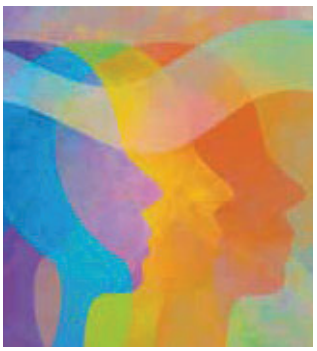
Alliance to leave no-one behind



ICAR 2022
Bergamo
14-16 Giugno
2022
14° CONGRESSO NAZIONALE

Italian Conference on **AIDS** and **Antiviral Research**

Presidenza del Congresso: **A. Antinori, M. Cernuschi, F. Maggiolo, M. Zazzi**

Promosso da
SIMIT Società Italiana di Malattie Infettive e Tropicali

e da
INMI, Istituto Nazionale per le Malattie Infettive
ISS, Istituto Superiore di Sanità
AMCLI, Associazione Microbiologi Clinici Italiani
SIICA, Società Italiana di Immunologia, Immunologia Clinica e Allergologia
SIMaST, Società Interdisciplinare per lo Studio delle Malattie Sessualmente Trasmissibili
SITA, Società italiana per la Terapia Antinfettiva
SIV-ISV, Società Italiana di Virologia - Italian Society for Virology
ANLAIDS, Associazione Nazionale per la lotta all'AIDS
ARCIGAY, Associazione LGBT Italiana
ARCOBALENO Aids ODV, Associazione ARCOBALENO Aids ODV
ASA Onlus, Associazione Solidarietà AIDS Onlus
C.I.C.A., Coordinamento Italiano delle case alloggio per persone con HIV/AIDS
EpaC Onlus, Associazione EpaC Onlus
LILA, Lega Italiana per la Lotta contro l'AIDS
MARIO MIELI, Circolo di Cultura Omosessuale
Milano Check Point, Associazione Milano Check Point
NADIR, Associazione Nadir
NPS Italia Onlus, Network Persone Sieropositive
PLUS, Rete persone LGBT+ sieropositive Aps

ABSTRACT BOOK

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PrEP: new data and issues

OC 1 IMPACT OF SIMIT PREP ELIGIBILITY CRITERIA ON RETENTION IN CARE AND NEW SEXUALLY TRANSMITTED INFECTIONS ACQUISITION

R. Rossotti[1,5], G. Mulé[2,5], A. Tavelli[3], A. De Bona[2,5], C. Muccini[4,5], D. Moschese[5,6], S. Bossolasco[4,5], D. Calzavara[5], A. Foschi[5,6], V. Ferrara[5], R. Repossi[5], M. Cernuschi[4,5], A. d'Arminio Monforte[2,7]

[1]Department of Infectious Diseases, ASST Grande Ospedale Metropolitano Niguarda, Milan, [2]Department of Infectious Diseases, ASST Santi Paolo e Carlo, Milan, [3]ICONA Foundation, Milan, [4]Unit of Infectious Diseases, IRCCS San Raffaele Scientific Institute, Milan, [5]Milano Checkpoint, Milan, [6]I Division of Infectious Diseases, ASST Fatebenefratelli Sacco, Milan, [7]University of Milano, Milan

Background: SIMIT Italian guidelines recommend offering pre-exposure prophylaxis (PrEP) to MSM or TGW who are sexual partners of viremic HIV-positive patients, have inconsistent condom use with casual partners, had a recent sexually transmitted infection (STI), practice Chemsex, or have had a non-professional post-exposure prophylaxis (nPEP) course. Eligibility criteria might not be equally sensitive in defining individuals at major risk of HIV acquisition, thus they could under- or overestimate the need of PrEP. Aim of this study is to evaluate whether the eligibility criteria have an impact in terms of retention in care, STIs acquisition, and adverse events (AE) complaint.

Material and Methods: This retrospective analysis included all subjects who started PrEP attending a community-based service. Demographic, clinical, and behavioral features were collected though self-administered questionnaires. Median and interquartile range (IQR) for continuous variables, absolute and relative values for categorical variables were calculated. Nonparametric tests were applied to compare variables. STIs incidence rates were assessed. Cox regression analyses were performed to test factors associated to PrEP drop out.

Results: The analysis included 659 individuals: the vast majority had 0 (168, 25%) or 1 (254, 39%) eligibility criteria. Study population was then dichotomously divided in subjects with 0/1 criteria (0/1C, 422, 64%) and ≥2 criteria (≥2C, 237, 36%). Age, geographic origin, sexual orientation, level of education and employment status were similar in the two groups (Figure, A).

After the first informative interview, the rate of not started, or immediate and delayed initiation was similar in both groups (p=0.729). The rate of PrEP withdrawal was 29% in the 0/1C group and 38% in the ≥2C group (p=0.031). The main reason for discontinuation in both groups was the start of a steady relationship (20%). Figure B shows Cox models to test factors associated to drop out: among SIMIT criteria, only inconsistent condom use was negatively associated to PrEP discontinuation.

Over a follow up of 437 years, 0/1C subjects had 135 STIs with an incidence of 31 per 100 PYFU. Subjects in the ≥2C group had 135 STIs over 221 years of follow up, with an incidence of 61 per 100 PYFU. Incidence rate ratio was 1.97 (95% CI 1.54-2.52, p<0.001). All the eligibility criteria (except previous STIs and nPEP) were associated to higher incidence of new infections.

AE complaints were similar in both groups (22% vs 26%, p=0.336). The most reported AEs were gastrointestinal symptoms (19%), again with no significant differences (p=0.540).

Conclusions: The validated behavioral score by Smith was proposed to help clinicians in the selection of PrEP candidates, but it did not consider U=U and is unbalanced on the age matter, thus it might overestimate subjects in need of PrEP. Conversely, SIMIT eligibility criteria seem to better identify individuals at major risk of new STIs acquisition.

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PrEP: new data and issues

OC 2 SEXUALLY TRANSMITTED INFECTION AND ADHERENCE IN AN ITALIAN ACCESS PROGRAM OF HIV PRE-EXPOSURE PROPHYLAXIS (ITAPREP)

V. Mazzotta[1], S. Lanini[1], D. Calzavara[2], A. Tavelli[3], A. De Bona[3], F. De Zottis[1], V. Ferrara[2], S. La Monica[4], S. Mattioli[5], A. Bianchi[6], G. Mulè[3], L. Badia[5], S. Bossolasco[2], E.Rozenn[7], R. Bellagamba[1], D. Tesoro[3], R. Rossotti[8], M. Pedone[5], S. Nozza[9], P. Tomasi[5], L. Biasoli[3], F. Gili[7], M. Bonanni[5], A. Copes[3], A. Castagna[9], A. Gori[10], M. Puoti[8], G.Rizzardini[11], M. Andreoni[12], C. Mastroianni[13], R. Cauda[4], V. Puro[7], A. Cingolani[4], G. M. Corbelli[5], M. Cernuschi[2,6], A. d'Arminio Monforte[3], A. Antinori[1]

[1]HIV/AIDS Unit, INMI L. Spallanzani IRCCS, Roma, [2]Milano Checkpoint, Milano, [3]ASST Santi Paolo e Carlo, University of Milano, [4]Fondazione Policlinico A. Gemelli, Catholic University, Roma, [5]PLUS aps (BLQ Checkpoint), Bologna, [6]ASA Onlus, Milano, [7]CRAIDS, INMI L. Spallanzani IRCCS, Roma, [8]ASST Niguarda Hospital, Milano, [9]HSR San Raffaele Scientific Institute, Milano, [10]IRCCS Policlinico Ospedale Maggiore, Milano, [11]ASST L. Sacco Hospital, Milano, [12]Tor Vergata University, Roma, [13]Sapienza University, Roma

Background: Pre-exposure prophylaxis (PrEP) is one of the most effective methods to reduce HIV transmission globally. Despite the proven effectiveness and rapid spread of PrEP, there are still many barriers to taking PrEP properly. Enhancing adherence and increasing availability are some of the main goals of a PrEP program. We reported HIV and sexually transmitted infections (STI) infection rate, adherence, and factors associated in a multicentric access program in Italy.

Methods: Multicenter prospective cohort study on people taking PrEP in 8 Italian centers. Incidence of HIV and other sexually transmitted infections (STIs) was calculated using mixed-effect Poisson regression.

Poor adherence was defined as a wrong reported schedule of assumption for on-demand PrEP, temporary interruption for daily PrEP, or reporting of at least one sexual intercourse with neither PREP nor condom

Unadjusted mixed effect logistic model, with random intercept on PREP center, was used to explore potential risk factors associated with poor adherence. Proportion of patients with optimal adherence was expressed as marginal estimates and relative 95% CI. Adjusted analysis of risk for poor adherence was carried out with by a multivariable mixed effect logistic model. Strength of association between risk factor and adherence was expressed in OR, relative 95% CI and LRT P-value

Results: 1,099 persons (prs) were evaluable for this analysis (Flow chart in Fig.1): 98% men; 92% MSM, 59% younger than 40 years; 11% non-Italian origin, 60% university degrees. 463 prs (42%) chose on-demand and 365 (33%) daily schedules: 271 prs (25%) changed their schedule during observation (Fig.2). 655 (60%) prs were chem-sex users. Median follow-up was 305 days (IQR 2.8-10.9). 4 HIV seroconversion were observed for 1167 person-years follow-up (PYFU), with an incidence rate (IR) of 0.34 per 100 PYFU (95%CI 0.13-0.91). IR per 100 PYFU of STIs was 19.25 for syphilis, 23.75 for chlamydia, and 24.22 for gonorrhea with a risk of subsequent events of 3.56, 3.70, and 3.32, respectively (Fig.3). Proportion of prs with optimal adherence according to bivariate analysis was 57.46% (95%CI 40.6-74.32) (Tab.2). Multivariable analysis suggested that poor adherence was significantly associated with chemsex (OR 0.62 95%CI 0.43-0.87) and either on-demand (OR 0.60 95%CI 0.41 -0.90) or changing PrEP schedule (OR 0.29 95%CI 0.18-0.47).

Conclusions: During PrEP implementation program, the incidence rate of new HIV infections remained low. PrEP was a helpful tool not only for the prevention of HIV infection but also for monitoring changing trends of other sexually transmitted diseases. Optimal adherence remains a difficult goal to achieve during a PrEP program, and the analysis of predictors of poor adherence in the real-world, such as chemsex and on-demand or changing schedules in our cohort, is crucial to address strategies for improving and spreading PrEP.

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PrEP: new data and issues

OC 3 PREVALENCE OF ANAL HPV INFECTION AMONG PREP USERS SCREENED THROUGH A SELF-ADMINISTERED POINT-OF-CARE TEST: DATA FROM A COMMUNITY-BASED PREP PROGRAMME IN MILAN

L. Biasioli[1,3], R. Rossotti[1,4], A. Tavelli[1,3], A. De Bona[1,3], C. Tincati[3], D. Calzavara[1], P. Vinti[1], C. Baiguera[1,4], R. Repossi[1], V. Ferrara[1], S. Bossolasco[1,2], C. Muccini[1,2], D. Tesoro[1,3], A. D'Arminio Monforte[1,3], M. Cernuschi[1,2] on behalf of the Milano Check Point Group

[1]Milano Check Point, Milano, [2]IRCCS San Raffaele Scientific Institute, Milano, [3]ASST Santi Paolo e Carlo, Milano, [4]ASST Niguarda Hospital, Milano

Background: Human papillomavirus (HPV) infection is the most common sexually transmitted infection worldwide, especially among people living with HIV and MSM, and it can lead to serious complications, including anal cancer. There are currently little data on HPV prevalence in PrEP users. In recent years WHO has promoted the use of Point-of-Care Tests (POCTs) for STIs screening to ensure greater coverage and effectiveness of prevention campaigns.
In this study we evaluated the prevalence of high-risk HPV strains in the anal site among PrEP users through a self-administered POCT. We then compared the performance of the POCT with laboratory gold standard test.
Methods: We enrolled PrEP users from a local community-based PrEP programme (Milano Check Point). They were tested for anal HPV with a PCR POCT (Xpert® HPV) capable of detecting 14 high-risk HPV genotypes on a sample collected through a self-performed anal swab. They were also referred to a local clinic (Niguarda or S. Paolo Hospital) to collect a new sample to be analyzed with the standard sequencing assay. The median time elapsed between the two tests was 11.7 months (IQR 8.2-15), due to COVID-19-related service interruptions. The data were evaluated through descriptive statistical methods. Associations between demographic/behavioral factors and a positive POCT result were evaluated through logistic regression. Agreement between POCT and gold standard test was measured with Cohen's kappa. POCT performance was expressed through sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) calculation. A value of $p<0.05$ was considered significant.
Results: Globally, 200 subjects were enrolled, most of them male (98%) and MSM (88%). 71% of them tested positive for at least one high-risk HPV strain on POCT. Factors associated with a positive POCT result were being non-Italian (p=0.017), previous STI diagnosis (p=0.019) and a higher number of sexual partners in the previous 3 months (median 10 IQR 4-20 vs 6 IQR 2-15, p=0.037) (Tab.1). For 117 subjects, laboratory gold standard test was also performed: 83% tested positive for at least one high-risk HPV strain. Agreement between POCT and gold standard was 80.3% (Cohen's kappa= 0.46). POCT showed a sensitivity of 80.4%, a specificity of 83.3%, a PPV of 95.1% and a NPV of 45.7%. Considering only HPV16, the most common strain, agreement between POCT and laboratory gold standard was 87.9% (Cohen's kappa=0.70). In this case POCT showed a sensitivity of 86.7%, a specificity of 88.4%, a PPV of 72.2% and a NPV of 95% (Tab.2).
Conclusions: Prevalence of anal HPV infection in PrEP users was high. POCT showed a moderate agreement with laboratory gold standard and a discrete sensitivity and specificity (especially for HPV16): even if a long time had passed between the two tests, data suggest that it could be an useful additional instrument to reach a wider number of people, especially among high risk populations.

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PrEP: new data and issues

OC 4 PREP USE DISCLOSURE TO SEXUAL PARTNERS, FRIENDS AND RELATIVES: A PSYCHO-SOCIAL ANALYSIS

A. Bianchi[1,2], A. Tavelli3, P.L. Vinti[2], D. Calzavara[2], V. Ferrara[2], A. Antonino[1,2], F. Rossi[1,2], M. Massa[2], A. De Bona[3], D. Rossotti[2,4], S. Bossolasco[2,5], D. Canetti[5], A. Foschi[2,6], D. Tesoro[3], G. Mulé[2,3], R. Repossi[1,2], N. Frattini[1,2], E. Garavaglia[1,2], C. Ferrara[1,2], D. De Cia Warzanowski[2], M. Cernuschi[1,2,5]

[1]ASA. Associazione Solidarietà AIDS, Milan, Italy, [2]Milano Checkpoint, Milan, [3]San Paolo Hospital, Milan, Italy, [4]ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy, [5]San Raffaele Hospital, Milan, Italy, [6]Luigi Sacco Hospital, Milan, Italy

Background: If correctly taken, PrEP is an effective tool to reduce new HIV infections. The service provides a visit with an ID physician who informs about medication schedules, side effects, and how to care about other STIs. Aim of this study is to describe motivations for starting PrEP and its psychosocial consequences.

Method: A psychologist discussed motivations for starting PrEP, sexual behavior (including chemsex use), attitude towards HIV, thoughts and expectations regarding medication giving opportunity to reflect over themselves. During the first appointment sexual habits, how & until when they would remain on PrEP were mainly discussed. Further appointments were focused on their relationship with PrEP use and changes in sexual life. Self-administered questionnaires (July 2021-March 2022) have been analyzed by descriptive statistics. Bio-psycho-social and medical features, sexual habits and risk behaviors were collected. Qualitative analysis on interviews with counselors have been conducted.

Results: The analysis included 638 clients (males 99%; MSM 87%; graduated 67%; Italians 80%; employed 86%; Chems users 17%). More than half of users takes PrEP as an additive tool to condom use, but 39% of clients younger than 24 years stated they need it because of difficult-to-control risky behaviors: only 16% of them said they always use condoms. More than 50% discuss PrEP use with sexual partners, a smaller portion with friends, while only 4% discuss it with the family. Women did not discuss PrEP with anyone, in two thirds of cases for fears of a bad judgment. A reaction of interest to this tool was observed in almost half of the population, even if 25% reported misinformation and prejudice. During the first interview, 29% of our clients also affirm to experience stigma: such stigma significantly decreased over time but resulted still an important concern.

Conclusions: PrEP is an essential preventive tool both in terms of HIV protection and STI early diagnosis and treatment. Also decreasing, fear of stigma and shame is still common: psychological interventions might be important to reduce barriers to PrEP use.

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Immunological efficacy of SARS-CoV-2 vaccine I

OC 5 POOR HUMORAL IMMUNOGENICITY TO SARS-COV-2 VACCINATION IN PEOPLE LIVING WITH HIV (PLWH) WITH LOW CD4 COUNT

A. Vergori[1], A. Cozzi-Lepri[2], M. Giannella[3], A. Tavelli[4], A.M. Azzini[5], L. Marconi[3], S. Cicalini[1], A. Rodanò[4], S. Meschi[1], M. Fusto[1], A. Sartor[6], G. Matusali[1], S. Piconi[7], G.Pellicano[8], A. Cascio[9], G. Levy-Hara[10], A. Costantini[11], G. Madeddu[12], G. Marchetti[4], P. Viale[3], E. Tacconelli[5], A. d'Arminio Monforte[4], A.Antinori[1] for the VAXICONA-ORCHESTRA Study Group

[1]National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Roma, Italy, [2]CREME, Institute for Global Health, UCL, London, UK, [3]Unit of Infectious Diseases, ASST Santi Paolo e Carlo, Department of Health Sciences, University of Milan, Milan, Italy, [4]Department of Medical and Surgical Sciences, Alma Mater Studiorum University of Bologna, Bologna, Italy, [5]Division of Infectious Diseases, Department of Diagnostics and Public Health, University of Verona, Verona, Italy, [6]Microbiology Unit, Udine University Hospital, Udine, Italy, [7]Infectious Diseases Unit, A. Manzoni ASST Lecco, Lecco, Italy, [8]Department of Human Pathology of the Adult and the Developmental Age "G. Barresi", Unit of Infectious Diseases, University of Messina, Messina, Italy, [9]Infectious and Tropical Diseases Unit, PROMISE, University of Palermo, Palermo, Italy, [10]Instituto Alberto Taquini de Investigación en Medicina Traslacional, Facultad de Medicina, Universidad de Buenos Aires, Buenos Aires, Argentina, [11]Clinical Immunology Unit, Azienda Ospedaliero-Universitaria Ospedali Riuniti, Marche Polytechnic University, Ancona, Italy, [12]Unit of Infectious Diseases, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy

Background: Data on SARS-CoV-2 vaccine immunogenicity in PLWH are currently limited, mostly collected in persons with high CD4 count from randomized trials. Large population studies characterizing the immune response after vaccination by CD4 count are lacking. Aim of this analysis was to investigate real-world antibody response against SARS-CoV-2 spike protein elicited after primary vaccination according to CD4 count in a large cohort of PLWH.

Methods: We included PLWH of the VAXICONA-ORCHESTRA cohort who received SARS-CoV-2 vaccine and for whom anti-S serology was available. Serologic titres were standardized in BAU/mL. Participants were stratified by CD4 count pre-vaccination (T0) (LCD4=CD4 count <200 cell/mm3; ICD4=CD4 count 201-500 cell/mm3; HCD4=CD4 count >500 cell/mm3). Immune response was defined as having anti-S ≥7.1 BAU/mL for Abbott, ≥0.82 BAU/mL for Roche and ≥4.8 BAU/mL for DiaSorin, while low response was defined as ≤46 BAU/mL regardless of assay. ANOVA was used to compare titres (log2 scale); association between CD4 groups and risk of undetectable/low level anti-S was evaluated by means of logistic regression.

Results: 2,017 PLWH were included (LCD4=145; ICD4=539; HCD4=1333); median age 53 years (IQR 45-59), median time from HIV diagnosis 12 years (6-22), median CD4 nadir 200 cell/mm3 (64-363), 89% HIV-RNA <50 copies/mL, 25% with a previous AIDS diagnosis, 25% with ≥1 comorbidity (Table 1). The proportion with undetectable/low immune response after a median of 28 days (21-28) after 1st dose was 33.9/75.6% for LCD4, 9.5/58.6% for ICD4 and 4.9/44.7% for HCD4 (P<0.0001/P<0.0001). Odds ratios from fitting a logistic regression are reported in Table 2. At a median of 50 days (31-77) from 2nd dose, the proportion with undetectable/low response were 9.8/30.8% for LCD4, 1.8/9.0% for ICD4 and 0.9/7.2% for HCD4 (P<0.0001/P<0.0001) (Figure 1). The adjusted mean (SD) levels of anti-S were 6.7 (3.7) log2 BAU/mL for LCD4, 8.6 (2.5) for ICD4 and 8.9 (2.4) for HCD4 (Fisher test P<0.0001, Figure 2).

Conclusions: In this large real world population sample, humoral immunogenicity after primary cycle of SARS-CoV-2 vaccination was lacking or poorly elicited in a consistent proportion of PLWH with CD4 count <200/mm3. Having a CD4 count >500 cell/mm3 as comparator, a significant higher risk of lack of response after 1st dose and lower average levels after 2nd dose were also observed in PLWH with CD4 count of 201-500/mm3. CD4 count was confirmed as a strong predictor of humoral response to SARS-CoV-2 vaccination in PLWH. These findings are useful to inform policy makers regarding the use of additional and booster doses in PLWH

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Immunological efficacy of SARS-CoV-2 vaccine I

OC 6 HUMORAL IMMUNOGENICITY TO SARS-COV-2 MRNA VACCINE THIRD ADDITIONAL/BOOSTER SHOT IN PEOPLE LIVING WITH HIV (PLWH) BY CURRENT CD4 COUNT

A. Antinori[1], A. Cozzi-Lepri[2], A. Vergori[1], A. Tavelli[3], M. Giannella[4], S. Cicalini[1], L. Marconi[4], V. Yellenki[3], S. Meschi[1], G. Pellicanò[5], N. Carroccia[4], G. Matusali[1], A. Latini[6], M. Lichtner[7], S. Lo Caputo[8], F.M. Fusco[9], G. Marchetti[3], E. Tacconelli[10], A. d'Arminio Monforte[3] for the VAXICONA-ORCHESTRA Study Group

[1]National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Roma, Italy, [2]CREME, Institute for Global Health, UCL, London, UK, [3]Unit of Infectious Diseases, ASST Santi Paolo e Carlo, Department of Health Sciences, University of Milan, Milan, Italy, [4]Department of Medical and Surgical Sciences, Alma Mater Studiorum University of Bologna, Bologna, Italy, [5]Dertment of Human Pathology of the Adult and the Developmental Age "G. Barresi", Unit of Infectious Diseases, University of Messina, Messina, Italy, [6]Department of Dermatology, San Gallicano Institute IRCCS, Roma, Italy, [7]Santa M. Goretti Hospital, Sapienza University, Latina, Italy, [8]Department of Clinical and Experimental Medicine, University of Foggia, Foggia, Italy, [9]AORN Ospedali Dei Colli, Cotugno Hospital, Naples, Italy, [10]Division of Infectious Diseases, Department of Diagnostics and Public Health, University of Verona, Verona, Italy

Background: In Italy, from September 2021, administration of a 3rd additional/booster dose (3D) of SARS-CoV-2 vaccine was approved for PLWH with advanced disease. Observational data on immunogenicity after a 3D in PLWH are currently limited. Aim was to investigate real-world antibody response against SARS-CoV-2 spike protein elicited after a 3D of mRNA vaccination, according to CD4 count, in a large cohort of PLWH.

Methods: We included PLWH of the VAXICONA-ORCHESTRA cohort who previously received a primary cycle of SARS-CoV-2 mRNA vaccine, who were infused with a mRNA 3D and for whom anti-S serology was available. Serologic titres were standardized in BAU/mL. Participants were stratified by CD4 count pre-vaccination (T0) (LCD4=CD4 count <200 cell/mm3; ICD4=CD4 count 201-500 cell/mm3; HCD4=CD4 count >500 cell/mm3). Immune response was defined as having anti-S ≥7.1 BAU/mL for Abbott, ≥0.82 BAU/mL for Roche and ≥4.8 BAU/mL for DiaSorin, while low response was defined as ≤46 BAU/mL regardless of assay. ANOVA was used to compare titres (log2 scale); association between CD4 groups and risk of undetectable/low level anti-S was evaluated by means of ANOVA and logistic regression.

Results: 625 PLWH included (LCD4=96; ICD4=199; HCD4=330); median age 56 years (IQR 48-61), median time from HIV diagnosis 11 years (5-23), median CD4 nadir 124 cell/mm3 (39-299), 89% HIV-RNA <50 copies/mL, 30% with a previous AIDS diagnosis, 39% with ≥1 comorbidity. PLWH received the 3D at a median of 164 days (151 -173) from the second dose (Table 1). The proportion with undetectable/low response after a median of 31 days (30-62) after the 2nd dose was originally 12.5/38.9% for LCD4, 1.4/10.9% for ICD4 and 0.9/12.2% for HCD4 (P<0.0001/P<0.0001). After a median of 164 days (151-193) from the 2nd dose the same proportion increased to 15.6/72.7% for LCD4, 5.6/33.9% for ICD4 and 8.8/27.5% for HCD4 (P<0.0001/P<0.0001). After at a median of 29 days (16-56) after the 3D, the proportion of PLWH with undetectable/low immune response showed a sharp decline to 5.21/12.5% for LCD4, 0.5/2.0% for ICD4 and 0.3/1.2% for HCD4 (P<0.0001/P<0.0001). Odds ratios from fitting a logistic regression for the 3D are reported in Table 2. The adjusted mean (SD) levels of anti-S after 2nd dose were 3.4 (3.4) log2 BAU/mL for LCD4, 5.9 (3.2) for ICD4 and 6.1 (3.3) for HCD4, (Fisher test P<0.0001, Figure 1a) and 8.7 (3.4) log2 BAU/mL for LCD4, 10.6 (2.0) for ICD4 and 11.1 (2.2) for HCD4, after 3D (Fisher test P<0.0001, Figure 1b).

Conclusions: In PLWH, a 3D of SARS-CoV-2 mRNA vaccine, elicited a strong humoral immune response, higher that observed after the primary vaccination, even in patients with poor CD4 count. The 3D quickly over-compensated the waning of immune response already seen a few months after the 2nd dose. A CD4 count <200 cell/mm3 was independently associated with a 3-fold higher risk of low antibody response after 3D vs. >500 cell/mm3. These data are essential for targeted strategies for appropriate delivery of a 4th dose in PLWH.

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Immunological efficacy of SARS-CoV-2 vaccine I

OC 6 HUMORAL IMMUNOGENICITY TO SARS-COV-2 MRNA VACCINE THIRD ADDITIONAL/BOOSTER SHOT IN PEOPLE LIVING WITH HIV (PLWH) BY CURRENT CD4 COUNT

A. Antinori[1], A. Cozzi-Lepri[2], A. Vergori[1], A. Tavelli[3], M. Giannella[4], S. Cicalini[1], L. Marconi[4], V. Yellenki[3], S. Meschi[1], G. Pellicanò[5], N. Carroccia[4], G. Matusali[1], A. Latini[6], M. Lichtner[7], S. Lo Caputo[8], F.M. Fusco[9], G. Marchetti[3], E. Tacconelli[10], A. d'Arminio Monforte[3] for the VAXICONA-ORCHESTRA Study Group

[1]National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Roma, Italy, [2]CREME, Institute for Global Health, UCL, London, UK, [3]Unit of Infectious Diseases, ASST Santi Paolo e Carlo, Department of Health Sciences, University of Milan, Milan, Italy, [4]Department of Medical and Surgical Sciences, Alma Mater Studiorum University of Bologna, Bologna, Italy, [5]Dertment of Human Pathology of the Adult and the Developmental Age "G. Barresi", Unit of Infectious Diseases, University of Messina, Messina, Italy, [6]Department of Dermatology, San Gallicano Institute IRCCS, Roma, Italy, [7]Santa M. Goretti Hospital, Sapienza University, Latina, Italy, [8]Department of Clinical and Experimental Medicine, University of Foggia, Foggia, Italy, [9]AORN Ospedali Dei Colli, Cotugno Hospital, Naples, Italy, [10]Division of Infectious Diseases, Department of Diagnostics and Public Health, University of Verona, Verona, Italy

Background: In Italy, from September 2021, administration of a 3rd additional/booster dose (3D) of SARS-CoV-2 vaccine was approved for PLWH with advanced disease. Observational data on immunogenicity after a 3D in PLWH are currently limited. Aim was to investigate real-world antibody response against SARS-CoV-2 spike protein elicited after a 3D of mRNA vaccination, according to CD4 count, in a large cohort of PLWH.

Methods: We included PLWH of the VAXICONA-ORCHESTRA cohort who previously received a primary cycle of SARS-CoV-2 mRNA vaccine, who were infused with a mRNA 3D and for whom anti-S serology was available. Serologic titres were standardized in BAU/mL. Participants were stratified by CD4 count pre-vaccination (T0) (LCD4=CD4 count <200 cell/mm3; ICD4=CD4 count 201-500 cell/mm3; HCD4=CD4 count >500 cell/mm3). Immune response was defined as having anti-S ≥7.1 BAU/mL for Abbott, ≥0.82 BAU/mL for Roche and ≥4.8 BAU/mL for DiaSorin, while low response was defined as ≤46 BAU/mL regardless of assay. ANOVA was used to compare titres (log2 scale); association between CD4 groups and risk of undetectable/low level anti-S was evaluated by means of ANOVA and logistic regression.

Results: 625 PLWH included (LCD4=96; ICD4=199; HCD4=330); median age 56 years (IQR 48-61), median time from HIV diagnosis 11 years (5-23), median CD4 nadir 124 cell/mm3 (39-299), 89% HIV-RNA <50 copies/mL, 30% with a previous AIDS diagnosis, 39% with ≥1 comorbidity. PLWH received the 3D at a median of 164 days (151 -173) from the second dose. The proportion with undetectable/low response after a median of 31 days (30-62) after the 2nd dose was originally 12.5/38.9% for LCD4, 1.4/10.9% for ICD4 and 0.9/12.2% for HCD4 (P<0.0001/P<0.0001). After a median of 164 days (151-193) from the 2nd dose the same proportion increased to 15.6/72.7% for LCD4, 5.6/33.9% for ICD4 and 8.8/27.5% for HCD4 (P<0.0001/P<0.0001). After at a median of 29 days (16-56) after the 3D, the proportion of PLWH with undetectable/low immune response showed a sharp decline to 5.21/12.5% for LCD4, 0.5/2.0% for ICD4 and 0.3/1.2% for HCD4 (P<0.0001/P<0.0001). Odds ratios from fitting a logistic regression for the 3D are reported in Table 1. The adjusted mean (SD) levels of anti-S after 2nd dose were 3.4 (3.4) log2 BAU/mL for LCD4, 5.9 (3.2) for ICD4 and 6.1 (3.3) for HCD4, (Fisher test P<0.0001, Figure 1a) and 8.7 (3.4) log2 BAU/mL for LCD4, 10.6 (2.0) for ICD4 and 11.1 (2.2) for HCD4, after 3D (Fisher test P<0.0001, Figure 1b).

Conclusions: In PLWH, a 3D of SARS-CoV-2 mRNA vaccine, elicited a strong humoral immune response, higher that observed after the primary vaccination, even in patients with poor CD4 count. The 3D quickly over-compensated the waning of immune response already seen a few months after the 2nd dose. A CD4 count <200 cell/mm3 was independently associated with a 3-fold higher risk of low antibody response after 3D vs. >500 cell/mm3. These data are essential for targeted strategies for appropriate delivery of a 4th dose in PLWH.

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Immunological efficacy of SARS-CoV-2 vaccine I

OC 7 LONGITUDINAL CHARACTERIZATION OF INTERFERON AND ANTIBODY RESPONSE FOLLOWING VACCINATION AGAINST SARS-COV-2 IN PATIENTS WITH HIV-1 INFECTION

M. Scordio[1], F. Frasca[1], L. Santinelli[2], L. Maddaloni[2], L. Sorrentino[1], M. Fracella[1], E.N. Cavallari[2], A. Napoli[2], L. Cinti[2], P. Roberto[2], G. Ceccarelli[2], A. Gaeta[2], G. Antonelli[1,3], C. M. Mastroianni[2], G. d'Ettorre[2], C. Scagnolari[1]

[1]Laboratory of Virology, Department of Molecular Medicine, Sapienza University, Rome, Italy, [2]Department of Public Health and Infectious Diseases, Sapienza University, Rome, Italy, [3]Microbiology and Virology Unit, Sapienza University Hospital "Policlinico Umberto I", Rome, Italy

Background: COVID-19 vaccine has been reported to elicit humoral and T cell immune response in HIV-1 patients. Remarkably, some studies suggest that Interferon (IFN) signature might correlate with immunological and clinical efficacy of COVID-19 vaccines, as reported for Influenza vaccines. Understanding the early innate response to vaccine exposure and the humoral activation is needed to characterize mechanisms related to immunization in HIV-1 individuals. Therefore, the aim of this study was to evaluate the humoral response and IFN signature in HIV-1 positive individuals receiving COVID-19 vaccine.

Material and Methods: Longitudinal effects of mRNA-based SARS-CoV-2 vaccine on humoral response in HIV-1 patients (n=82) were investigated measuring antibodies levels using LIAISON SARS-CoV-2 Trimerics IgG assay in serum samples collected before vaccination (T0), at the time of the second dose (T1), and 1 or 6 months following the second dose (T2). Expression level of mRNA encoding for distinct type I IFNs (i.e. IFN-Alpha2, IFN-Beta, IFN-Epsilon and IFN-Omega), and IFN-stimulated genes (ISGs), ISG15 and ISG56, were quantified by RT/Real time PCR assays in peripheral blood mononuclear cells (PBMCs) collected at T0, T1 and T2.

Results: Eighty-two HIV-1 patients (57 males (70%), 25 females (30%), mean age 56 years) on long-term ART were enrolled in this study. Results showed that humoral response following immunization increased significantly from T0 to T1 ($p<0.001$), and from T1 to T2 ($p<0.001$). Stratyfing patients according to CD4 T cell count, no differences in antibody production were observed up to 1 month after the second dose. However, individuals with CD4 T cell count <400 cells/mm3 maintained a lower anti spike-antibody response 5 months after full vaccination compared to those with high (>400 cells/mm3) CD4 T cell count ($p<0.05$). Gene expression analysis performed in 55 HIV-1 infected patients before and after COVID-19 vaccination, indicated an overall increased of IFN response up to 1 month after the second dose. Also, transcript levels of IFN-Alpha2, IFN-Beta, IFN-Epsilon and IFN-Omega, and of ISG15 and ISG56 were positively correlated with antibody production. By contrast, IFNs and ISGs mRNA levels decreased ($p<0.05$) at 5 months after the second dose, concomitantly with the reduction of antibody levels.

Conclusion: Our results confirmed that mRNA-based SARS-CoV-2 vaccine successfully promote antibody production in ART-treated HIV-1 patients and that the levels of CD4 T cells can impact on the rate of humoral immune response activation. Moreover, we demonstrated that transcript levels of IFN related genes changed in patients receiving COVID-19 vaccine according to the amount of anti-spike antibodies.

Immunological efficacy of SARS-CoV-2 vaccine I

OC 8 T-CELL AND HUMORAL RESPONSES TO MRNA-1273 VACCINE UP TO 6 MONTHS IN LATE PRESENTER PEOPLE LIVING WITH HIV (PLWH)

M. Augello, V. Bono, R. Rovito, M. Hadla, V. Yellenki, C. Tincati, A. d'Arminio Monforte, G. Marchetti

Clinic of Infectious Diseases and Tropical Medicine, San Paolo Hospital, ASST Santi Paolo e Carlo, Department of Health Sciences, University of Milan, Milan, Italy

Background: Immune responses to SARS-CoV-2 mRNA vaccines in PLWH with a history of late presentation (LP) as well as their durability have not been fully characterized. We hereby longitudinally evaluated T-cell and humoral responses to mRNA-1273 vaccination up to 6 months in LP-PLWH.

Materials and methods: SARS-CoV-2-specific T-cell and humoral responses were comparatively assessed in LP-PLWH (CD4 nadir<350/μL and/or previous AIDS diagnosis) on effective cART, who received mRNA-1273, and in age-matched HIV-negative healthcare workers (HCWs), who received BNT162b2. We determined antigen-specific activation induced markers (CD69+CD137+)-expressing CM, EM, TEMRA, Tfh/Tfc (CCR7/CD45RA, CXCR5) and cytokines (IFNγ, TNFα, IL2, IL4, IL17A)-producing CD4 and CD8 T-cells after wild-type SARS-CoV-2 spike (S) peptides challenge (flow cytometry) as well as anti-RDB antibodies (Abs) (ELISA) before vaccination (T0), 1 month (T1) and 5 months (T2) after 2nd dose. Wilcoxon and Mann-Whitney tests were used for statistical analyses.

Results: 20 LP-PLWH (median CD4 nadir=67/μL; current median CD4=403.5/μL, CD4/CD8=0.57, HIV-RNA<20 cp/mL) (Fig.1A) and 20 HCWs were included. In each group, 10 had a clinical history of previous COVID-19 (experienced) and 10 had not (naïve). LP-PLWH showed an expansion of S-specific total, CM, EM, TEMRA and Tfh CD4 T-cells at T1 (P=.0003, .0017, <.0001, .0012, .0012) and T2 (P= .0002, .0017, .0001, .0049, .0002) (Fig.1B). A rise of Th1-cytokine (IFNγ, TNFα, IL2)- and Th2-cytokine (IL4)-producing S-specific CD4 T-cells (by both % and iMFI) at T1 (P=.2609, .3910; P=.0026, .0637; P=.0938, .0803; P=.0244) and T2 (P=.0635, .0537; P=.0178, .0266; P=.0012, .0049; P=.0078) was further registered (Fig.1C). Besides, 17/20 LP-PLWH developed polyfunctional Th1 cells (Fig.1D). A significant rise of anti-RBD Abs at T1 (P<.0001) and T2 (P<.0001) was also observed (Fig.1E). Of note, T-cell and humoral responses to vaccine in LP-PLWH were not inferior to HCWs (Fig.1B-E).

Interestingly, SARS-CoV-2-experienced PLWH and HCWs displayed higher anti-RBD Abs at T0 vs naïve (P=.0220; P=.0355, respectively) but not at T1 and T2. Conversely, while experienced HCWs showed higher S-specific Th1 cells vs naïve at both T0 (IFNγ+ CD4+ %, iMFI: P=.0251, .0090) and T1 (IFNγ+ CD4+%, iMFI: P=.0325; TNFα+ CD4 T-cells iMFI: P=.0289), the same was not seen in LP-PLWH (Fig. 1E).

Conclusions: In PLWH with pre-cART advanced immunodeficiency and full immunovirological control on cART, a 2-dose mRNA-1273 vaccine cycle is able to induce S-specific polyfunctional Th1 and Th2 memory as well as Tfh cells, besides anti-RBD Abs, not inferior to HIV-uninfected peers, still detectable after 6 months. Interestingly, in our cohort of LP-PLWH, a previous COVID-19 diagnosis, while able to sustain S-specific Ab response, seems less efficacious in inducing a T-cell immune memory both prior and after vaccination, possibly reflecting an enduring immunodeficiency specific to the T-cell compartment.

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Metabolic issues in effective HAART

OC 9 ROLE OF EMTRICITABILE/TENOFOVIR ALAFENAMIDE/BICTEGRAVIR ON METABOLIC AND HEPATIC SAFETY: DATA FROM SURVEILLANCE COHORT LONG-TERM TOXICITY ANTIRETROVIRALS/ANTIVIRALS (SCOLTA) PROJECT

N. Squillace[1], E. Ricci[2], B. Menzaghi[3], G.V. De Socio[4], G. Orofino[5], B.M. Celesia[6], F. Vichi[7], A. Di Biagio[8], L. Taramasso[8], C. Molteni[9], E. Sarchi[10], L. Valsecchi[11], G.F. Pellicanò[12], P. Bonfanti[1], for the CISAI Study Group

[1]Infectious Diseases Unit ASST-MONZA, San Gerardo Hospital-University of Milano-Bicocca, Monza, [2]Fondazione ASIA Onlus, Buccinasco (MI), Italy, [3]Unit of Infectious Diseases, ASST della Valle Olona, Busto Arsizio, Varese, [4]Unit of Infectious Diseases, Santa Maria Hospital, Perugia, [5]Division I of Infectious and Tropical Diseases, ASL Città di Torino, [6]Unit of Infectious Diseases, Garibaldi Hospital, Catania, [7]Unit of Infectious Diseases, Santa Maria Annunziata Hospital, Florence, [8]Infectious Diseases, San Martino Hospital Genoa, University of Genoa, Genoa, [9]Unit of Infectious Diseases, A. Manzoni Hospital, Lecco, [10]Infectious Diseases Unit, S.Antonio e Biagio e Cesare Arrigo Hospital, Alessandria, Italy, [11]1st Department of Infectious Diseases, ASST Fatebenefratelli Sacco, Milan, Italy, [12]Infectious Diseases, G. Martino Hospital -University of Messina, Messina

Background: Our aim was to investigate the role of emtricitabine/tenofovir alafenamide/bictegravir (FTC/TAF/BIC) regimen on metabolic and hepatic safety in a real-life setting.

Material and Methods: Consecutive patients living with HIV infection (PLWH) enrolled in SCOLTA project switching to or initiating their first antiretroviral treatment (ART) with FTC/TAF/BIC were included. T0 and T1 were defined as results at baseline and 6-month follow-up respectively. For AST and ALT data until T2 (12 months) were analyzed.

Results: Four hundred ninety-nine PLWH were enrolled, and 377 had at least one follow-up visit and were included in the analysis (see table 1 for patients' characteristics at baseline).

At T1, in patients naïve at baseline, total cholesterol (TC) (mean change from baseline +16.0 ± standard error 5.2 mg/dL, p=0.004), LDL-C (+11.2 ± 4.4, p=0.02) and estimated glomerular filtration rate (eGFR) (-14.8 ± 2.3 mL/min, p<0.001) showed a remarkable variation.

Experienced PLWH showed a significant variation in TC (-8.0 ± 2.0 mg/dL, p<0.0001), LDL-C (-4.9 ± 1.8, p=0.008), and triglycerides (TGL) (-15.6 ± 4.8 mg/dL, p=0.002). Finally, eGFR showed a small but significant decrease (-3.2 ± 0.8 mL/min, p<0.0001). Splitting by previous regimen, patients from FTC/TAF/DTG (n=55) had a significant variation in HDL-c (+2.0 ± 0.8 mg/dL, p=0.01), while PLWH from FTC/TAF/ELV/COBI (n=133) experienced significant changes in TC (-8.8 ± 3.3 mg/dL, p=0.0003) and LDL (-7.4 ± 2.5 mg/dL, p=0.004).

Weight increased in naïve patients (+1.2 ± 0.6 Kg, p=0.053) and to a lesser extent in experienced ones (+0.5 ± 0.3 Kg, p=0.12).

Among 18 experienced diabetic patients, mean glucose increase was statistically significant (+14.8 ± 6.4 mg/dL, p=0.03), whereas no significant change was observed in non-diabetic experienced subjects.

In non-diabetic PLWH, blood glucose did not modify, by previous regimen. Weight showed a not significant increase (+1.2 ± 0.9 Kg from FTC/TAF/DTG and +0.6 ± 0.5 Kg from FTC/TAF/ELV/COBI).

At T1 and T2 , AST and ALT remained stable, with the exception of naïve patients both with and without HBV (Figure). The latter showed a borderline significant reduction (-8.3 ± 4.0, p=0.04 and -11.5 ± 5.7, p=0.05).

Among 34 ART-experienced subjects with detectable viral load (VL) at study entry, 13 (38.2%) still had detectable VL at T1. Five out of 290 (3.8%) subjects with undetectable baseline VL had 50<VL<200 and 6 VL ≥200 copies/mL at T1.

Conclusions: ART initiation with FTC/TAF/BIC determined TC elevation and eGFR reduction as expected.

Switching to FTC/TAF/BIC is associated with a significant amelioration of lipid profile (TC and TGL reduction), but with an increase of glucose in diabetic patients. In naïve PLWH FTC/TAF/BIC initiation is associated with a reduction of AST/ALT, especially but not exclusively in patients with HBV coinfection.

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Metabolic issues in effective HAART

OC 10 MACHINE LEARNING ALGORITHM TO PREDICT WEIGHT CHANGE IN ART EXPERIENCED PWH

F. Motta[1], J. Milic[1], S. Barbieri[1], L. Gozzi[2], E. Aprile[2], M. Belli[2], M. Venuta[2], G. Cuomo[2], F. Carli[2], G. Dolci[2], V. Iadisernia[2], G. Burastero[2], C. Mussini[1,2], F. Mandreoli[3], G. Guaraldi[1,2]

[1]Department of Surgical, Medical, Dental and Morphological Sciences, University of Modena and Reggio Emilia, Modena, Italy, [2]Department of Infectious Diseases, Azienda Ospedaliero-Universitaria Policlinico of Modena, Modena, Italy, [3]Department of Physics, Informatics and Mathematics, University of Modena and Reggio Emilia, Modena, Italy

Background: Weight gain (WG) is a well-described phenomenon in PWH. Machine learning (ML) methods can generate models able to identify patients at risk of WG. The objective of the study was to develop a ML algorithm that predicts weight change in a given interval of time in ART experienced PWH.

Methods: This was an observational study of ART-experienced PWH attending Modena HIV Metabolic Clinic from 2001 to 2022. Data were assessed at each patient visit. Variables with availability ≥80% were considered as valuable observations and accounted for 142 variables used in model A. Additional models were trained in order to test ML performance on parsimonious datasets available in tertiary level clinics (model B) and standard HIV outpatient clinics (model C). Data were partitioned in an 80/20 training/test set to generate predictive models. The study outcome was the prediction of weight change % at any given follow-up. A clinically meaningful WG cut-off was set at 5% at the following annual visit. Intelligible explanations were obtained through Shapley Additive exPlanations values (SHAP), which quantified the positive or negative impact of each variable on the predicted outcome.

Results: A total of 3516 patients generated 18874 observations, and 3 predictive models with different sets of variables were trained (Table 1, panel L). At last observation, median age was 50 years; 70% were males. Median BMI was 23.5, and 7.5% had obesity. The following ART switches were registered in the dataset: 304 from TDF to TAF, 3656 from non-INSTI to INSTI without TAF, 293 from non-INSTI to INSTI with TAF, and 3128 from EFV to INSTI. Table 1, panel L depicts performance metrics of the ML model with 5% WG threshold. Out of 3776 observations in the test set (16.7% with WG≥5%), 596 correctly predicted with WG≥5% (true positive [TP]), 35 overestimated WG≥5% (false positive [FP]), 35 underestimated WG<5% (false negative [FN]), and 3110 correctly predicted with WG<5% (true negative [TN]). ML algorithm built in model A had excellent performance (>90%) in predicting WG in terms of accuracy, sensitivity, specificity, and ROC AUC. The global SHAP values for the 11 top variables and ART regimens (out of 142 included in the model A) are depicted in Figure 1, panel R. Values of each variable have a positive or negative impact depending on their SHAP value. High values in red negatively contribute to WG, while low values in blue contribute strongly to WG. ART switch did not have a significant impact on WG (Figure 1).

Conclusions: ML models A and B had excellent performance in WG prediction due to the inclusion of body composition, metabolic and endocrinological variables. The parsimonious model (model C) with a restricted subset of anthropometric HIV and ART variables is insufficient to obtain reliable prediction. These models stress the multi-factorial nature of WG in which the impact of INSTI or/and TAF switch/exposure is diluted in the universe of variables that contribute to WG.

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Metabolic issues in effective HAART

OC 11 IN VITRO MODEL OF ADYPOCITE DIFFERENTIATION UNDER TAF, TDF AND INSTIS SELECTIVE CHALLENGE

M.A. Carleo[1], A. Perna[2], A. Guida[1], P. Rosario[1], S. Mascolo[1], A. Lucariello[3], G. Palmiero[1], V. Rizzo[1], A. M. Rossomando[1], A. Baldi[4], A. De Luca[5], P. Maggi[6], V. Esposito[1]

[1]Infectious Diseases and Gender Medicine Unit "D. Cotugno" Hospital – AO dei Colli, Naples Italy, [2]Department of Medicine and Health Sciences "Vincenzo Tiberio", University of Molise, Campobasso, Italy, [3]Department of Sport Sciences and Wellness, University of Naples "Parthenope", Naples, Italy, [4]Department of Environmental, Biological and Pharmaceutical Sciences and Technologies, Università degli Studi della Campania "L. Vanvitelli", Caserta, Italy, [5]Department of Mental and Physical Health and Preventive Medicine, Section of Human Anatomy, University of Campania "Luigi Vanvitelli", Naples, Italy, [6]University of Campania "Luigi Vanvitelli", Caserta Italy

Background: The Integrase Strand Transfer Inhibitors (INSTI) class of antiretroviral drugs is characterized by a good tolerability profile and a relatively high genetic barrier to HIV drug resistance. Several studies reported greater weight gain among persons receiving INSTI-based regimens for initial therapy as compared to other regimens. In association with INSTI one of the most widely used regimens are nucleotide analog reverse-transcriptase inhibitor (NRTI) whose effect on adipogenesis pathway is not well understood. Since adipocyte differentiation recognize an important regulatory checkpoint by two families of transcription factors, the CCAAT/enhancer-binding proteins (C/EBPs) and the peroxisome proliferator-activated receptors (PPARs), the evaluation of the expression of adipocytic differentiation markers, such as PPAR-γ and C/EBP-α, is routinely used to evaluate fat tissue differentiation and it has been already assessed to investigate adipocyte differentiation in studies on HIV infected patients.

Material and methods: In experimental setting, we used the in vitro model of adipogenesis of 3T3-L1 cells, to investigate the effects of the newer NRTI, tenofovir alafenamide fumarate (TAF), alone or in combination with the four INSTIs, raltegravir (RAL), elvitegravir (EVG), dolutegravir (DTG) and bictegravir (BIC) on adipose differentiation. Protein expression levels of PPARɣ and C/EBPα, and the intracellular lipid accumulation by Red Oil staining, were used to monitor adipose differentiation. In a second step, we compared the effects of tenofovir disoproxil fumarate (TDF) with the effects of TAF on adipose differentiation by using the same model of investigation.

Results: Compared to the control, RAL, EVG, DTG and BIC were all able to increase adipogenesis, being RAL and ELV somehow more efficient, while TAF slightly inhibited adipogenesis. However, when used in combination with the other INSTIs, TAF was able to reduce the adipogenic effects of all the four drugs. This effect was more evident when TAF was used in combination with DTG and BIC. Similarly TDF was related to a reduction in adipocyte proliferation. In addition when TDF was added to 3T3L1 differentiating cells a morphological change was noted and a deregulation of PPAR-γ and C/EBP-α pathway was evident.

Conclusions: Our results confirm that INSTIs could increase adipogenesis; whereas, TAF shows an inhibitory effect, being able to effectively counteract the increase in adipogenesis caused by other INSTIs, in particular DTG and BIC. Differently, TDF seems to determine changes in the differentiation pathway of 3T3L1 cells whose effects on clinical practice deserves careful considerations. We can therefore conclude that the interaction between INSTIs and TAF leads to an antagonistic effect on the differentiation of adipocytes, while the apparently toxic effect of TDF in adipogenesis needs to be further elucidated with more detailed evidences from experimental and clinical settings.

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Metabolic issues in effective HAART

OC 12 LIVER ENZYMES LEVELS, METABOLIC AND RENAL PROFILE MODIFICATIONS AFTER SWITCHING FROM TDF TO TAF- BASED REGIMENS AMONG ART EXPERIENCED PLWH IN ICONA COHORT

M. Poliseno[1], S. Lo Caputo[1], A. Tavelli[2], R. Gagliardini[3], L. Gazzola[2], A. Saracino[4], T.A. Santantonio[1], M. Puoti[5], S. Cicalini[3], A. Antinori[3] , A. d'Arminio Monforte[2], A. Cozzi-Lepri[6]

[1]Unit of Infectious Diseases, University of Foggia, Foggia, Italy, [2]Clinic of Infectious Diseases, San Paolo Hospital, ASST Santi Paolo e Carlo, Department of Health Sciences, University of Milan, Milan, Italy, [3]National Institute for Infectious Diseases "L. Spallanzani" IRCCS, Rome, Italy, [4]Operative Unit of Infectious Diseases, Hospital-University Polyclinic of Bari, Bari, Italy, [5]Infectious Diseases Unit, Niguarda Hospital, Milan, Italy, [6]Institute for Global Health UCL, University College London, London, UK

Background: Liver enzymes elevation during treatment with Tenofovir Disoproxil Fumarate (TDF) and reduction in Alanine aminotransferase (ALT) values after TDF replacement with Tenofovir Alafenamide (TAF) have been described among ART-experienced PLWH. However, the rate of change of liver enzymes concomitantly with that of other markers after a switch to TAF have been seldom investigated and the possible role of the anchor drug used on markers trajectories remains unclear.

Materials and Methods: The analysis includes >18 years, ART-experienced PLWH enrolled in the ICONA Foundation Study cohort who at any time were switched from a TDF-based to a TAF-based regimen while they had a VL≤50 copies/mL. PLWH had to have ≥2 values of the markers while receiving TDF and TAF to be included. Pearson rho was used to evaluate baseline correlations. Mean changes in liver enzymes (AST, ALT, GGT, ALP), metabolic profile (Glucose, Triglycerides, Total, LDL and Total/HDL Cholesterol) and serum creatinine/eGFR using pair of values measured before and after the switch were compared using a paired t-test. Mixed models with random intercept and slope were used to evaluate the trajectories of the markers. A step-linear model with a change in slope at 1 year after switch was used for all markers. A quadratic model with interactions was used to assess the effect of the anchor drug class (NNRTI, PI, INSTI) used in the TAF regimen on ALT changes.

Results: 2,911 PLWH, mainly males (81%), median age 45 (37-53) years, after having received TDF for a median (IQR) of 31 (19-47) months, were switched to a regimen containing TAF in combination with a NNRTI (N=1337), PI/r (N=489) or INSTI (N=1105). At baseline, 347 subjects (12%) presented with chronic viral hepatitis, while only 44 (2%) had liver enzyme elevation. At baseline, weak correlations were found between ALT and HDL Cholesterol, Triglycerides and Glucose (ρ=-.07, p<0.0001; ρ=.13, p<.001; ρ=.08, p<.001, respectively).

We noticed differences in the changes of some of the parameters when comparing the periods while participants were on TDF vs. TAF, although none of these were clinically significant (Table 1). Over a median of 42 (34-47) months follow-up after switch, for liver enzymes we observed a moderate reduction over the 1st year followed by a slight increase; the opposite trend was observed for the metabolic and renal profiles, although again within the normal limit range (Table 2). U-shape trajectories for ALT after the switch was confirmed when we fitted a quadratic model, suggesting a difference in the evolution of ALT according to the anchor drug class (interaction p-value=0.04, Figure 1).

Conclusions: In our cohort of PLWH who were switched from TDF to TAF-based regimens with a VL≤50 copies/mL, no clinically significant changes in markers over a median of 42 months after the switch were observed. The class of the anchor drug used appeared to have an effect on the shape of ALT changes.

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COVID-19: clinical management

OC 13 HOME PRESCRIPTION TREATMENT AND MORTALITY RISK AFTER HOSPITALIZATION WITH SYMPTOMATIC COVID- 19 DISEASE

A. Dessilani, A. Cozzi-Lepri, E. Franceschini, G. Guaraldi, V. Borghi, M. D. Di Trapani, M. Del Monte, F. Medioli, I. Baldisserotto, S. Esperti, A. Mazzocchi, J. Conti, A. Gallerani, N. Barp, A. Spadoni, V. Menozzi, C. Mussini

Struttura Complessa di Malattie Infettive, AOU Policlinico di Modena, Modena

Background: International and national guidelines do not suggest a specific home-treatment (HT) for mild COVID -19. On the basis of the results of the RECOVERY trial, steroid prescription is contra- indicated in subjects not requiring oxygen support. Nevertheless, at least in Italy, a proportion of individuals who are hospitalized with symptomatic COVID-19 disease have previously received home prescribed medications. Few studies evaluated whether the type of medication received at home may have an impact on the risk of death after hospitalization.
Methods: Single center cohort study of patients with COVID-19 pneumonia, admitted to Modena Hospital over February 2020-Dec 2021. History of HT was collected at entry in the hospital (baseline) and participants were classified according to: no treatment, use of steroids, of heparin, of steroids + heparin and use of other drugs (hydroxychloroquine, macrolides, beta-lactams). Participants' characteristics at baseline were compared by HT groups. Kaplan-Meier curves were used to estimate day 28 mortality rate by HT groups. Cox regression analysis was conducted to control for potential key confounders (DAG, Figure 1).
Results: 2,458 participants were included, 62% males, median age 71 years. Before admission, 1784 (73%) were prescribed no treatment, 104 (4%) steroids, 103 (4%) heparin, 94 (4%) steroids + heparin and 373 (15%) other drugs. Treatment groups differed significantly by ischemic cardiomyopathy, cerebrovascular disease, diabetes, chronic renal insufficiency, dementia and Charlson co-morbidity index (Table 1). Compared to other treatment groups, dyspnea was more prevalent in participants treated with steroids or with steroids + heparin (p=0.001), and this latter group also had lower baseline PaO2/FiO2 ratio (p=0.017) and were more frequently treated with high-flow nasal oxygen after admission (p=0.002) (Table 1). Overall, 339/2458 patients died by day 28 from admission (14%). There was a significant difference in mortality by HT group (day 28 KM estimates: no treatment 15.0.%, steroids 16.3%, heparin 7.8%, steroids + heparin 7.4% and other drugs 10.7% p=0.02, Figure 2). Results were confirmed after controlling for key potential confounders, suggesting that using heparin alone before hospitalization led to a 58% reduction in day 28 mortality as compared to no treatment (Table 2).
Conclusions: In our cohort of patients admitted to hospital for Covid-19 pneumonia home treatment with heparin alone was associated with a lower in-hospital mortality. Role of home treatment with heparin in presence of newly developed antivirals should be tested in future randomized trials.

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COVID-19: clinical management

OC 14 IN VIVO EFFICACY OF MONOCLONAL ANTIBODIES AND DIRECT ANTIVIRAL AGENTS AGAINST THE SARS-COV-2 BA.1 AND BA.2 OMICRON SUBLINEAGES

V. Mazzotta[1,2], A. Cozzi Lepri[3], F. Colavita[1], S. Lanini[1], R. Rosati[1], E. Lalle[1], C. Cimaglia[1], I. Mastrorosa[1], J. Paulicelli[1], S. Vita[1], E. Caraffa[1], G. Matusali[1], A. Vergori[1], G.Giannico[1], G. Maffongelli[1], E. Milozzi[1], D. Donno[1], P. Vittozzi[1], F. De Zottis[1], P. Piselli[1], E. Girardi[1], A.R. Garbuglia[1], F. Vaia[1], E. Nicastri[1], A. Antinori[1]

[1]National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [2]PhD course in Microbiology, Immunology, Infectious Diseases, and Transplants (MIMIT), University of Rome Tor Vergata, Rome, Italy, [3]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, UCL, London, UK

Background: Omicron variant questioned the efficacy of the approved therapies for the early COVID-19. In vitro data show retained neutralizing activity against BA.1 and BA.2 for remdesivir (RDV), molnupiravir (MLN), and nirmatrelvir/ritonavir (NRM/r), while poor efficacy for Sotrovimab (STR) against BA.2. No data about the risk of clinical failure and in vivo antiviral activity are available.

Material and Methods: Single-center observational comparison study enrolling all consecutive pts seen for care at INMI Spallanzani, Rome with a confirmed SARS-CoV-2 Omicron (BA.1 or BA.2) diagnosis and who met the AIFA criteria for eligibility for treatment with RDV, MLN, NRM/r, or STR. Treatment allocation was subject to drug availability, time from symptoms onset, and comorbidities. Patients were followed through day 30. Nasopharyngeal swab (NPS) VL was measured on day 1 (D1) and D7 and was expressed by log2 cycle threshold (CT) scale. Comparisons between groups were made by Chi-square and Wilcoxon paired-test. Primary endpoint was D1-D7 VL variation. Potential decrease in VL and average treatment effect (ATE) were calculated from fitting marginal linear regression models weighted for calendar month of infusion, duration of symptoms, and immunodeficiency. Secondary endpoints were the proportion of D7 undetectable VL in NPS and clinical outcomes compared by treatment groups using a Chi-square test.

Results: A total of 522 pts received treatments (STR 203, MLN 117, NRM/r 84, and RDV 118): female 250 (48%), median age 66 yrs (IQR 55-76), 91% vaccinated; 15% with negative baseline serology. At D1, median time from symptoms onset was 3 days (2,4). 379 (72.6%) pts were infected with BA.1 and 143 (27.4%) with BA.2. D1 mean viral load was 4.12 log2 (4.16 for BA.1 and 4.01 for BA.2), Table 1. The adjusted analysis showed that NRM/r significantly reduced VL compared to all the other drugs in pts infected with BA.1 while no evidence for a difference vs. MLP was seen in those infected with BA.2. (Fig 1,2). MLN had comparable activity to STR against BA.1 and to NRM/r against BA.2. There was no significant difference between STR and RDV for BA.2. Tables 2 showed ATE for all possible 2-by-2 treatment comparisons separately for BA.1 and BA.2. At D7, 35/522 (6.7%) pts had undetectable VL. Of these, 31 were infected with BA.1 [9 (9%) MLN, 7 (14%) NRM/r, 7 (8%) RDV, and 8 (5%) STR), and only 4 with BA.2, all treated with NRM/r. After 30 days of follow-up, 9/568 pts experienced COVID-19-related clinical failure [7/226 STR (5 BA.1) and 2/87 NRM /r (2 BA.1)].

Conclusions: In this analysis of in vivo early VL reductions, NRM/r appears to be the drug showing the greatest antiviral activity regardless of the VoC, together with MLN, although the latter limited to people with BA.2. In the Omicron era, due to the high prevalence of vaccinated people and the lower probability of hospital admission, VL decrease can be a valuable surrogate of drug activity.

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COVID-19: clinical management

OC 15 ANEMIA IS STRONGLY ASSOCIATED WITH SEVERITY AND MORTALITY OF COVID-19 IN HOSPITALIZED PATIENTS

F. Di Gennaro, G. Brindicci, M. Cormio, V. Guerra, A. Lugli, L. De Santis, A. Procopio, D.F. Bavaro, E. Milano, N. De Gennaro, G. De Iaco, R. Lattanzio, C.R. Santoro, A. Saracino

Clinic of Infectious Diseases, University of Bari, University Hospital Policlinico, Bari Italy

Introduction: Limited studies are available on the association between anemia and COVID-19 outcomes in patients with moderate-severe pneumonia, with controversial findings. Therefore, in this research, we aimed to investigate the impact of anemia registered at admission on COVID-19 outcomes in patients who were hospitalized in the Clinic of Infectious Diseases, University Hospital of Bari, Italy.

Methods: In this retrospective study, data of all consecutive patients admitted to hospital due to COVID-19 from March 2020 to January 2022 were evaluated. The first available hemoglobin (Hb) value at the entrance was used for classifying patients as anemic or not anemic; anemia was defined as a hemoglobin (Hb) concentration <13 g/dL and <12 g/dL in males and females, respectively. Patients with qSOFA scores ≥2 or CURB-65 scores ≥3 were considered as severe COVID-19. Our primary objective was to assess the association between anemia at admission and COVID-19 severity and mortality in hospitalized patients.

Results: Overall, 865 consecutive patients admitted at University Hospital of Bari with SARS CoV2 infection were included in the study [44% F, mean age: 53.8 (15.0)], 43 % (n.372) of whom were defined as anemic. Patients with anemia had a higher frequency of comorbidities, hypertension, renal failure, diabetes, and cancer (P < 0.001, Table 1). Furthermore, anemic patients had more elevated PCR at admission, PCR and troponin peak (P < 0.001), and required more frequently High Flow Nasal Cannula or Noninvasive ventilation (NIV) (P < 0.001) and prone position during the hospital stay (P < 0.001). According to the multiregression analysis, mortality was more frequent in patients with anemia (OR: 3.41, 95% CI: 1.84- 6.69), in females (OR: 1.83, 95% CI: 1.02- 3.36), and in patients with at least one comorbidity (OR: 5.63, 95% CI: 2.41- 16.7), dyspnea at admission (OR: 3.54, 95% CI: 1.92- 6.82), higher procalcitonin (OR: 4.19, 95% CI: 2.31- 7.63), higher D-dimers (OR: 23.9, 95% CI: 5.25- 558), higher troponin (OR: 4.62, 95% CI: 2.54- 8.43), and higher IL – 6 levels (OR: 5.14, 95% CI: 1.85- 22.1).

In addition, severe COVID-19 was also associated with anemia (OR: 13.2, 95% CI: 8.96- 20.0), presence of at least one comorbidity (OR: 1.83, 95% CI: 1.38- 2.44), dyspnea at admission (OR: 2.77, 95% CI: 2.05- 3.78), higher D-dimers (OR: 2.23, 95% CI: 1.67- 2.98), higher PCR (OR: 4.26, 95% CI: 2.77- 6.69), higher ferritin (OR: 1.69, 95% CI: 1.28- 2.24) and higher LDH value (OR: 2.07, 95% CI: 1.56- 2.75).

Conclusion: The prevalence of anemia in hospitalized patients with COVID-19 was high and associated with poorer outcomes and more severe clinical manifestations of disease. Anemia should be considered as an early marker of alert in COVID-19 patients.

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COVID-19: clinical management

OC 16 CLINICAL CHARACTERISTICS AND OUTCOMES OF COVID-19 IN VACCINATED VERSUS NOT-VACCINATED HOSPITALIZED PATIENTS: DATA FROM AN ITALIAN REFERENCE HOSPITAL

A. Mondi, I. Mastrorosa, A. Navarra, S. Lanini, A. D'Annunzio, F. Vaia, E. Girardi, A. Antinori

National Institute for Infectious Diseases L. Spallanzani IRCCS, Rome, Italy

Background: The aim of the study was to describe and compare clinical characteristics and outcomes of COVID -19 hospitalized patients (pts) according to vaccination status.

Methods: Retrospective observational study including all pts admitted to INMI L. Spallanzani, from Jan 1st to Dec 31st 2021, with confirmed COVID-19 diagnosis and with data on SARS-CoV-2 vaccination available from hospital records and/or regional vaccination registry. According to vaccination status at the admission, pts were classified as unvaccinated (NV = no vaccine doses or only the first dose of a 2-dose series <14 days before), partially vaccinated (PV= only the first dose of a 2-dose series >14 days before or the second dose received <14 days before), fully vaccinated (FV=complete vaccine schedule >14 days before). FV pts were further stratified according to the distance from the last dose (≤ or >120 days) and to the receipt of the booster dose. Main characteristics at hospital admission were compared between NV, PV and FV pts by Chi-square test. The predictive factors of clinical progression (admission in Intensive Care Unit [ICU]/death) within 29 days both in total population and in FV +PV pts were assessed by multivariable logistic regression.

Results: Overall 2072 pts were included: 1609 (77.7%) NV, 80 (3.9%) PV and 383 (18.5%) FV. Among FV, 72% received the last dose > 120 days from baseline and 7.3% received the booster dose.

NV pts were more likely to be younger (p<0.001), without comorbidities (p<0.001) and to have pneumonia (p<0.001). Over a median follow-up of 14 (IQR 9-22) days, 299 (14.4%) pts were admitted to ICU, 136 (6.5%) pts died within 29 days. The three groups did not significantly differ for the length of hospital stay (0.621), the ICU admission (0.061) and the 29-day death (0.199).

By multivariable logistic regression, having received complete vaccination compared to be unvaccinated halve the risk of death or ICU admission within 29 days. No differences were observed between PV and NV pts. Similarly, female gender and having received remdesevir (RDV) or monoclonal antibodies (MoAb) during hospitalization were associated to a lower risk of clinical progression whereas older, having baseline comorbidities and pneumonia predicted a higher chance of death/ICU admission [Table 1a]. Restricting the analysis to FV and PV pts, only female gender and RDV use were associated to a lower risk of clinical progression whereas MoAb showed a trend through significance as a protective factor. No significant association with the time from the last dose and the booster dose were observed [Table 1b].

Conclusions: Our data confirm the efficacy of complete vaccination in preventing severe clinical progression of COVID-19. In FV pts, a longer time from last dose does not seem to be associated to higher risk of severe progression but this finding needs further confirmation. Efforts to promote SARS-CoV2 vaccination are critical to prevent COVID-19–associated severe outcomes.

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Pathogenesis and Immunology

OC 17 IMPACT OF SARS-COV-2 INFECTION IN A RELEVANT THREE-DIMENSIONAL HUMAN BRONCHIAL CELL CULTURE MODEL OF CYSTIC FIBROSIS

I. Pagani[1], L. JV. Galietta[2], N. Pedemonte[3], V. Capurro[3], A. Venturini[2], C. Cigana[4], B. A. Franco[4], A. Bragonzi[4], E. Vicenzi[1]

[1]Viral Pathogenesis and Biosafety Unit, IRCCS-Ospedale San Raffaele, Milan, Italy, [2]Telethon Institute of Genetics and Medicine (TIGEM), Pozzuoli, NA, Italy, [3]UOC Genetica Medica, IRCCS Istituto Giannina Gaslini, Genova, Italy, [4]Infections and Cystic Fibrosis Unit, IRCCS-Ospedale San Raffaele, Milan, Italy

Background: SARS-CoV-2 does not cause a more serious infection in Cystic Fibrosis (CF) patients compared to the general population and the outcomes have been better than initially predicted from previous viral respiratory infections. This epidemiological evidence raises the question of whether the determinants of CF pathophysiology might interfere with virus replication and/or COVID-19 disease progression.

Materials and Methods: We investigated SARS-CoV-2 infection in ten primary human bronchial epithelial cells (HBEC) obtained from individuals with CFTR-diverse mutations compared with HBEC from nine wild type CFTR (non-CF) subjects. Once HBEC were seeded on snapwells inserts, they were let in culture for three weeks in air-liquid interface condition to differentiate and self-organise as a three-dimensional bronchial epithelium (BE) with an apical/basolateral polarisation. The SARS-CoV-2 isolate (GISAID accession ID: EPI_ISL_413489) was used to carry out the infection experiments and added to the apical surface of BE. The CF vs. non-CF BE susceptibility to infection was determined both by plaque forming assay by collecting apical supernatants at 24-48-72 days post-infection and by indirect immunofluorescence using different antibodies specific for either SARS-CoV-2 or cellular components. Perturbation of gene expression by viral infection was determined by RNAseq at 72 hours post-infection.

Results: Productive infection was detected in all HBEC although the efficiency of viral replication varied among the different donors. By comparing the kinetics of viral replication, SARS-CoV-2 replicated less efficiently in CF vs. non-CF donors. Immunofluorescence staining confirmed plaque assay results, indeed with two antibodies specific for either SARS-CoV-2 Nucleoprotein or Spike protein, less positive cells were observed in CF vs. non-CF BE. Moreover, no alteration in the overall epithelium architecture was observed during infection; in fact, tight junction staining with ZO-1 antibody showed no difference in uninfected vs. infected condition. Preliminary transcriptome analysis showed higher basal levels of viral replication an upregulation of interferon-stimulated genes with antiviral functions and pro-inflammatory cytokines and chemokines in CF compared to non-CF culture.

Conclusion: Our results suggest that CFTR mutations are associated with a pre-existing pro-inflammatory and antiviral-state that might curtail SARS-CoV-2 replication in human BE.

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Pathogenesis and Immunology

OC 18 ORAL IMMUNITY CHARACTERIZATION IN SALIVA FROM ASYMPTOMATIC AND SEVERE COVID19 PATIENTS

I. Saulle[1,2], M. Garziano[1,2], O. Utyro[2], S. Lo Caputo[3], M. Poliseno[3], T.A. Santantonio[3], M. Clerici[1,4], M. Biasin[2]

[1]Laboratory of Immunology, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy, [2]Laboratory of Immunobiology, Department of Biomedical and Clinical Sciences L. Sacco, University of Milan, Milan, Italy, [3]Unit of Infectious Diseases, Department of Clinical and Experimental Medicine, University of Foggia, Foggia, Italy, [4]Don C. Gnocchi Foundation, Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) Foundation, Milan, Italy

Background: The oral mucosa is the first site of SARS-CoV-2 entry and replication, and it plays a central role in the early defense against infection. Thus, profiling the immune response in the oral mucosa of patients with different degrees of COVID19 could be key to infer their outcome. To address this issue, cytokines, miRNA and neutralizing activity were assessed in saliva and plasma from asymtomatyc and severe COVID19 patients.

Material and Methods: This study included a total of 20 COVID19 patients (as determined by SARS-CoV-2 molecular test of nasopharyngeal swabs) hospitalized at Infectious Diseases Unit, Policlinic “Riuniti” of Foggia (Italy), from 1 March to 31 May 2020. According to COVID19 disease severity, patients were divided into asymptomatic (AP) (n°=10) and severe (SP) (n°=10). Saliva and plasma samples were collected at hospital admission and stored at −80 °C until use. MiRNA profile (PCR array), viral load (qPCR) and neutralizing antiviral assay (NA) as well as cytokine and chemokine release (Multiplex ELISA) were evaluated on both biological specimens. Results were compared to those of SARS-CoV-2 uninfected subjects (US).

Results: As a whole viral entry was associated with the activation of immune response as for US, AS and SP sample comparison. Thus, of the 84 miRNAs analysed, 13 were differently expressed in AP compared to SP. In particular, nine antiviral miRNAs (let-7a-5p; let-7b-5p; let-7c-5p, miR-23a and b, miR-29c, miR-30, miR-545 miR -497-5p) and four immunomodulatory miRNAs (miR-34a-5p, miR-144-3p, miR-181d-5p, miR-146) were significantly upregulated in SP. Such differences were evident at both local and plasma level, though they were far more marked in saliva. Notably, disease severity was not correlated with NA. As expected, an increased secretion of pro-inflammatory cytokines, including IL-1a, IL-4, IL-6, IL-17, IFNγ, as well as CCL2 and CCL5 chemokines was observed in both saliva and plasma from SP.

Conclusions: According to this results, SARS-CoV-2 is able to subvert the immune balance at both systemic and local level with an intensity proportional to the severity of the disease: US<AP<SP. Notably, miRNA specifically induced in saliva from SP were predicted to directly bind SARS-CoV-2 genes or cellular factors that indirectly influence SARS-CoV-2 replication and immune response; as if the immune system would attempt to contain SARS-CoV-2 infection at the site of entry. Monitoring these parameters over time could help to predict the outcome of the disease and to identify new markers of disease progression.

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Pathogenesis and Immunology

OC 19 THERAPEUTIC MONOCLONAL ANTIBODY TREATMENT RESTORES IMMUNE HOMEOSTASIS AND DID NOT PREVENT THE EXPANSION OF ANTI-SARS-COV-2 ADAPTIVE IMMUNE RESPONSE IN MILD/MODERATE COVID-19 PATIENTS

R. Casetti[1], A. Sacchi[1], V. Mazzotta[2], F. Cristofanelli[1], E. Cimini[1], S. Notari[1], G. Grassi[1], V. Bordoni[1], I. Mastrorosa[2], M.L. Giancola[2], A. Vergori[2], M. Tempestilli[1], S. Vita[2], M. Rubino[1], D. Mariotti[1], S. Gili[1], E. Lalle[3], S. Meschi[3], F. Colavita[3], A.R. Garbuglia[3], E. Girardi[4], E. Nicastri[2], A. Antinori[2], C Agrati[1]

[1]Cellular Immunology and Pharmacology Laboratory, INMI L Spallanzani, Rome, Italy, [2]Clinical Department, INMI L Spallanzani, Rome, Italy, [3]Virology Laboratory, INMI L Spallanzani, Rome, Italy, [4]Scientific Directorate, INMI L Spallanzani, Rome, Italy

Background: The impact of anti-Spike monoclonal antibody (mAbs) treatment of COVID-19 patients on innate and adaptive immunity are lacking. Aim of this longitudinal study was to investigate the impact of mAb treatment on innate inflammatory response, immune activation, cytotoxic profile and on the differentiation of specific immune response.

Material and Methods: SARS-CoV2-infected patients (n=39) were enrolled before (T0) and after 7 (T7) and 30 (T30) days from mAb infusion. Patients showed comorbidities, such as thyroid illnesses, dyslipidemia, multiple sclerosis, hypercholesterolemia, cutaneous LNH B cells, lymphoma, depression and schizophrenia. Immune phenotyping of innate (NK and γδ T cells) and adaptive (CD4 and CD8 T) cell subsets and inflammatory cytokine (IL-6) were evaluated by flow cytometry. Finally, the Spike-specific T cell response was analyzed by quantifying IFN-γ after specific stimulation and anti-Nucleocapside IgG by chemiluminescence assay.

Results: SARS-CoV-2 RNA was negative in the nasopharyngeal swabs at day 30 in all patients. According to the viral decay, a significant reduction of CD38 expression was observed both in γδ T cells ($p<0.001$, T7 and T30 vs T0) (Fig. A) and NK cells ($p<0.0001$, T7 and T30 vs T0) (Fig. B) of the innate compartment. Also in adaptive immune compartment a significant reduction of CD38 expression was observed at T7 ($p<0.0001$, T7 vs T0 in CD8 T cells) (Fig. D) and even more at T30 ($p<0.0001$, T30 vs T0 in both CD4 and CD8 T cells) (Fig. C and Fig. D). Moreover, a significant reduction of perforin expression was observed in γδ T cells ($p<0.05$, T7 and T30 vs T0) (Fig. E) and NK cells ($p<0.01$, T7 and T30 vs T0) (Fig. F). A significant reduction of perforin expression was observed in CD8 T cells ($p<0.01$; T7 and T30 vs T0) (Fig. H), as well. Nevertheless, respect to healthy controls, a higher frequency of activated CD8 T cells ($p<0.01$) (Fig. D) and of perforin-positive CD4 ($p<0.0001$) (Fig. G) and perforin-positive CD8 T cells ($p<0.01$) (Fig. H) persisted overtime. At T0, circulating monocytes were enriched of IL-6 inflammatory cytokine whose frequency significantly decreased after treatment but persisted higher than healthy controls ($p<0.01$) (Fig. I). Similarly, IL-6 significantly decreased after treatment but persisted higher than healthy controls in neutrophils ($p<0.0001$) (Fig. L). Accordingly, a reduction of plasmatic IL-6 showed a similar kinetic ($p= 0.056$, patients vs HD) (Fig. M). Finally, the expansion of Spike specific T cells ($p<0.05$, T7 vs T0) (Fig. N) and anti-N IgG ($p<0.0001$, T7 vs T0) (Fig. O) increased already at T7.

Conclusions: We provided evidences that early effective mAbs treatment of SARS-CoV2 patients restored immune homeostasis and did not prevent the expansion of endogenous Spike-specific T cells and anti-N antibodies.

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Pathogenesis and Immunology

OC 20 EVIDENCE OF EXTENSIVE TRANSCRIPTIONALLY ACTIVE HBV INTEGRATIONS INVOLVING GENETIC REGIONS CRUCIAL FOR CELL PROLIFERATION IN THE EARLY PHASES OF CHRONIC INFECTION EVEN IN THE SETTING OF LIMITED LIVER DAMAGE

S. D'Anna[1], L. Carioti[1], L. Piermatteo[1], A. Battisti[1,2], L. Benedetti[1], F. Ceccherini-Silberstein[1], U.S. Gill[2], P.T.F. Kennedy[2], V. Svicher[1], R. Salpini[1]

[1]University of Rome Tor Vergata, Department of Experimental Medicine, Rome, [2]Barts Liver Centre, Blizard Institute, Barts and The London SMD, QMUL, London

Background: HBV integration into the human genome can mediate oncogenic activity. Limited data are available on HBV integration in the early phases of infection. Here, we characterize chimeric HBV-human RNAs reflecting transcriptionally active HBV integrations in eAg positive phases of HBV infection.

Methods: RNA-seq of liver tissues from 42 eAg+ chronically infected patients (27 with eAg+ hepatitis [eAg+CH] and 15 with eAg+ infection [eAg+CI]) was performed by NGS [Illumina, median(IQR) reads per sample: 22(18-27) millions]. An ad-hoc bioinformatic pipeline was applied to recognize chimeric HBV-human transcripts (present in >2 reads). Role of genes involved in HBV integration was assessed by GeneCards.

Results: Patients with eAg+CI were significantly younger than eAg+CH [Median(IQR): 27(22-29) vs 29(25-35) years; P<0.001). Median(IQR) serum HBV-DNA and HBsAg were 8.0(5.7-8.6) logIU/ml and 4.4(4.1-4.8) logIU/ml respectively, with no significant difference according to HBV infection status. Overall, >1 chimeric HBV-human RNA was revealed in almost all patients (98%) for a total of 1048 unique HBV-human transcripts, reflecting the abundance of transcriptionally active HBV integrations. The number of chimeric transcripts in each patient did not differ in eAg+CH and eAg+CI groups [median(IQR): 13(11-22) and 14(10-39); P=0.46], highlighting an early occurrence of HBV integration in young patients with limited fibrosis.

The landscape of transcriptionally active HBV integrations was similar in both CI and CH patients, involving all chromosomes in both groups. Notably, HBV integration was revealed in mitochondrial transcriptome (at levels of genes with a role in electron transport chain) only in CH group but never in CI group (48% vs 0; P<0.001).

69.6% of integrations originated from HBx/Core while 20.7% of chimeric transcripts involved HBsAg coding region, resulting in production of truncated/aberrant HBsAg forms.

By analyzing the number of chimeric transcripts according to HBV genotypes, we found that gen-C, -D and -E have a trend to harbor a higher number of transcriptionally active HBV integrations respect to gen-B and -A (P=0.07).

Notably, by gene ontology, 18% (189/1048) of chimeric transcripts involved human exons and splicing signals, crucial for gene expression. Among them, 35.4% corresponds to genes playing a pivotal role in modulating cell survival/proliferation, including genes (BIRC6, SYF2, EVI5, BTG1) known to be dysregulated in HCC.

Conclusions: Transcriptionally active HBV integrations occur frequently in the eAg-positive phases of HBV infection, even in young patients with limited liver fibrosis. These events lead to the production of chimeric HBV-human aberrant transcripts, that mostly involve genes with a role in crucial intracellular pathways, conferring a proliferative advantage to the hepatocytes. This further supports early treatment initiation in eAg positive chronic infection.

From HIV to SARS-CoV-2

OC 21 INTACT PROVIRAL DNA AND CHROMOSOME INTEGRATION SITES IN PERIPHERAL BLOOD LYMPHO-MONOCYTES OF EARLY TREATED ACUTE HIV INFECTIONS

G. Rozera[1], G. Sberna[1], G. Berno[1], C. Gruber[1], N. Orchi[2], V. Puro[2], A. Mondi[3], A. Antinori[3], I. Abbate[1]

[1]Virology Unit, [2]AIDS Referral Center, [3]HIV/AIDS Clinical Department of the National Institute for Infectious Diseases I.R.C.C.S. L. Spallanzani, Rome, Italy

Background: HIV-1 genomes integrate into human chromosomes and establish a lifelong reservoir of virally infected cells. Only a part of integrated proviral DNA is intact and able to generate viral progeny. Intact and defective proviruses are under distinct selective pressure during disease progression and antiretroviral therapy (ART). Aim of the study was to characterize proviral DNA in acute HIV infections, starting early ART, in terms of both fraction of intact/defective proviral genomes and human chromosome integration sites. Changes in a period of 48 weeks after early therapy start were also evaluated.

Material and Methods: Peripheral blood lympho-monocytes (PBMC) viral reservoir of a group of 8 acute (Fiebig II/III) HIV-1 infections was studied at the moment of diagnosis (T0) and after 48 weeks of early ART (TDF/FTC associated with either DRV/b and RAL or DTG) (T1). Intact and defective provirus was measured at T0 and T1 by digital droplet PCR and correlated to plasma HIV-1 viral load. To perform intact/defective provirus analysis, primers and probes to both packaging signal and env regions were used, together with a third additional unconjugated probe, targeting hypermutated env region. At T0 and T1, proviral integration sites in human chromosomes were analysed with a shot-gun next generation sequencing approach. Statistical analysis was carried out as appropriated.

Results: In PBMC of acute HIV infections, intact provirus was detected in 6 out of 8 subjects with a median (IQR) of 570 (135-1109) copies/million cells, representing a median (IQR) of 10.02 (5.08-11.00) % of total HIV-1 DNA. Median (IQR) plasma HIV-1 RNA was 6.12 (5.42-6.80) Log copies/ml and did not correlate with intact proviral DNA p=0.92 (Spearman correlation). After 48 weeks of early ART all subjects were virological suppressed. Intact provirus was detected in 5 out of 8 subjects with a median (IQR) of 35 (21-78) copies/million cells, representing a median (IQR) of 9.11 (8.07-14.07) % of total HIV-1 DNA. The median (IQR) of different chromosomal integration sites/subject were 5 (2.25-13.00) at T0 and 4 (3.00-6.75) at T1. Of all the different integration sites observed at T1, the 64 % was already present at T0.

Conclusions: In PBMC of acute HIV infections, about only 1/10 of the total HIV-1 DNA represents intact proviral DNA. In these subjects HIV provirus displayed a relatively small number of different integration sites in human chromosomes. The lack of correlation between plasma viremia and intact provirus in PBMC suggests an extra-peripheral blood origin of the virus during acute infection. Early effective ART after 48 weeks did not substantially change the frequencies of intact provirus as well as the number and quality of integration sites of provirus in human chromosomes. The persistence of intact virus in the presence of a successful therapy remains the major obstacle for a cure of HIV infection.

OC 22 PLASMA, INTRACELLULAR AND LYMPH NODE ANTIRETROVIRAL CONCENTRATIONS AND HIV DNA CHANGE IN PATIENTS TREATED DURING PRIMARY HIV INFECTION: RESULTS FROM THE INACTION P25 STUDY

A. De Nicolò[1], E. De Vivo[1], S. Dispinseri[2], G. Marchetti[3], M. Trunfio[4], A. Ianniello[1], A. D'Avolio[1], A. Muscatello[5], A. Gori[5], S. Rusconi[6,7], E. Bruzzesi[8], A. Gabrieli[9], D.P. Bernasconi[10], S. Nozza[11], A. Calcagno[4] on behalf of the INACTION (Italian Network of Acute HIV Infection) study group

[1]Laboratory of Clinical Pharmacology and Pharmacogenetics, Department of Medical Sciences, University of Turin, Turin, [2]Viral Evolution and Transmission Unit, IRCCS Ospedale San Raffaele, Milan, [3]Clinic of Infectious Diseases, Department of Health Sciences, ASST Santi Paolo e Carlo, University of Milan, Milan, [4]Unif of Infectious Diseases, Department of Medical Sciences, University of Turin, Turin, [5]Infectious Diseases Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, [6]UOC Malattie Infettive, Ospedale Civile di Legnano, ASST Ovest Milanese, Legnano, [7]University of Milan, Milan, [8]Vita-Saluta San Raffaele University, Milan, [9]Dipartimento di Scienze Biomediche e Cliniche, Ospedale L Sacco, Milan, [10]Bicocca Bioinformatics Biostatistics and Bioimaging Centre - B4 School of Medicine and Surgery, University of Milano-Bicocca, Monza, [11]Department of Infectious Diseases, IRCCS Ospedale san Raffaele, Milan, Italy

Background: Antiviral treatment during primary HIV Infection (PHI) has been shown to be beneficial in terms of antiviral efficacy and long-term patients' outcomes. Preliminary data suggest that a higher antiretroviral (ARV) exposure in lymphatic tissues may be associated with a higher decrease in tissue reservoire size. Aim of this analysis was to explore the association between ARV concentration in plasma and PBMCs with HIV DNA decay at weeks 12 and 48.

Material and Methods: PHI was the inclusion criterion of this randomized, open-label, multicentric Italian study. Participants were randomly assigned (10:10:8) to a fixed-dose combination of tenofovir alafenamide (TAF, 25 or 10mg)/emtricitabine (FTC, 200 mg) plus darunavir/cobicistat (DRV/c, 800/150 mg, "group A"), dolutegravir (DTG, 50 mg, "group B") or DRV/c and DTG ("group C"). The study was funded by a Ministry of Health for GRANT NET -2013-02355333.

HIV-DNA was quantified by Droplet digital PCR (Biorad QX100) and normalized to RPP30 reference gene. Samples for plasma and intra-PBMC concentrations (including tenofovir-diphosphate [TFV-DP] and emtricitabine triphosphate [FTC-TP]) were collected at the end of the dosing interval. Lymph node (LN) samples were collected at W12 through needle-biopsy: tissues were homogenated and concentrations measured. All samples were analysed through validated ultra high performance liquid chromatography associated to mass spectrophotometry methods (UHPLC/MS-MS). Data are described as median values (interquartile range).

Results: Seventy-two participants (out of 78) with available PK/virological analysis were included. Sixty-eight were male (94.4%). Median age, CD4 cell count and HIV RNA were 34.1 years [28.3-43.9], 658 [474-796] cells/mm3 and 5.66 [4.62-6.50] Log10 copies/mL. The majority of participants were in Fiebig stage V (29, 40.8%) or II (13, 18.3%). At baseline, W12 and W48 HIV DNA was 4.46 [4.08-4.81], 4.22 [3.79-4.49] and 3.87 [3.46-4.34] Log10 (copies/10^6 PBMCs). LN PK was available for 9 (TFV and FTC intracellular metabolites), 5 (DTG) and 4 (DRV) samples. Plasma, PBMCs, LN and ratios at W12 and W48 as well as geometric means of available concentrations are shown in Table 1. We observed a border-line association between higher PBMCs TFV-DP and higher HIV DNA decay at week 48 (R=0.33, p=0.053). Non-significant higher decays in HIV DNA at week 12 were observed in participants with higher DTG LN ratios (R=0.3, p=0.68) and lower DRV LN ratios (R=-0.40, p=0.52).

Conclusions: We here report for the first time DTG LN concentrations in humans showing a moderate penetration of the drug; while DRV exposure in LNs was similar TFV and FTC were higher to previously published data.* With the exception of higher HIV DNA decay in participants showing higher TFD-DP PBMC concentrations we observed no other PK/PD association in this trial of patients treated during PHI.

*Scholz EMB and Kashuba ADM. Clin Pharm Ther 2021

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OC 23 EFFICACY, TOLERABILITY AND PHARMACOKINETICS OF DORAVIRINE IN THE CLINICAL SETTING

S. Fantino[1], M. Ferrara[1], G. Trevisan[1], G. Accardo[1], F. Alladio[1], E. Drappero[1], S. Biffi[1], A. Serra[1], L. Trentini[1], M. Tettoni[1], E. De Vivo[2], A. Ianniello[2], J. Mula[2], A. De Nicolò[2], A. D'Avolio[2], A. Calcagno[1], G. Di Perri[1], S. Bonora[1]

[1]Unit of Infectious Diseases, Department of Medical Sciences, University of Torino, Torino, [2]Laboratory of Clinical Pharmacology and Pharmacogenetics,, Department of Medical Sciences, University of Torino, Torino

Background: Doravirine (DOR) is a novel non-nucleoside reverse transcriptase inhibitor (NNRTI) characterized by an optimal efficacy, tolerability and safety in clinical trials. Efficacy and safety of DOR have been poorly described in the clinical setting as well as data variability on pharmacokinetics (PK) have been obtained. Therefore, our aim was to evaluate DOR efficacy, tolerability, plasma and intracellular (IC) pharmacokinetics in real-life experienced patients (pts).

Methods: Pts who switched to a DOR-based regimen according to clinicians' judgement were included. At baseline (BL), 4 (W4) and 24 weeks (W24) after switch immunovirological and metabolic assessments were considered. In a subset of pts, plasma and IC (PBMCs) concentrations of DOR were measured as Ctrough (24+/-4 hours after last drug intake), by means of UHPLC-MSMS validated methods. Pts characteristics were analysed by Mann-Whitney, Wilcoxon and Spearman's rank test, as appropriate. Non-compartmental PK parameters were expressed as geometric mean (CI95%).

Results: 85 pts were included, 76% were male, age and BMI were 57 years (50-64) and 26.7 kg/m2 (25.3-28.2), respectively. Most used companion drugs were TAF/FTC (54%) and DTG (27%). A significative viral load (VL) decrease was observed at W4 and W24 both in pts with undetectable (p=0.001) and detectable VL (p<0.001) at BL. At W24, significative decreases of total cholesterol (p=0.017) and borderline significative decrease of triglycerides (p=0.050) were reported in the subgroup with total cholesterol > 200 mg/dL at BL, 38 pts were included in the PK analysis. DOR plasma, IC and IC/plasma ratio Cthrough were 724.6 (548.2-901.0) ng/mL, 1018.1 (737.4-1298.8) ng/mL and 1.378 (1.199-1.556), respectively. No difference in DOR plasma and IC Cthrough was reported in dual (36%) vs triple (64%) regimen. Correlation between DOR plasma and IC Cthrough (p<0.001), IC Cthrough and IC/plasma ratio (p<0.001), and IC/plasma ratio and CD4+ cell count (p=0.009) were reported. No significative correlation between DOR PK and VL, creatinine, BMI or age was found.

Conclusions: DOR showed good short-term (24 weeks) efficacy and tolerability in real-life experienced pts. A favourable effect on lipids was observed in initially dyslipidemic subjects. Moreover, in the first evaluation of intracellular concentration of DOR, the drug proved to highly accumulate in PBMCs, accounting for values 41% higher than in plasma. These data need to be confirmed over longer follow-up and larger sample size.

From HIV to SARS-CoV-2

OC 24 ARE MINIONS USEFUL IN THE LAB WORKFLOW? COMPARISON BETWEEN LONG AND SHORT SEQUENCING IN COVID-19 SURVEILLANCE

B. Bruzzone[1], V. Ricucci[1], V. De Pace[1], F. Stefanelli[1], N. Randazzo[1], G. Garzillo[2], M. Cavaletti[3], S. Casali[3], M. Rossi[3], A. Domnich[1], C. Trombetta[2], A. Orsi[1,2], G. Icardi[1,2]

[1]Hygiene Unit, San Martino Policlinico Hospital-IRCCS for Oncology and Neurosciences, Genoa, Italy, [2]Department of Health Science, Genoa University, Genoa, Italy, [3]4bases Italia srl, Campospinoso, Pavia, Italy

Background: Recent long-read sequencing technologies such as Oxford Nanopore Technologies (ONT) seem to have the potential to improve SARS-CoV-2 surveillance procedures. Nanopore sequencing enables real-time analysis of long DNA or RNA fragments. It works by monitoring changes to an electrical current as nucleic acids, after amplification, are passed through a protein nanopore. The resulting signal is decoded to provide the specific DNA or RNA sequence. The usage of MinION nanopore sequencing platform, was well documented in the first part of the COVID19 pandemic, less regarding new variants, such as Delta and Omicron variants, the latter harbouring an elevated number of mutations. In the present study a comparison between ONT performance on MinION with a well-established short-read platform for sequencing was evaluated.

Materials and methods: Viral sequencing with ONT MinION MK1B and Illumina iSeq platform on 25 matched SARS-CoV-2-positive patient specimens, collected at Hygiene Laboratory, Policlinico San Martino Hospital (Genoa, Italy), using the COVID panel CE-IVD kit developed at 4Bases and CleanPlex SARS-CoV-2 NGS Panel by Paragon Genomics, respectively, both enabling sequencing of the entire SARS-CoV-2 genome, was performed. Data analysis was carried out using the 4Bases proprietary platform 4eVAR, and consensus sequence was analysed using Nextclade webservice; each variant was classified according to World Health Organization (WHO), Clade and Lineage.

Results: Both technologies identified 7 Delta and 18 Omicron variants. Mean coverage on MinION was 763x, after 3 hours of run, with reads spanning at least 98% of the genome. Accordingly, there was perfect match for the WHO, Clade and the Lineage classification. Only just one difference along the sub-lineage classification on an omicron variant (BA.2.3 in Paragon BA.2 in MinION).

Single mutations analysis showed 96% overlap on average in mutation classification between the two different technologies considering all mutations, 98% considering mutations on Spike protein.

Conclusions: The two different methodologies lead to a comparable analytical performance, with some differences concerning precise mutation classification. Thanks to its unique, unconventional technique, MinION is faster, cheaper and more flexible than standard sequencing techniques. By this analysis it is confirmed to be a promising platform, with the potential to represent a convenient portable and rapid tool for the analysis of SARS-COV2 sequencing.

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From HIV to SARS-CoV-2

OC 25 IN VITRO ACTIVITY OF MOLNUPIRAVIR IN COMBINATION WITH GC-376 OR PF-07321332 AGAINST SARS-COV-2

A. Gidari[1], S. Bastianelli[1], S. Pierucci[1], C. Busti[1], S. Sabbatini[2], G. Genga[1], E. Svizzeretto[1], A. Tommasi[1], E. Schiaroli[1], D. Francisci[1]

[1]Department of Medicine and Surgery, Clinic of Infectious Diseases, "Santa Maria della Misericordia" Hospital, University of Perugia, Perugia, Italy, [2]Department of Medicine and Surgery, Medical Microbiology Section, University of Perugia, Perugia, Italy

Introduction: The development of effective vaccines has partially mitigated the trend of the SARS-CoV-2 pandemic, however, the need for antiviral drugs persists, especially if they can be orally available. Molnupiravir and PF-07321332 have been recently released for treatment of mild-moderate Coronavirus Disease 2019 (COVID -19) in frail patients. GC-376 is a protease-inhibitor active against the feline coronavirus and it is the precursor of PF-07321332.

This study aims to investigate the activity of these compounds on SARS-CoV-2 in combination to verify the synergistic effect.

Methods: The experiments were conducted in a biosafety level 3 facility. In this study, we used a Vero E6 cell-based infection assay to investigate the in vitro activity of Molnupiravir, PF-07321332 and GC-376 alone and in the following combination: Molnupiravir-PF-07321332 and Molnupiravir-GC-376. All experiments were performed using a SARS-CoV-2 strain isolated from a symptomatic patient and identified as lineage 20A.EU.

Firstly, the compounds have been tested alone and using a four-parameter variable-slope regression modelling, EC90 was identified. The combinations were tested using 5 compound concentrations ≤EC90. Vero E6 cells were seeded in 96-well clear flat-bottom plates and incubated at 37°C with 5% CO2 for 24 h. After incubation, cells were infected using a multiplicity of infection (MOI) of 0.1. Subsequently, virus inoculum was removed, and cells were overlaid with media containing serial dilutions of the compounds.

After 48 h post-infection, viability was performed using MTT (3-(4,5-Dimethyl-2-thiazolyl)-2,5-diphenyl-2H-tetrazolium bromide) reduction assay. All experiments were conducted three times and in triplicate.

To test whether the drug combinations act synergistically, the observed responses were compared with expected combination responses. The expected responses were calculated based on the Highest Single Agent (HSA) reference model using SynergyFinder version 2.

Results: All compounds reached micromolar EC90. Molnupiravir and GC-376 showed a synergistic activity at 48 h with an HSA score of 19.33 ($p<0.0001$) and an additive activity at 72 h with an HSA score of 8.61 ($p<0.0001$) (Figure 1A-B). Molnupiravir and PF-07321332 showed a synergistic activity both at 48 h and 72 h with an HSA score of 14.2 ($p=0.01$) and 13.08 ($p<0.0001$), respectively (Figure 1C-D).

Conclusion: Molnupiravir associated with one of the two protease-inhibitors PF-07321332 and GC-376 showed good additive-synergic activity in vitro. Here, we identified novel synergistic combinations against SARS-CoV-2. The next goal could be to realize preclinical studies with these combinations and translate our findings into trials in patients. These combinations may have a global impact, improving the protection from severe COVID-19, especially for frail populations.

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Metabolic alterations: effect of drugs and diseases

OC 26 FROM NAFLD TO MAFLD: IMPLICATIONS OF CHANGE IN TERMINOLOGY IN PWH

L. Gozzi[1], J. Milic[2], S. Renzetti[3], F. Motta[2], A. Cervo[1], G. Burastero[1], V. Iadisernia[1], B. Lebouche[4], S. Al Hinai[4], M. Deschenes[4], M. Menozzi[1], P. Raggi[5], S. Calza[3], C. Mussini[1,2], G. Sebastiani[4], G. Guaraldi[1,2]

[1]Azienda Ospedaliero - Universitaria, Policlinico of Modena, Modena, Italy, [2]University of Modena and Reggio Emilia, Modena, Italy, [3]University of Brescia, Brescia, Italy, [4]McGill University Health Centre, Montreal, Canada, [5]University of Alberta, Edmonton, Canada

Background: Metabolic associated fatty liver disease (MAFLD) has been recently proposed as a new construct to describe nonalcoholic fatty liver disease (NAFLD), based on positive diagnostic criteria rather than exclusionary ones. The ongoing debate regarding NAFLD/MAFLD construct has not yet reached HIV arena. Our objective was to characterize MAFLD in comparison to NAFLD and to determine prevalence and predictors of both conditions in people with HIV (PWH).

Methods: This was a cross-sectional study of two prospective cohorts comprising PWH on stable ART, that were screened for fatty liver disease (FLD) defined as controlled attenuation parameter of ≥248 dB/m by transient elastography. NAFLD was defined as FLD in absence of significant alcohol intake and HBV or HCV co-infection. MAFLD was defined as the presence of FLD and at least one of the following criteria: 1) overweight/obesity; 2) diabetes; or 3) lean FLD (BMI<25 kg/m2) with at least two immune-metabolic alterations [Eslam M. JHepatol.2020;73(1):202-209]. Significant liver fibrosis was defined as liver stiffness ≥7.1 kPa. Predictors for both conditions were explored in logistic regression.

Results: We included 1947 PWH (mean age 54 years, 74% males, median HIV duration 21 years, median current CD4 703, 98% with undetectable HIV viral load, current ART exposure to INSTI 53%, PI/c 25%, 32% NNRTI). Prevalence of overweight/obesity and diabetes was 49.5% and 23.4%. NAFLD was diagnosed in 618/1714 (36.1 %) PWH, after excluding PWH with significant alcohol intake (1.8%), HBV (1.2%), HCV (9.2%). MAFLD was diagnosed in 648 (33.3%) PWH. Prevalence of significant liver fibrosis differed across the groups: 9.9% in no NAFLD-no MAFLD, 9.3% in NAFLD only, 26.5% in NAFLD/MAFLD overlap, 48% in MAFLD with diabetes and overweight/obesity, and 16.7% in lean MAFLD. Figure 1A depicts proportions of PWH with NAFLD, MAFLD and NAFLD/MAFLD overlap. Figure 1B shows that male sex, higher CD4, triglycerides and BMI were associated with NAFLD/MAFLD. Significant liver fibrosis was associated with MAFLD with diabetes and overweight/obesity.

Discussion: PWH displayed a substantial overlap between NAFLD and MAFLD, but those with MAFLD and diabetes or overweight/obesity had higher risk of significant liver fibrosis. Both HIV-related and metabolic variables were independent predictors of NAFLD/MAFLD. Change of terminology may help to prioritize PWH requiring surveillance and interventions for the management of FLD and associated liver fibrosis.

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Metabolic alterations: effect of drugs and diseases

OC 27 THE PATHWAY OF NAFLD VS MAFLD TOWARD SIGNIFICANT FIBROSIS

J. Milic[1], S. Renzetti[2], F. Motta[1], L. Gozzi[3], G. Besutti[4], G. Burastero[3], V. Iadisernia[3], A. Dessilani[3], M. Del Monte[3], M. Faltoni[3], S. Volpi[3], B. Lebouche[5], S. Al Hinai[5], M. Deschenes[5], S. Calza[2], P. Raggi[6], G. Mancini[3], C. Mussini[1,2], G. Sebastiani[5], G. Guaraldi[1,2]

[1]University of Modena and Reggio Emilia, Modena, Italy, [2]University of Brescia, Italy, [3]Azienda Ospedaliero-Universitaria, Policlinico of Modena, Modena, Italy, [4]Azienda USL - IRCCS di Reggio Emilia, Reggio Emilia, Emilia-Romagna, Italy, [5]McGill University Health Centre, Montreal, Canada, [6]University of Alberta, Edmonton, Canada

Background: The ongoing debate regarding nonalcoholic fatty liver disease (NAFLD)/metabolic-associated fatty liver disease (MAFLD) should consider risk of progression of fatty liver disease (FLD). We aimed to describe transition of NAFLD and MAFLD states towards significant fibrosis in people with HIV (PWH).

Methods: This was a longitudinal study of two prospective cohorts of PWH (Modena HIV Metabolic Clinic and Montreal LIVEHIV cohort) on stable antiretroviral therapy. FLD was assessed at least twice with controlled attenuation parameter (CAP ≥248 dB/m) by transient elastography. NAFLD was defined as FLD in absence of significant alcohol intake or HBV or HCV co-infections. MAFLD was defined as the presence of FLD and at least one criteria: 1) BMI≥25 kg/m2; 2) diabetes; or 3) lean (BMI<25 kg/m2) with at least two immune-metabolic alterations [Eslam M. JHepatol.2020;73(1):202-209]. Significant liver fibrosis was defined as liver stiffness ≥7.1 kPa. A continuous-time multi-state Markov model was used to describe the process in which a study patient moved through a series of states allowing joint analysis of care length, incidence of FLD or fibrosis progression or reversion. The probabilities to switch from one state to another were modelled according to an exponential distribution for time-to-event data, considering censored follow-up times. The events were the transitions between the states. The analyses were performed separately for NAFLD and three MAFLD categories in which minimum two and maximum four assessments for FLD were considered.

Results: A total of 888 PWH were screened for FLD, with a mean follow-up of 2 years, mean age 54.4 years, 77% males. At the first visit, after excluding PWH with alcohol intake and viral co-infections, prevalence of NAFLD was 42.9% (285/664), while the overall prevalence of the MAFLD was 34.3% (305/888). In detail, MAFLD with BMI≥25 kg/m2 was present in 244 (27.5%), MAFLD with diabetes in 86 (9.7%) and lean MAFLD in 33 (3.7%). Figure 1 shows alluvial plots of state transitions in NAFLD (panel A) and in MAFLD with BMI≥25 kg/m2 (Panel B), with diabetes (Panel C) and lean MAFLD (Panel D). Each panel is accompanied by table that summarizes probabilities to move from one state to another.

Discussion: Use of Markov models depicts dynamic changes of FLD with or without fibrosis over time. The highest risk of MAFLD and liver fibrosis progression was observed in PWH with BMI >25. The highest probability of MAFLD reversibility was observed in lean MAFLD group, while the highest probability of liver fibrosis reversibility was observed in PWH with diabetes. MAFLD categories offer the possibility to stratify PWH at highest risk of hepatic and extra-hepatic adverse outcomes.

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Metabolic alterations: effect of drugs and diseases

OC 28 WITH OR WITHOUT TAF? WHAT IS THE DIFFERENCE? DATA FROM A REAL-LIFE SETTING

N. Squillace[1], L. Taramasso[2], E. Ricci[3], B. Menzaghi[4], G. De Socio[5], G.Orofino[6], B.M. Celesia[7], E. Sarchi[8], C. Molteni[9], G. Pellicano[10], F. Conti[11], F. Vichi[12], A. Di Biagio[2], P. Bonfanti[1], for the CISAI Study Group

[1]Infectious Diseases Unit ASST-MONZA, San Gerardo Hospital-University of Milano-Bicocca, Monza, [2]Infectious Diseases, San Martino Hospital Genoa, University of Genoa, Genoa [3]Fondazione ASIA Onlus, Buccinasco (MI), [4]Unit of Infectious Diseases, ASST della Valle Olona – Busto Arsizio (VA), [5]Unit of Infectious Diseases, Santa Maria Hospital, Perugia, [6]Division I of Infectious and Tropical Diseases, ASL Città di Torino, [7]Unit of Infectious Diseases, Garibaldi Hospital, Catania, [8]Infectious Diseases Unit, S.Antonio e Biagio e Cesare Arrigo Hospital, Alessandria, [9]Unit of Infectious Diseases, A. Manzoni Hospital, Lecco, [10]Infectious Diseases, G. Martino Hospital -University of Messina, Messina, [11]Department of Infectious Diseases, Luigi Sacco Hospital, Milan, Italy, [12]Unit of Infectious Diseases, Santa Maria Annunziata Hospital, Florence

Background: Our aim was to investigate the role of switching from Emtricitabine/Tenofovir Alafenamide (FTC/TAF) based regimen to a dolutegravir (DTG) containing two-drug regimen (2DR) vs continuing FTC/TAF on metabolic parameters.

Material and methods: Consecutive people living with HIV infection (PLWH) enrolled in a multicenter observational cohort (SCOLTA) project, on a stable FTC/TAF based regimen with a HIV-RNA<50 copies/ml were included. Changes from baseline (T0) to follow-up (T1, week 24) were analyzed.

Results: 179 PLWH met the inclusion criteria, 137 (76.5%) were males, 12 (6.7%) diabetics.

At T0 main characteristics were (mean ± standard deviation [SD]) the following: age 49.6 ± 10.9 years, body mass index (BMI) 25.2 ± 3.6 kg/m2, total cholesterol (TC) 198 ± 40 mg/dL, HDL cholesterol (HDL-c) 51 ± 15 mg/dL, LDL-cholesterol (LDL-c) 117 ± 34 mg/dL, glucose 96 ± 26 mg/dL (92 ± 15 in non-diabetic patients). CD4+ cell count (CD4) median value was 736 cell/µL (interquartile range [IQR] 543-1000), triglycerides (TGL) 122 mg/dL (IQR 91 -170). 128 PLWH were on FTC/TAF/bictegravir (BIC), 13 on FTC/TAF/DTG, 32 on DTG/lamivudine (3TC) and 6 on DTG/rilpivirine (RPV).

PLWH switching to 2DR or continuing FTC/TAF had similar characteristics, except for baseline CD4 (median 838 and 710, p=0.01) and CDC stage C (0% vs 14.9%, p=0.008). The previous regimen included cobicistat (COBI) in 121 PLWH (44.7% in 2DR vs 73.8% in TAF, p=0.0007).

Comparing PLWH on 2DR vs FTC/TAF no difference was found at T1 for TC, LDL-c, TGL, and weight (see table 1). Mean changes for HDL-c and glucose were -0.7 vs +0.4 mg/dL (p=0.53) and 0.7 vs 1.4 mg/dL(p=0.81), respectively.

Splitting by previous regimens with vs without COBI, the following changes were observed at T1: TC (-12.1 vs +4.3 mg/dL, p=0.002), HDL-c (-0.7 vs +0.4 mg/dL, p=0.53), LDL-c (-6.6 vs 1.4, p=0.08), TGL (-27.7 vs +12.2 mg/dL, p=0.001), glucose (non-diabetic PLWH 1.0 vs 1.8 mg/dL, p=0.79), weight (0.05 vs 0.14 kg, p=0.91).

Evaluating only patients that switched from a regimen without COBI (21 PLWH on 2DR vs 37 on TAF/FTC), we observed no difference in lipid profile and a significant weight increase in FTC/TAF group as compared to 2DR (see table 1).

Conclusions: No difference was found in TC, HDL-c, LDL-c and blood glucose in PLWH continuing an FTC/TAF regimen vs those switching to 2DR. Switching from a previous COBI-including regimen was associated with a significant decrease of TC and TGL.

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Metabolic alterations: effect of drugs and diseases

OC 29 IMPACT OF COVID-19 PANDEMIC ON INCIDENCE AND PREVALENCE OF METABOLIC SYNDROME IN PLWH

R. Papaioannu Borjesson[1], L. Galli[2], C. Muccini[1,2], A. Poli[2], T. Clemente[1], M. Bottanelli[1], N. Gianotti[2], S. Nozza[2], A. Castagna[1,2], V. Spagnuolo[2]

[1]Vita-Salute San Raffaele University - Milan (Italy), [2]Infectious Diseases Unit, San Raffaele Scientific Institute - Milan (Italy)

Background: Our aim was to analyze the impact of restrictions due to COVID-19 pandemic on incidence and prevalence of Metabolic Syndrome (MS), and to identify its predictors in people living with HIV (PLWH).

Material and Methods: This cohort study included 1564 PLWH followed at Infectious Diseases Unit of IRCCS San Raffaele, Milan, Italy, with ≥1 body mass index (BMI) determination during pre-pandemic (1 Dec 2018-29 Feb 2020) and pandemic period (1 Mar 2020-31 May 2021).

MS diagnosis was based on NCEP ATP III 2005 criteria as the presence of at least three of the followings: BMI ≥30 kg/m2 (as a surrogate of abdominal obesity); triglycerides (TG) ≥150 mg/dL (or drug therapy); HDL <40 mg/dL in males, <50 mg/dL in females (or drug therapy); fasting plasma glucose ≥100 mg/dL (or previous diabetes diagnosis).

We used univariable Poisson regression model to compare crude MS incidence rates, calculated as the number of people who developed MS within each time period, divided by the total person-years of follow-up (PYFU) in that time period.

We applied univariable mixed linear models to estimate crude mean change in some parameters during each time period.

Multivariable Cox proportional hazard model was applied to assess MS risk factors; adjusted hazard ratio (AHR) with the respective 95% confidence intervals (95%CI) are presented.

Results: At the beginning of pre-pandemic period there were 460 and 1104 PLWH with and without MS, respectively. During pre-pandemic period 528 PLWH had MS, with a prevalence of 33.8% (95%CI=31.5%-36.1%), while during pandemic period people with MS diagnosis increased to 628, with a prevalence of 40.2% (95%CI 37.8%-42.6%), p<0.0001 at McNemar test.

The median age of the 1104 individuals was 51.2 years (IQR=43.5-55.7), 77% were males, 45% were smokers; median CD4+ was 729 cells/μL (IQR=552-945) and 92% of individuals had HIV-RNA <50 copies/mL.

During pre-pandemic, the estimated mean value of BMI was 23.8 kg/m2 (95%CI 23.6-24.0), of total cholesterol 182 mg/dL (95%CI 180-184), HDL cholesterol 52 mg/dL (95%CI 51–53), LDL cholesterol 122 mg/dL (95%CI 120 -124), while the mean values of triglycerides and glucose were 115 mg/dL (95%CI 112-119) and 92 (95%CI 92 -93), respectively. Crude mean changes in weight, BMI and metabolic parameters between the two periods are reported in Figure1.

The MS incidence rate increased from 13.7/100-PYFU (95%CI=11.7-16.0) in the pre-pandemic period to 18.5/100-PYFU (95%CI 16.2-21.1) in the pandemic period (p=0.004), with 201 subjects who developed MS during pandemic.

After adjusting for HIV risk factor, HBV, HCV, ART duration, duration of virological suppression and use of INSTI, age (AHR per 3-year older=1.12 (95%CI=1.08-1.17)), gender (AHR F vs M=0.62 (95%CI=0.44-0.87)) and CD4+ cell count (AHR per 100-cells/μL=1.05 (95%CI=1.01-1.09)) were associated with the risk of MS.

Conclusions: COVID-19 pandemic had an impact on metabolic profile of PLWH, especially increasing prevalence and incidence rate of MS.

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Special issues in clinical HIV

OC 30 FINAL IMMUNOVIROLOGICAL DATA FROM THE P25- ITALIAN NETWORK OF ACUTE HIV INFECTION (INACTION) COHORT

E. Bruzzesi[1], A. Gabrieli[2], D. Bernasconi[3], G. Marchetti[4], M. Trunfio[5], D. Ripamonti[6], A. Antinori[7], N. Squillace[8], R. Cauda[9,10], M. Parisi[11], A. Muscatello[12], A. Bandera[12,13], G.Tambussi[11], S. Nozza[11], S. Rusconi[14] on behalf of INACTION study group

[1]Vita-Salute San Raffaele University, Milan, Italy, [2]Dipartimento di Scienze Biomediche e Cliniche, Ospedale L. Sacco, Milan, Italy, [3]Bicocca Bioinformatics Biostatistics and Bioimaging Centre - B4 School of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy, [4]Clinic of Infectious Diseases, Department of Health Sciences, ASST Santi Paolo e Carlo, University of Milan, Milan, Italy, [5]Unif of Infectious Diseases, Department of Medical Sciences, University of Turin, Turin,Italy, [6]Infectious Disease Unit; ASST Papa Giovanni XXIII; Bergamo, Italy, [7]National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS; Rome, Italy, [8]Infectious Diseases Unit; Department of Internal Medicine; ASST San Gerardo; Monza, Italy, [9]Istituto Clinica di Malattie Infettive, Università Cattolica del Sacro Cuore, Rome, Italy, [10]UOC Malattie Infettive, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [11]Unit of Infectious Diseases, IRCCS Ospedale san Raffaele, Milan, Italy, [12]Infectious Diseases Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan,Italy, [13]School of Medicine and Surgery, University of Milan, Milan, Italy, [14]UOC Malattie Infettive, Ospedale Civile di Legnano, ASST Ovest Milanese, Legnano, Italy

Background: As the introduction of antiretroviral therapy (ART) during primary HIV-1 infection (PHI) could restrict the establishment of HIV reservoirs, we aimed at assessing the effect of three different ART regimens on HIV-DNA load in people living with HIV (PLWH), who started ART in PHI. The primary endpoint was the decrease of HIV-DNA copies/10^6 peripheral blood mononuclear cells at weeks (W) 12 and 48. Secondary endpoints were increase in CD4+ cells and in CD4+/CD8+ ratio and percentage of PLWH reaching undetectable HIV-RNA.

Materials and Methods: Randomized, open-label, multicentric study, including subjects in PHI (defined as an incomplete HIV-1 Western blot and detectable plasma HIV-RNA) in the INACTION (Italian Network of Acute HIV Infection) cohort. Participants were randomly assigned (10:10:8) to a fixed-dose combination of tenofovir alafenamide (TAF) 25 mg plus emtricitabine (FTC) 200 mg, darunavir 800 mg, and cobicistat 150 mg once daily (group A), or TAF 25 mg plus FTC 200 mg, dolutegravir 50 mg once daily (group B), or an intensive four-drug regimen (TAF 25 mg plus FTC 200 mg, dolutegravir 50 mg, darunavir 800 mg, and cobicistat 150 mg once daily) (group C) . HIV-DNA was quantified by Droplet digital PCR (Biorad QX100) and normalized to RPP30 reference gene. Kruskall-Wallis test was used for continuous variables, Chi-square test for categorical variables and linear regression for multivariable analysis, adjusted for age, HIV-RNA and CD4 T cell count.
This study was registered in ClinicalTrials.gov (number NCT04225325).

Results: Among seventy-eight participants enrolled, 30 belong to group 1, 28 to group 2 and 20 to group 3. At baseline, median CD4+ count was 658/uL (476- 790), HIV-RNA 5.37 (4.38, 6.12) log10 copies/mL (as shown in Table 1), without statistical difference in their change among groups at week 12 and 48 (p: 0.432 and p=0.234, respectively) (Figure 1).
In the per-protocol analysis, PLWH (=72) with undetectable viral load were 54.3% at W12 and 86.4% at W48. Interestingly, CD4/CD8 ratio progressively increased over time, up to normalization in almost half of the cohort by week 48, despite a deflection in group 3; no difference was observed by Fiebig stage (I-III vs IV-VI). HIV-DNA decreased from 4.46 (4.08, 4.81) Log10copies/10^6 PBMCs to 4.22 (3.79, 4.49) at week 12 and 3.87 (3.46, 4.34) at week 48, without difference among groups. At multivariable analysis, HIV-DNA delta at W48 was associated only with the increase of CD4+ count by 100 cells/mm3 but not with Fiebig stage, CD4+/CD8+ ratio and treatment arm, despite a higher decrease in group 3. Six adverse events were recorded during our study, which did not cause any withdrawal from study.

Conclusions: We observed a decrease in HIV-DNA from baseline to W48 in PLWH treated during PHI, associated with an increase in CD4 count and CD4/CD8 ratio, regardless treatment arm.
The authors would like to thank Ministry of Health for the support for GRANT NET-2013-02355333.

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Special issues in clinical HIV

OC 31 EFFECT OF 12-WEEK CART ON GUT MUCOSAL IMMUNITY AND MICROBIOME IN PHI

C. Tincati[1], M. Hadla[1], M. Falleni[2], D. Tosi[2], V. Yellenki[1], R. Rovito[1], V. Bono[1], S. Rusconi[3], A. Giacomelli[4], A. Muscatello[5], S. Dispinseri[6], A. d'Arminio Monforte[1], A. Calcagno[7], S. Nozza[6], A. Gori[5], G. Marchetti[1] for the Inaction (Italian Network of Acute HIV Infection) Study Group

[1]Clinic of Infectious Diseases, Department of Health Sciences, ASST Santi Paolo e Carlo, University of Milan, Milan, [2]Pathology Unit, Department of Health Sciences, ASST Santi Paolo e Carlo, University of Milan, Milan, [3]UOC Malattie Infettive, Ospedale Civile di Legnano, ASST Ovest Milanese, Legnano, [4]Clinic of Infectious Diseases, Department of Biomedical and Clinical Sciences, L. Sacco Hospital, University of Milan, Milan, [5]Infectious Diseases Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, [6]Viral Evolution and Transmission Unit, IRCCS Ospedale San Raffaele, Milan, [7]Unit of Infectious Diseases, Department of Medical Sciences, University of Turin, Turin

Background: The short-time effects of cART in primary HIV (PHI) on mucosal immune and microbiome imbalances in the gastrointestinal (GI) tract are largely unknown.
Methods: PHI subjects were studied prior to (T0) and after 12 weeks (T12) of cART. Chronically-infected, untreated, HIV-individuals (C-Naïve) were enrolled as controls. The Th17/Treg ratio, linked to intestinal homeostasis, was analyzed in colon, ileum and PBMCs by flow cytometry. The mucosal microbiome (MiSeq Illumina) and tissue structure, M1/M2 macrophage polarization (CD14, CD68 and CD163) were studied in colon. Gut integrity (E-cadherin) and peripheral inflammation (sCD14, IL-6) were measured in plasma (ELISA).
Results: 11 PHI and 10 C-Naïve were included (A). In PHI, cART was introduced at 12, (IQR 9-24) days from PHI diagnosis and lead to viral decay (T0; 5.58 log10 cp/mL, 5.16-5.92; T12: 1.59 log10 cp/mL 1.56-1.73, p<0.0001) and CD4+ reconstitution (T0: 538/mmc, 446-615; T12: 756/mmc, 681-938, p=0.0003). We observed a significant reduction of the Th17/Treg ratio in PHI colon biopsies (T0: 5.34, IQR 2-10; T12: 3.32, IQR 0.5-4.5; p=0.04) and PBMCs (T0: 0.665, IQR 0.35-1.2; T12: 0.26, IQR 0.18-0.36; p=0.04) a similar trend in ileum, yet no differences compared with C-Naïve (B).
A trend to consistently higher E-Cadherin was found in PHI than C-Naïve (C). In contrast, sCD14 and IL-6 were lower in PHI than C-Naïve at T0 (sCD14: 4.54 ug/mL, IQR 3-5 vs 5.6 ug/mL, IQR 5-5.9; p= 0.03; IL-6: 2.46 pg/mL, IQR 1.5-3.6 vs 3.9 2.46 pg/mL, IQR 2-10, p=0.2) and showed a non-significant change during cART (C).
Progressive collagen deposition and loss of E-cadherin in treated PHI was seen in colon, regardless cART; highest fibrosis and lowest E-cadherin were detected in C-Naïve (D). Macrophage distribution also changed despite cART introduction in PHI with migration of CD14- and CD163 (M2)-expressing cells toward the gut lumen. Macrophages maintained this location in C-Naïve but were lower in number (D). High variability was found in taxonomic composition within the GI at T0 and decreased at T12; variability was lowest in C-Naïve (E). Samples clustered per patient rather than per tissue/group (E). No major differences were noted in α-and β-diversity between study time-points and groups, yet LeFSE showed lower proportions of Fusobacteriaceae and predominance of Lachnospiraceae at T12 compared to T0 for both GI districts in PHI. Instead, higher proportions of Ruminococcaceae, Christensenellaceae, Oscillospiraceae, Bacteroidales, Lachnospiraceae and lower Lactobacillales were found in the GI of C-Naïve compared to PHI at T0.
Conclusions: PHI features GI damage, low Th17/Treg and increased microbiota variability; together with the finding of lower sCD14 and IL-6 in PHI than C-Naive our data show major perturbations within the GI which are not linked to systemic activation. 12-week cART appears to have little/no effect on the immune, structural and microbiome imbalances in PHI.

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Special issues in clinical HIV

OC 32 PLWH WITH ADVANCED HIV DISEASE ARE AT HIGHER RISK FOR BECOMING DIFFICULT TO TREAT: DATA FROM A LARGE COHORT OF PLWH STARTING MODERN ART REGIMENS

R. Gagliardini[1], A. Cozzi-Lepri[2], A. Tavelli[3], S. Rusconi [4,5], V. Spagnuolo[6], A. Giacomelli[7], G. Burastero[8], C. Agrati[1], M.M. Santoro[9], G. Madeddu[10], A. d'Arminio Monforte[11], A. Antinori[1]

[1]INMI Lazzaro Spallanzani IRCCS, Rome, Italy, [2]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, UCL, [3]Icona Foundation, Milan, Italy, [4]Unità Operativa Malattie Infettive, Ospedale Civile di Legnano, Legnano, Italy, [5]Dipartimento di Scienze Biomediche e Cliniche "Luigi Sacco" Università degli Studi di Milano, Milan, Italy, [6]IRCCS San Raffaele Scientific Institute, Infectious Diseases Unit, Milan, Italy, [7]III Infectious Diseases Unit, ASST Fatebenefratelli Sacco, Ospedale Luigi Sacco, Milan, Italy, [8]Infectious Disease Clinic, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy, [9]University of Rome Tor Vergata, Department of Experimental Medicine, Rome, Italy, [10]Infectious Diseases Department of Medical, Surgical, and Experimental SciencesUniversity of Sassari, Italy

[11]University of Milan, Department of Health Sciences, Milan, Italy

Background: Discontinuation of ART due to simplification, toxicities/intolerance and, less frequently, virological failure (VF), may potentially limit future ART options. Data which describe the characteristics and incidence rate of treatment failure of PLWH initiating modern ART are scarce.

Methods: All PLWH of the ICONA Foundation Study cohort who started a modern first-line ART (2NRTI + DRV/b; 2NRTI+ INSTI; 2NRTI+ RPV; 2NRTI+ DOR; DTG+3TC) were included. They were classified as "difficult to treat" (DTT) if, after starting ART, experienced ≥1 of the following events: i) ≥2 VF (VF defined as 2 consecutive viral load, VL>50 copies/mL) followed by ART change; ii) ≥2 treatment discontinuations due to toxicity/intolerance/failure on 2 different regimens; iii) ≥1 VF followed by ART change plus ≥1 treatment discontinuation due to toxicity/intolerance/failure. Comparison according to stage of HIV disease at ART initiation and outcome were performed by chi-square test for categorical and non-parametric Mann-Whitney test for continuous variables. Time to first fulfilling the DTT definition was estimated using the Kaplan-Meier (KM) method. Weighted and standard unweighted survival analysis by KM curves and Cox regression model were employed. The model was controlled for age, VL at ART starting, calendar year of ART and nationality.

Results: Among 8,061 PLWH included, 320 (4%) experienced one of the DTT-defining events (75% had ≥2 discontinuations, 18% had ≥1 VF + ≥1 discontinuation, 7% had ≥2 VF). DTT PLWH had a significantly higher prevalence of AIDS diagnosis, were slightly older, had lower CD4 cells count at nadir, had greater VL at ART starting, when compared to the non-DTT PLWH (Table 1). PLWH with advanced HIV disease (CD4<200 and/or AIDS) were 2,402 (30%) were more frequently females, infected through heterosexual contacts, not Italians, older and had greater viral load than PLWH without advanced HIV disease. Overall KM probabilities of becoming DTT were 9.95% (8.50-11.41%) by 8 years, with a significantly higher probability for PLWH with advanced HIV disease at unweighted (13.66% vs 8.55% p<0.0001) and weighted analysis (p=0.0426) (Figure 1). PLWH with advanced HIV disease had higher adjusted hazard rate of becoming DTT (aHR=1.30, 95% CI 0.98-1.74, p=0.072) when compared to PLWH without advanced HIV. ART started after fulfilling DTT definition was PI-based (±1-2 NRTI) in 16% of PLWH, INSTI-based in 56%, NNRTI-based in 13%, with ≥2 anchor drugs in 12%, with other drugs in 2% of them.

Conclusions: The probability of satisfying the definition of DTT after starting modern ART was of 9.95% by 8 years; PLWH with advanced HIV disease at ART initiation were at significantly higher risk of becoming DTT after controlling for confounding factors. Most PLWH after satisfying the DTT definition started a regimen with 1 anchor drug + 1-2 NRTI, mainly INSTI-based, but more complex regimens were prescribed in 12% of cases indicating potential lack of therapeutic options.

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Special issues in clinical HIV

OC 33 WEIGHT CHANGE IN OBESE AND OVERWEIGHT PWH: THE IMPACT OF SARS-COV-2 PANDEMIC

S. Dettori[1,2], S. Lerta[1], L. Taramasso[2], S. Bianchi[1], F. Magnè[2], S. Mora[3], M. Giacomini[3], M. Bassetti[1,2], A. Di Biagio[1,2]

[1]Department of Health Sciences (DISSAL), University of Genoa - Genoa, Italy, [2]Infectious Diseases Unit, Ospedale Policlinico San Martino IRCCS - Genoa, Italy, [3]Department of Informatics Bioengineering, Robotics, and Systems Engineering (DIBRIS), University of Genoa - Genoa, Italy

Background: Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic started in March 2020 changed habit of life, especially in periods with lockdown measures. During this time, daily routine for work, food, sleep and sport was deeply modified. Some authors talked about “covibesity” to indicate the tendence to weight gain (WG) during this period. In the context of increasing prevalence of overweight and obesity among people living with HIV (PWH), the aim of this study was to evaluate if the pandemic period played a role in excessive WG in obese or overweight PWH.

Material and methods: Retrospective, single-centre observational cohort study conducted from Jan 2010 to Jan 2022. Data about overweight (BMI ≥25 kg/m²) or obese (BMI ≥30 kg/m²) PWH in antiretroviral therapy (ART) were collected, using an electronic data capture system. Variables about annual WG, ART regimen and comorbidities were tested with a linear regression model. Pre-pandemic period was considered Jan 2010 - Feb 2020 (period 1) and the SARS-CoV-2 pandemic period was Mar 2020- Jan 2022 (period 2). Data about daily routine (sleep and physical activity) were collected through questionnaires in a subgroup of PWH.

Results: 285 PWH were enrolled, 73% male, with mean age 53.8 (range 23-81) years, mean BMI at enrolment 29.5 kg/m², 33% were obese. During period 2 WG was found in 183 (64.2%) PWH; among them, 43/190 (23%) became overweight and 27/95 (28%) obese. Mean WG during period 2 was +1.16 kg/year (+2.71); +0.72 (+2.38) kg/year in overweight and +2.07 (+3.11) kg/year in obese PWH. Instead, during period 1 the average WG was +1.03 kg/year (+1.65); +0.73 (+1.27) kg/year in overweight and +1.65 (+2.10) kg/year in obese PWH. WG was statistically different comparing overweight and obese ($p<0.001$) PWH in both periods, but was similar in period 1 and period 2 ($p=0.521$). During period 2, 20 (21%) steatosis and 40 (56%) metabolic syndromes were newly diagnosed, not statistically related to WG. The univariate analysis showed that obesity in 2021 was significantly associated to greater WG, ($p<0.001$), while PWH with previous diagnosis of diabetes and with lower BMI in 2010 were those less likely to gain weight ($p=0.001$ and $p=0.006$). Also, greater WG was associated with increase of total and LDL cholesterol ($p=0.016$ and $p=0.017$), triglycerides ($p=0.008$) and blood glucose ($p=0.022$).

In multivariable analysis obesity ($p=0.002$), glucose ($p=0.036$) and cholesterol LDL ($p=0.022$) increase confirmed a significant association with greater WG. No relation was found between WG and ART regimen (Table). From questionnaires available (49 in total), obese PWH reported fewer physical activity and worst sleep quality compared to overweight (figure).

Conclusions: Being obese, as well as higher glucose and cholesterol LDL were correlated with weight gain during period 2. No relationship was found with any ART regimen.

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Resistance to antiretrovirals

OC 34 EVALUATION OF INTEGRASE RESISTANCE AND ITS PREDICTORS IN INDIVIDUALS WHO FAILED A REGIMEN CONTAINING DOLUTEGRAVIR IN FRENCH AND ITALIAN CLINICAL SETTINGS

M.M. Santoro[1], D. Armenia[2], C. Charpentier[3], A. Bertoli[4], F. Forbici[5], V. Calvez[6], D. Descamps[3], F. Ceccherini-Silberstein[1], A.G. Marcelin[6], P. Flandre[7], on behalf of the ANRS-MIE AC43 group and the Italian HIV-drug resistance group

[1]University of Rome "Tor Vergata", Rome, Italy, [2]Saint Camillus International University of Health Sciences, Rome, Italy, [3]Paris University, AP-HP, Hôpital Bichat-Claude-Bernard, IAME, Paris, France, [4]Polyclinic of Rome "Tor Vergata", Rome Italy, [5]National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy, [6]Sorbonne Université, AP-HP, Hôpital Pitié Salpêtrière, INSERM UMR-S1136, Paris, France, [7]Sorbonne Université, INSERM UMR-S1136, Paris, France

Background: This work aims at evaluating the potential selection of integrase resistance and its predictors in HIV -1 infected individuals who failed a DTG-based regimen.

Materials and Methods: We retrospectively analysed 467 HIV-1 infected c-ART experienced individuals who experienced a failure (two consecutive plasma HIV RNA values >50 copies/mL) under a DTG-based treatment among several French and Italian clinical centers. People for whom a plasma genotypic resistance test (GRT) was available at DTG failure were included. Major resistance mutations (MRM) and genotypic susceptibility score (GSS, used as a binary variable: ≥2 vs.<2) of DTG-companion drugs of the current regimen were evaluated at failure according to Stanford Drug resistance algorithm (version 9.0). Logistic regression analyses were used to evaluate factors associated to the risk of having at least one INSTI MRM under DTG pressure.

Results: Individuals who failed DTG were mostly male (62%), with a median (IQR) age of 49 (39-55) years, and were HIV-infected since a median (IQR) time of 15 (5-22) years. At DTG start median (IQR) plasma HIV-RNA and CD4 count were 2.6 (1.6-4.6) log10 copies/mL and 358 (170-632) cell/mm3, respectively. Around half of individuals were subtype B HIV-1 infected (53%) and were INSTI-naïve before receiving DTG (52%). Regarding the previous INSTI-experience, 32%, 19%, and 9% received raltegravir, DTG and elvitegravir, respectively. A small proportion (10.7%) of individuals failed DTG as first-line regimen. At the moment of GRT at failure, individuals were under DTG since a median (IQR) time of 11 (5-20) months . Regarding resistance at DTG failure, 12.4% of individuals showed at least one INSTI MRM. N155H was the most prevalent MRM (5.4%), followed by G140S (4.5%), Q148H (4.3%), E138K (2.8%), S147G (2.4%) and R263K (1.7%). T66I/A, E92Q, G118R, E138A/T, G140A/C showed a prevalence <1%. GSS from 0 to 4 was observed in 17.1%, 21.9%, 56.5%, 4.2%, 0.3% of individuals, respectively. At univariable logistic regression, an older age (per 10 years higher, odd ratio [OR, 95% C.I]: 1.29 [1.01-1.60], P=0.040) and a longer history of HIV infection (per 5 years increase OR: 1.21 [1.04-1.40], P=0.010) were positively associated with having at least one INSTI MRM at failure. Whereas, to be INSTI-naïve before receiving DTG (OR: 0.22 [0.12-0.43], P<0.001) and having a GSS for the regimen ≥2 at failure (OR: 0.07 [0.03-0.17], P<0.001) were negatively associated with INSTI-resistance at failure. At multivariable analysis, only these two last variables were confirmed as independent negative predictors of INSTI-resistance at DTG failure.

Conclusions: In a large set of individuals failing DTG in real-life, INSTI-resistance was found in a low proportion of individuals (12%). People who never experienced first-generation INSTI and those who showed a susceptible GSS to companion drugs had a low risk of having INSTI resistance at DTG-failure.

Resistance to antiretrovirals

OC 35 EFFICACY OF DOLUTEGRAVIR VERSUS DARUNAVIR IN FIRST-LINE REGIMENS ACCORDING TO RESISTANCE MUTATIONS AND VIRAL SUBTYPE

P.F. Salvo[1], D. Farinacci[1,2], A. Ciccullo[3], V. Borghi[4], P. Laghetti[5], S. Rusconi[6], A. Saracino[7], W. Gennari[4], B. Bruzzone[8], I. Vicenti[9], A. Callegaro[10], A. Di Biagio[11], M. Zazzi[9], A. Borghetti[2]

[1]Istituto di Clinica delle Malattie Infettive, Università Cattolica del Sacro Cuore, Roma, [2]UOC Malattie Infettive, Fondazione Policlinico Universitario A.Gemelli IRCCS, Roma, [3]Malattie Infettive, Ospedale San Salvatore, L'Aquila, [4]Clinica delle Malattie Infettive e Tropicali, Università di Modena e Reggio Emilia, Modena, [5]Microbiologia e Virologia, Università degli Studi di Bari, Bari, [6]UOC Malattie Infettive, Ospedale Civile di Legnano, ASST Ovest Milanese, Legnano, [7]Clinica Malattie Infettive, Università degli Studi di Bari, Bari, [8]UO Igiene, Ospedale Policlinico San Martino, Genova, [9]Dipartimento di Biotecnologie Mediche, Università di Siena, Siena, [10]UO Microbiologia e Virologia, ASST Papa Giovanni XXIII, Bergamo, [11]Clinica di Malattie Infettive, Ospedale Policlinico San Martino, Dipartimento di Scienze della Salute (DISSAL), Università di Genova, Genova

Background: Dolutegravir (DTG)-based first line regimens have shown superior efficacy versus darunavir (DRV)-based ones in randomized trials. We compared these two strategies in clinical practice, particularly considering the role of transmitted drug resistance mutations (TDRMs) and of HIV-1 subtype.

Material and methods: The multicentre Antiviral Response Cohort Analysis (ARCA) database was queried to identify HIV-1-positive patients (pts) starting a first line-therapy with 2NRTIs (ABC, 3TC/FTC or TDF/TAF) plus either DTG or DRV between 2013 and 2019. Only adults (≥18 years) pts with a genotypic resistance test (GRT) prior to therapy and with HIV-1 RNA≥1000 copies/mL were selected. Through multivariable Cox regressions we compared DTG versus DRV-based regimens in the time to virological failure (VF, as identified by the first HIV-1 RNA≥50 copies/mL after 3 months from therapy start), by stratifying for TDRMs and viral subtype (B versus non-B).

Results: Six hundred and forty-nine pts were enrolled, 359 (55.3%) and 290 (44.7) starting DRV and DTG, respectively. Main characteristics of study groups are reported in table 1.

In 12 months of median follow-up time, there were 41 VF (0.7 per 100 pts-years follow-up, PYFU) and 15 VF (0.4 per 100 PYFU) in the DRV and DTG groups, respectively (p=0.067). After adjusting for age, gender, baseline CD4 count and concurrent AIDS diagnosis, DTG was associated with a reduced risk of VF (versus DRV, aHR 0.51, 95% CI 0.27-0.98; p=0.043). Non-B viral subtypes (particularly, C vs B: aHR 2.96, p=0.044 and circulating recombinant forms vs B: aHR 2.07, p=0.044), a higher baseline HIV-1 RNA (versus ≤100k cps/mL: >100k up to 500k cps/mL, aHR 3.84, p<0.001; >500k cps/mL, 5.22, p<0.001), and a longer time since HIV-1 diagnosis (>1 versus ≤1 month, aHR 2.89, p=0.015) were predictors of VF. After adjusting for the same variables, a second Cox model was performed to compare DTG and DRV-based regimens according to the presence of TDRM. Compared with a fully active DTG regimen, the risk of VF was confirmed to be higher with DRV compared with DTG (aHR 2.30, p=0.017), as well as in patients on a DTG-containing regimen in the presence of TDRM (aHR 14.14, p=0.001). The effect of DTG (with and without TDRM) on the outcome was similar in the subgroup of pts harbouring an HIV-1 B-subtype, whereas no protective effect was shown in the subgroup with non-B subtypes. Of note, in the latter the use of DTG plus ABC/3TC was associated with VF when compared with DTG plus TDF(TAF)/FTC (aHR 7.69, p=0.024) after adjusting for confounders. No comparison could be done between DTG and DRV-based regimens in the setting of TDRM, due to the lack of VF in the latter group.

Conclusions: In line with randomized trials, DTG-based first line regimens showed overall superior efficacy compared with DRV-based regimens. GRT may still play a role in identifying pts more at risk of VF and in guiding the choice of antiretroviral backbone.

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Resistance to antiretrovirals

OC 36 CLINICAL AND VIROLOGICAL OUTCOMES OF DIFFICULT TO TREAT PATIENTS IN A LARGE COHORT OF PLWH STARTING MODERN ART REGIMENS

R. Gagliardini[1], A. Tavelli[2], S. Rusconi[3,4], A. Costantini[5], S. Cicalini[1], F. Maggiolo[6], V. Spagnuolo[7], E. Quiros Roldan[8], S. Lo Caputo[9], A. d'Arminio Monforte[10], A. Antinori[1], A. Cozzi-Lepri[11]

[1]INMI Lazzaro Spallanzani IRCCS, Rome, Italy, [2]Icona Foundation, Milan, Italy, [3]Unità Operativa Malattie Infettive, Ospedale Civile di Legnano, Legnano, Italy, [4]Dipartimento di Scienze Biomediche e Cliniche "Luigi Sacco" Università degli Studi di Milano, Milan, Italy, [5]Clinical Immunology Unit, Azienda Ospedaliero-Universitaria Ospedali Riuniti, Marche Polytechnic University, Ancona, Italy, [6]ASST Papa Giovanni XXIII, Bergamo, Italy, [7]IRCCS San Raffaele Scientific Institute, Infectious Diseases Unit, Milan, Italy.

[8]Department of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili of Brescia, Brescia, Italy, [9]Infectious Diseases Unit, University of Foggia, Foggia, Italy, [10]University of Milan, Department of Health Sciences, Milan, Italy, [11]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, UCL

Background: While virological failures (VF) rate in PLWH is declining, approximately 30% of PLWH discontinue 1st-line ART in recent years. Treatment failures to modern ART regimens are of concern, as they might limit future drug options and lead to clinical failure. Real world estimates of the rate of multiple failures to modern regimens are lacking and long-term consequences of these events remain unclear.

Methods: All participants of the ICONA Foundation Study cohort who started a modern first-line ART (2NRTI + DRV/b; 2NRTI + any INSTI; 2NRTI+ RPV; 2NRTI+ DOR; DTG+3TC) were included in this analysis. Patients were classified as "difficult to treat" (DTT) if, after starting ART, experienced ≥1 of the following events: i) ≥2 VF (VF defined as 2 consecutive viral load, VL>50 copies/mL) followed by ART change; ii) ≥2 treatment discontinuations due to toxicity/intolerance/failure on 2 different regimens; iii) ≥1 VF followed by ART change plus ≥1 treatment discontinuation due to toxicity/intolerance/failure. Time to fulfill DTT definition at its first occurrence (index date) was estimated using the Kaplan-Meier (KM) method. We then identified PLWH who, after the same time from starting ART, were still free from DTT events. In a subset of these who subsequently initiated a new regimen, we compared the treatment response between DTT (exposed) and matched unexposed (Figure 1) with respect to the following endpoints: a) VF b) discontinuation of ≥1 drug due to intolerance/toxicity/failure; c) treatment failure (composite of VL>200 cp/ml or b)) and d) clinical failure (AIDS/death, SNAE (Serious non-AIDS event)/death). Standard survival analysis by means of KM curves and Cox regression model were employed. The model was controlled for VL at ART, year of index date, nadir and current CD4 count fitted as time fixed covariate at index date.

Results: Among 8,061 PLWH included, 320 (4%) entered in the DTT definition. KM probabilities of becoming DTT were 2.2% (95% CI: 1.8-2.6%) by 2 years and 6.5% (5.8-7.4%) by 6 years.

In unadjusted analyses and compared to the matched unexposed group (matched analysis performed on 858 PLWH, Table 1), DTT showed higher probabilities of experiencing all the outcomes (Table 2). Associations were stronger for time to virological failure (p<0.0001), discontinuation of ≥1 drug due to intolerance/toxicity/failure (p=0.0001) and SNAE/death (p=0.003). After controlling for confounders, the association with the risk of discontinuation and time to AIDS/death was no longer significant. In contrast, for the associations remained significant after the adjustment (Figure 2).

Conclusion: A total of 6.5% of PLWH starting modern first-line ART satisfied our arbitrary definition of DTT by 6 years from ART initiation. This appears to be a more vulnerable PLWH population who in the long-term experiences higher risk of treatment and clinical failures. PLWH showing early signs of DTT events should be carefully managed to prevent morbidity and mortality.

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Resistance to antiretrovirals

OC 37 DURABILITY OF MEGA ART IN A LARGE COHORT OF TREATMENT EXPERIENCED PEOPLE LIVING WITH HIV: DATA FROM ARCA DATABASE

L. Labate[1,2], B. Rossetti[3], C. Russo[1,2], M. Bottanelli[4,5], C. Cassol[6,7], F. Bracchitta[8], L. Graziani[9], M. Tilli[9], I. Rancan[6,7], C. Malcontenti[10], S. Mora[11], R. Papaioannu[4,5], A. Bezenchek[12,13], A. Shallvari[12,13], A. Di Biagio[1,2]

[1]Infectious Diseases Unit, San Martino Policlinico Hospital - IRCCS for Oncology and Neuroscience, Genoa, Italy, [2]Department of Health Sciences (DISSAL), University of Genoa, Genoa, Italy, [3]Infectious Disease Department, USL SUDEST, Toscana, Misericordia Hospital, Grosseto, Italy, [4]Vita-Salute San Raffaele University- Milan (Italy), [5]Infectious Diseases Unit, San Raffaele Scientific Institute-Milan (Italy), [6]Department of Medical Biotechnologies, University of Siena, Siena, Italy, [7]Department of Medical Sciences, Infectious and Tropical Diseases Unit, University Hospital of Siena, Siena, Italy, [8]Laboratory of Clinical Microbiology, Virology and Bioemergencies, ASST Fatebenefratelli Sacco, L. Sacco University Hospital, Milan, Italy, [9]Department of Experimental & Clinical Medicine, University of Florence, Florence, Italy, [10]SOD Malattie Infettive e Tropicali AOU Careggi, Firenze, [11]Department of Informatics, Bioengineering, Robotics and System Engineering, University of Genoa, Genoa, Italy, [12]INFORMAPRO Srl, Rome, Italy, [13]EURESIST Network GEIE, Rome, Italy

Background: Providing effective and durable ART is a challenge in people living with HIV (PLWH) who require a combination of multiple drugs due to previous failures. The aims of the study were to evaluate the durability of the mega combinations regimen (Mega ART) and to identify predictors of treatment discontinuations.

Patients and Methods: A retrospective observational cohort study in PLWH selected from the ARCA database, who started Mega ART between January 1st, 2009 to December 31st, 2019.

Mega ART was defined as more than 3-drugs therapy, belonging to different classes of antiretroviral drugs. We classified Mega ART in: a) 2 NRTI+INSTI+PI or 2 NRTI+INSTI+PI+others b) 2 NRTI+PI+others c) 2 NRTI+INSTI +others c) NRTI+NNRTI+others or NNRTI+INSTI+PI+others or 2 NRTI+NNRTI+others or 3 NRTI+ others or others.

Causes of discontinuation of Mega ART were: any regimen modification (excluding the switch intraclass of NRTIs and from ritonavir to cobicistat), death, loss to follow up (for more than 1 year).

The durability of regimens was analyzed by Kaplan–Meier analysis, while predictors of discontinuation were investigated by using Cox regression models.

Results: Overall, 1,514 PLWH were selected and 1,575 Mega ART were started among 43,371 (3.6%) ART collected in ARCA during the rime span analyzed.

The median age at the start of Mega ART was 48.1 years (IQR 42.8-53.7), 68% were males, 76.5% Caucasians, with reported sexual risk factor in 57.5%. At baseline median HIV-1 RNA log10 was 1.7 (IQR 1.5-2.7), zenith HIV-1 RNA log10 5.4 (IQR 4.7-5.7), CD4+ cell count 372 cells/mmc (188.5-591.5), nadir CD4 +cell count 75 cells/mmc (IQR 18-185). The Subtype was B in 65.6% individuals. Median cumulative GSS was 2.25 (IQR 1.25-3). Mega ART with 2NRTI+INSTI+PI/booster was administered to 535/1575 subjects (34%).

Over a median follow-up of 47 weeks (IQR 15-127), 1,299 (83%) Mega ARTs were interrupted with an incidence of 85.62 per 100 person-years of follow-up (PYFU).

The estimated 96-week risk of mega ART interruption was 64% (95% CI 61-66) (Fig.1).

At time of discontinuation 513 (34%) patients had HIV-RNA below 50 copies/ml. At multivariate analysis, predictors of discontinuation were higher number of antiretroviral drugs in baseline regimens (aHR 1.206, CI 95% 1.016 -1.431, p=0.032), higher baseline HIV-1 RNA log10 (aHR 1.113, CI 95% 1.048-1.181, p<0.001) and shorter duration of ART (aHR 0.982, CI 95% 0.965-0.999, p=0.037).

Conclusions: Mega ART was a small proportion of all regimens prescribed during the study period.

Higher viral load, a greater number of antiretrovirals and shorter duration of ART were involved in the discontinuation of this therapy.

In our experience, Mega ARTs were characterized by limited durability and poor virological success.

In the future, the arrival of new drugs with new mechanisms of action will allow to reduce the number of drugs used and probably improve the outcome.

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HIV and SARS-CoV-2 two intersecting epidemics

OC 38 THE CASCADE OF HIV CARE (COC) OF MILAN AS COMPARED TO ITALY: DATA DERIVED FROM THE COA REGISTRY AND THE ICONA COHORT- MILAN FAST TRACK CITY

A. d'Arminio Monforte[1,3,7], A. Navarra[2], A. Tavelli[3,7], B. Suligoi[4], V. Regine[4], L. Pugliese[4], L. Timelli[5], A. Caraglia[5], M. Oldrini[6], L. Cosmaro[3,7], D. Calzavara[7], M. Cernuschi[3,7], G. Rizzardini[8], A. Gori[3,9], S. Antinori[10], M. Puoti[3,11], A. Castagna[3,12], E. Girardi[2,3]

[1]ASST Santi Paolo e Carlo, Unità Malattie Infettive e Tropicali, Milano, Italia, [2]Istituto Nazionale per le Malattie Infettive "Lazzaro Spallanzani"- IRCCS, Roma, Italia, [3]Fondazione Icona, Milano, Italia, [4]Istituto Superiore di Sanità, Roma, Italia, [5]Ministero della Salute, Roma, [6]Fondazione LILA Milano, Milano, Italia, [7]Milano Check Point, Milano, Italia, [8]ASST Fatebenefratelli-Sacco, Divisione 1 Malattie Infettive, Milano, Italia, [9]IRCCS Ca' Granda Ospedale Maggiore Policlinico, Clinica di Malattie Infettive, Milano, Italia, [10]ASST Fatebenefratelli-Sacco, Divisione 3 Malattie Infettive, Milano, Italia, [11]ASST Grande Ospedale Metropolitano Niguarda, Unità Malattie Infettive, Milano, Italia, [12]IRCCS Ospedale San Raffaele, Unità di Malattie Infettive, Milano, Italia

Background: Even if effective ART results in non-transmittable HIV infection, still a consistent number of individuals can transmit HIV as unaware to be infected, or not receiving ART. It is important to establish the achievement of UNAIDS target of cascade of HIV care (CoC) (90-90-90 by 2020) at local level to support targeted preventive campaigns. We aim to define the Milan CoC and to compare it to the Italian one.

Methods: We evaluated the HIV diagnosed, and successfully cared in Italy and in Milan metropolitan area based on data of HIV diagnoses starting from 2012 in the Italian Institute of Health (ISS- COA) Registry and in the Icona cohort.

The Icona cohort covers the 48.6% of 2012-2015 HIV diagnoses, and the 74.6% of those in 2016-2019. In 2012, 0.3% of Lombardy residents were on HIV care, 44.5% of which were resident in Milan, equivalent to 13098 individuals. We determined: the HIV continuum of care in Milan and Italy, taking into account % of PLWH on ART and those on virological suppression (VS) over total estimated PLWH (2012-2019); and the CoC, counting % of PLWH on ART out of PLWH diagnosed and those on VS out of PLWH on ART. For the estimate of undiagnosed PLWH we used the adapted London Method2 (Mammone, 2016). PLWH on ART and those on VS were calculated using weighted data from the Icona cohort. High and low estimates (when considering or not the lost to follow-up) were calculated and mid-point between the two was used. We also calculated the Milan CoC in subpopulations (Italian vs non-Italian; MSM vs heterosexual vs Injecting Drug Users (IDU); males vs females; age strata).

Results: Data on the HIV continuum of care of Milan compared to Italy are shown in the Table1. Of note, the % of PLWH diagnosed, on ART and on virological suppression is higher in Milan as compared to Italy ($p<0.001$ for all years) and is increasing in more recent calendar years (p-value for trend <0.001).

UNAIDS targets of CoC were reached in 2017 for Italy and 2016 for Milan (Table 2).

In detail for Milan, younger (<25 years) and non-hetero individuals reached later than 2016 the 2nd 90 (starting ART), and IDU never passed it (Figure 1). Once on ART, only non-Italians showed lower % VS (Figure 2).

Conclusions: The CoC has improved from 2012 to 2019 both in Italy and Milan, reaching the 90-90-90 UNAIDS targets by 2017 and 2016 respectively. In Milan the new target of 95-95-95 is almost reached. Campaigns should be focused on several subpopulation, such as younger, non-Italian and IDU.

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HIV and SARS-CoV-2 two intersecting epidemics

OC 39 EFFECT OF COVID-19 PANDEMIC ON THE HIV CASCADE OF CARE AT A PROVINCIAL LEVEL

F. Maggiolo[1], R. Teocchi[1], P. Meli[2], D. Valenti[3], F. Radici[4], I. Mercurio[5], A.P. Callegaro[6]

[1]ASST Papa Giovanni XXIII, [2]Comunità Emmaus & Caritas Bergamasca, [3]Associazione FROM, [4]Arcigay Bergamo Cives, [5]CRI-Comitato di Bergamo, [6]ASST Bergamo Est, Bergamo

Background: Measuring progress towards the HIV care cascade allows to identify processes that should be improved to achieve UNAIDS 95-95-95 2030 goal. This goal is of paramount relevance as it could put the HIV epidemic curve under control. We focused our attention on the effect of the Covid-19 pandemic on our cascade of care.

Methods: We calculated the number of PLWH using the eCDC HIV modeling tool (version 1.3.0) that estimates the size of the undiagnosed population. Data on the diagnosed and treated populations were derived from the clinical database of the only Provincial Center authorized to treat HIV infection. Virologic response to ART was defined according to the last available HIV-RNA measure. Data of the last four solar years were compared to assess the dynamics of the cascade of care over time and to verify the weight of the COVID-19 pandemic that in our province was particularly present in the year 2020

Results: In the last 4 years we observed a decrement of new diagnosis, this reduction was particularly marked in 2020 and was paired by an increment of deceases (figure upper left panel). As a consequence expected patients in active FU in 2020 was higher than those effectively followed. In 2021 the number of new diagnosis incremented compared to 2020, but still confirmed the overall decrease trend. Furthermore, in 2021 we had a sustained increment of effective PLWH in FU above the expected number (figure upper right panel). This unexpected increment was due to a relevant number of PLWH previously (before 2019) lost to FU that re-engaged care. These temporal variations, induced a 4.3% reduction of the estimated PLWH and a 4.1% increment of PLWH on active care. At January 2022, according to our calculations the total estimated number of PLWH was 3225 (figure lower panel); 2834 of them (87.9%) were on active FU . All diagnosed and alive subjects were actively taking ART and 98.5% of them had their last viral load < 200 copies/ml. That brought to a final proportion of people living with HIV and virally suppressed of 86.4% just above the 95-95-95% goal (figure).

Conclusions: The COVID-19 pandemic we faced mainly in 2020 slightly reduced the attendance of our outpatient clinic, but increased death rate in our cohort. New diagnosis were lower, but no rebound was observed in 2021 (e. g. delayed diagnosis). The number of new diagnosis in 2021 confirmed the positive trend of the last four years indicating a steadily reduction of new diagnosis. In 2021 the number of PLWH on active FU exceeded the expected one because of the re-engagement of several PLWH lost to follow-up before the pandemic. This increment improved our cascade of care leasing to an overall positive outcome in 86.4% of PLWH.

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HIV and SARS-CoV-2 two intersecting epidemics

OC 40 SARS-COV-2 INFECTION AND VACCINATION COVERAGE AMONG FRAGILE POPULATIONS IN A LOCAL HEALTH AREA OF NORTHERN ITALY

G. Maifredi[1], I. Izzo[2], C. Gasparotti[1], C.V. Sileo[1], S. Storti[2], M. Degli Antoni[2], G. Tiecco[2], S. Amadasi[2], E. Focà[2], F. Castelli[2], E. Quiros-Roldan[2]

[1]ATS Brescia (Brescia Health Protection Agency), Brescia, Italy, [2]Department of Clinical and Experimental Sciences, Unit of Infectious and Tropical Diseases, University of Brescia and ASST Spedali di Brescia, Brescia, Italy

Introduction: Italy was dramatically hit by the COVID-19 pandemic, with over 13 million cases and the province of Brescia was one of the epicentres of the outbreak. Also, Brescia has one of the highest incidences of PLWH (People Living With HIV) and a substantial presence of migrants: both are considered vulnerable populations for COVID-19. The study aimed to assess COVID-19 incidence and vaccination coverage among PLWH and migrants compared to the general population.

Methods: We conducted a retrospective cohort study involving all citizens >18 years old connected to the Brescia HPA Health Protection Agency, assessing SARS-CoV 2 burden, COVID-19 prevalence, and vaccination coverage.

Results: A total of 1 004 210 persons aged >18 years were included, 3.817 (0.38%) PLWH and 134 492 foreigners (13.39%); 111319 (11%) had a confirmed positive swab for SARS-COV-2. SARS-CoV-2 infection (11.4% vs 9% p<0.001), hospitalization (1.6% vs 0.9% p<0.001), ICU admission (1.5% vs 1.1% p=0.002) and death (4.3% vs 0.5% p<0.001) were more frequent among Italians than foreigners. SARS-CoV-2 infections and deaths were more frequent in HIV-uninfected people than in PLWH. PLWH and foreigners were less likely to have a SARS-Cov-2 diagnosis compared to HIV-negative patients (OR: 0.77; 95% CI 0.69–0.80, p<0.001 and OR: 0.72; 95% CI 0.30–1.76, p<0.001, respectively). PLWH were similarly likely to be hospitalized, admitted to the ICU, or die compared to HIV-negative patients. Migrants, instead, were more likely to be hospitalized or admitted to the ICU but had a lower risk of death compared to HIV-negative patients. Regarding vaccination, 89.1% of the population received at least one dose of vaccine, while 70.4% of the Italian citizens and 36.3 % of the foreigner subjects received 3 doses of vaccine (p<0.001). Moreover, 8.7% of the Italian subjects and 25.3% of foreigners did not receive a vaccine (p<0.001). Only 11% of PLWH remained unvaccinated. Among Italian PLWH, only 9.3% were unvaccinated and 72.4% had received 3 doses whereas not vaccinated foreign PLWH were 21.5%, and only 49.40% had received 3 doses.

Conclusions: Foreigners showed a lower risk of being diagnosed with SARS-CoV-2 but a higher risk of complications. SARS-CoV-2 infection diagnosis could prove less achievable for foreigners, due to misinformation and language barriers. HIV infection was not associated with a higher risk of SARS-CoV-2 severe manifestations compared to the general population, probably due to the conservative approach applied to PLWH to prevent potential complications. COVID-19 vaccine hesitancy was not different between PLWH and HIV uninfected people, but foreigners were more hesitant.

Conclusively, further studies are needed to identify key social and demographic determinants of health that contribute to the high risk of severe SARS-CoV-2 manifestations and vaccine hesitancy in vulnerable populations.

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HIV and SARS-CoV-2 two intersecting epidemics

OC 41 NEW DIAGNOSIS OF HIV AMONG TRANSGENDER WOMEN SEX-WORKERS ACROSS TIME: RESULTS FROM A MULTI-YEAR STREET-BASED INTERVENTION (2017-2020)

G. Lapadula[1,2], E. Beretta[1], P. Columpsi[1], M. Comolatti[1], N. Corti[2], S. Limonta[1], A. Rugova[1], A. Ranzani[1], A. Soria[1], N. Squillace[1], E. Lungu[3], A. Monopoli[3], V. Cristiano[3], P. Bonfanti[1,2]

[1]School of Medicine, University of Milano-Bicocca, Milan, Italy, [2]San Gerardo Hospital, ASST Monza, Monza, Italy, [3]ALA Milano Onlus, Milan, Italy

Background: Transgender (TG) women, particularly those who are sex workers (SW), are disproportionally affected by HIV and have inconsistent access to testing. During COVID-19 pandemic, a sharp decrease of HIV testing and new HIV diagnosis was observed in Italy. Continuous monitoring of HIV prevalence and access to healthcare is necessary in this fragile population.

Methods: Herein, we describe the results of the activity of our mobile HIV-testing unit between 2017 and 2020. Three interventions specifically addressed to street-based TG SW were conducted in prostitution venues in Monza and Milan, two before (2017 and 2019) and one after (2020) the beginning of COVID-19 pandemic. TG women SW were offered rapid oral HIV tests and were interviewed regarding their access to HIV testing. Tests were not administered if the individual reported to know already to be HIV-positive.

Results: Overall, 136 tests were administered, 99 before and 37 after COVID-19 spread in Italy. Sixteen new HIV-diagnosis were done. The prevalence of new HIV diagnosis was 12.7% (7/55) in 2017, 11.4% (5/44) in 2019 and 10.8% (4/37) in 2020, with no evidence of change across time (Chi-square for trend, P>0.05). The time elapsed since the last HIV testing was comparable between the first two interventions. The proportions of TG women who had previously tested for HIV at least once in the preceding 6 and 12 months were 85% and 41% in 2017 and 85% and 43% in 2019, respectively. These proportions increased in 2020, when they were 90% and 75%. Lack of time represented the most commonly reason for not testing more often (reported in 60% of cases in 2019 and 18% in 2020). Other reasons were: not knowing where to test (32% of the respondents in 2019 and 18% in 2020) and believing not to be at risk for HIV acquisition (12% and 27% in 2019 and 2020, respectively). Only one respondent reported that the COVID-19 pandemic and the subsequent lock-down prevented her from testing. The mobile unit was the only way to access HIV testing for a limited number of TG SW.

Discussion: We found no evidence of reduced access to HIV testing over time among TG women who engage in paid sex. Nonetheless, a stable and high proportion of the tests administered on the street led to a new HIV diagnosis (approximately 12% for each intervention). The access to healthcare of marginalized and highly vulnerable groups should be constantly monitored and facilitated. Community-based approach can mitigate the effect of COVID-19 pandemic on the access to HIV-testing facilities.

Diabetes, cardiovascular diseases and STIs. A wide range of comorbidities

OC 42 INCIDENT DIABETES IN COURSE OF ANTIRETROVIRAL THERAPY

L. Taramasso[1], N. Squillace[2], E. Ricci[3], B. Menzaghi[4], G. Orofino[5], G.V. De Socio[6], C. Molteni[7], C.V. Martinelli[8], G. Madeddu[9], F. Vichi[10], L. Valsecchi[11], B.M. Celesia[12], P. Maggi[13], F. Conti[14], G.F. Pellicanò[15], A. Cascio[16], E. Sarchi[17], R. Gulminetti[18], G. Parruti[19], L. Calza[20], K. Falasca[21], A. Di Biagio[1,22], P. Bonfanti[2] on behalf of CISAI Study Group

[1]Infectious Disease Clinic, IRCCS Policlinico San Martino Hospital, Genoa, Italy, [2]Infectious Diseases Clinic, San Gerardo Hospital, University of Milano-Bicocca, Monza, Italy, [3]Fondazione ASIA Onlus, Buccinasco (MI), Italy, [4]Unit of Infectious Diseases, ASST della Valle Olona, Busto Arsizio Hospital, Busto Arsizio, Italy, [5]Unit of Infectious Diseases, "Divisione A", Amedeo di Savoia Hospital, Torino, Italy, [6]Clinic of Infectious Diseases, Department of Medicine, Azienda Ospedaliera di Perugia, Santa Maria Hospital, Perugia, [7]Infectious Disease Unit, Ospedale A. Manzoni, Lecco, Italy, [8]SOD Malattie Infettive e Tropicali AOU Careggi, Florence, Italy, [9]Unit of Infectious and Tropical Diseases, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy, [10]Infectious Diseases Department, SOC 1, USLCENTROFIRENZE, Santa Maria Annunziata Hospital, Florence, Italy, [11]Infectious Disease Unit (I Divisione), ASST Fatebenefratelli Sacco, Milan, Italy, [12]Unit of Infectious Diseases, University of Catania, ARNAS Garibaldi, Catania, Italy, [13]Department of Infectious Disease, University of Campania Luigi Vanvitelli, Naples , Italy, [14]Infectious Diseases Unit, Department of Biomedical and Clinical Sciences 'Luigi Sacco', Università degli Studi di Milano, Milan, Italy, [15]Department of Human Pathology of the Adult and the Developmental Age 'G. Barresi', Unit of Infectious Diseases, University of Messina, [16]Infectious and Tropical Diseases Unit- Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties (PROMISE) - University of Palermo, Palermo, Italy, [17]Infectious Diseases Unit, SS. Antonio e Biagio e Cesare Arrigo Hospital, Alessandria, Italy, [18]Fondazione IRCCS Policlinico San Matteo, University of Pavia, Pavia Italy, [19]Infectious Diseases Unit, Pescara General Hospital, Pescara, Italy, [20]Department of Medical and Surgical Sciences, Clinics of Infectious Diseases, S. Orsola-Malpighi Hospital, "Alma Mater Studiorum" University of Bologna, Bologna, Italy, [21]Clinic of Infectious Diseases, Department of Medicine and Science of Aging, University 'G. d'Annunzio' Chieti-Pescara, Chieti, Italy, [22]Department of Health Sciences, Infectious Disease Clinic, University of Genoa, Genoa, Italy

Background: Recent reports of excessive weight gain in course of integrase inhibitor (INSTIs) therapy have raised increasing concerns on the possible increase of diabetes mellitus (DM) risk in people living with HIV (PWH) treated with INSTIs. On the other hand, INSTIs have a neutral profile on plasma lipids and have been associated with improved insulin resistance. In this study, we aimed at describing DM incidence in course of antiretroviral therapy and identifying the factors associated with new DM onset.

Methods: Observational prospective SCOLTA (Surveillance Cohort Long-Term Toxicity Antiretrovirals) cohort. Diabetes was defined as confirmed fasting glycaemia ≥126 mg/dl or single value ≥200 mg/dl at any time or new starting of an antidiabetic drug. All people enrolled in SCOLTA between December 2002 and November 2021 were included. Multivariable Cox regression yielded adjusted hazard ratios (HRs) and 95% confidence intervals (CI) for incident DM, using a backward selection method. Mediation analysis, with weight gain before incident DM or at last observation as mediator, was performed to assess the effect size attributable to weight gain in new diabetes onset.

Results: Among 4327 PWH enrolled in SCOLTA, 216 (5.0%) were excluded because of preexisting DM diagnosis. Excluded patients were older, heavier, more frequently males, treatment experienced, and more often in CDC stage B and C than A.

Among the remaining 4111 PWH, 2989 (72.7%) were male, mean age was 45.5 years, and median CD4 were 459 cells/mmc. At baseline, 344 (8.4%) were on statin treatment, and mean weight was 70.1 Kg. During the follow up, 120 incident cases of DM occurred, with an estimated incidence of 1.26 cases/100 patient years-follow up (95% CI 1.05-1.50).

The mean weight increase was 0.9 and 1.4 at 1- and 2-year follow-up (n=2988 and n=1711), different across ART (Table 1).

At multivariable analysis, baseline weight, but not the amount of weight gain, resulted significantly correlated to diabetes incidence, as well as older age, being under statin treatment and having an history of previous intravenous drug use as risk factor for HIV acquisition. PWH with detectable HIV RNA at study entry resulted more at risk of incident diabetes as compared to PLW with HIV RNA < 50 copies/mL (Table 2).

Among antiretrovirals, using dolutegravir as the reference, raltegravir showed a higher HR for diabetes (HR 1.97, 95%CI 1.14-3.41; p= 0.001). Of note, most PWH on raltegravir (75%) had a baseline triglyceride/HDL ratio>2, suggesting an increased insulin resistance even before starting the drug. According to the mediation analysis, for each Kg of baseline weight the DM risk increased by 3%, while no significant effect was found for the amount of weight gain during follow up.

Conclusions: Baseline weight and not weight gain was associated with risk of incident DM in this observational cohort. We did not observe an imbalance in DM incidence among different antiretroviral classes.

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Diabetes, cardiovascular diseases and STIs. A wide range of comorbidities

OC 43 TREATMENT WITH INTEGRASE INHIBITORS AMONG ANTIRETROVIRAL NAÏVE PATIENTS IS NOT ASSOCIATED WITH INCREASED RISK OF DIABETES MELLITUS

G. Lapadula[1,2], A. Soria[2], G. Micheli[3], M.V. Cossu[4], A. De Vito[5], G. Guaraldi[6], A. Castagna[7], A. Di Biagio[8], S. Cicalini[9], P. Bonfanti[1,2], A. Cozzi-Lepri, A. d'Arminio Monforte for ICONA cohort Study

[1]School of Medicine, University of Milano Bicocca, Milano, Italy, [2]Clinic of Infectious Diseases, San Gerardo Hospital, ASST Monza, Monza, Italy, [3]Università Cattolica del Sacro Cuore, Infectious Diseases Unit, Roma, Italy, [4]1st Division of Infectious Diseases, 'Luigi Sacco' University Hospital, Milan, Italy, [5]Unit of Infectious Diseases, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy, [6]Unit of Infectious Diseases, University of Modena and Reggio Emilia, Modena, Italy, [7]University "Vita Salute", San Raffaele Hospital, Milano, Italy, [8]Unit of Infectious Diseases, University of Genoa, Genoa, Italy, [9]National Institute for Infectious Diseases "L. Spallanzani", Rome, Italy

Background: Integrase-strand inhibitors (INSTI) are components of the majority of antiretroviral (ARV) regimens currently recommended for treatment naïve patients. However, some INSTI have been associated with unintended weight gain. While the underlying mechanisms of this side effect is yet to be determined, it has been suggested that it may lead to an increased risk of metabolic complications, such as diabetes mellitus (DM).
Methods: All ARV-naïve patients enrolled in the ICONA cohort initiating first line ARV after Jan 1st 2009 were included, provided that baseline and ≥1 follow-up fasting glucose and weight were available. Patients were classified according to their initial ARV regimen into 3 groups (INSTI-, protease inhibitor (PI)- or non-nucleoside reverse transcriptase (NNRTI)-based treatment). Weight change after 18 months (time-window: 7-24 months) of ARV was compared between them using a linear regression model. Hazards of DM, defined as two consecutive fasting glucose >126 mg/dl, were compared, using uni- and multivariable Cox regression analyses. The following possible confounders measured at baseline were considered: age, ethnicity, baseline body mass index (BMI), presence of dyslipidemia, calendar year and use of TAF.
Results: Among the 4,808 patients included, 1,331 had initiated a regimen based on INSTI, 1,866 on PI and 1591 on NNRTI. Table 1 represents the characteristics of the enrolled patients. Those on INSTI were slightly older, less likely to have dyslipidemia and more likely to receive TAF and to initiate ARV more recently than the others. After ARV initiation, mean weight gains of 3.6 (SD 7.1), 3 (SD 7.2) and 1.4 (SD 6.1) Kg were observed INSTI, PI or NNRTI groups, respectively. Use of INSTI and PI were associated with a significantly higher additional weight gain than NNRTI (weight gain difference, INSTI vs NNRTI +2.1 [95%CI 1.4-2.8]; PI vs NNRTI +1.5 [95%CI 0.91-2.17]). No statistically significant difference was found comparing those who received INSTI vs. PI (INSTI vs PI, +0.6 [95%CI -0.1-1.23]). Over a median follow-up of 62 (IQR: 35-90) months, 110 new diagnoses of DM were observed, 20 (1.5%) among INSTI recipients, 54 (2.9%) and 36 (2.3%) among those treated with PI and NNRTI. From fitting a univariable Cox regression model there was no evidence for an association between the class of the anchor dug of first line regimen and risk of DM (INSTI vs. PI HR 1.07; 95%CI 0.63-1.82; P=0.796 vs. NNRTI HR 0.83; 95%CI 0.47-1.45; P=0.504). Lack of a statistically significant association between anchor drug class and risk of DM was confirmed after adjustment for possible confounders (Table 2).
Conclusions: Although patients initiating ARV using INSTI experienced, on average, higher weight gain compared to those treated with other drug classes, this difference appears of little clinical importance. In addition, no evidence of increased risk of DM was found among INSTI recipients, regardless of weight gain and other possible risk factors.

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Diabetes, cardiovascular diseases and STis. A wide range of comorbidities

OC 44 NON-ALCOHOLIC TO METABOLIC ASSOCIATED FATTY LIVER DISEASE: CARDIOVASCULAR IMPLICATIONS OF A CHANGE IN TERMINOLOGY IN PATIENTS LIVING WITH HIV

J. Milic[1], S. Renzetti[2], F. Motta[2], L. Gozzi[3], A. Cervo[3], G. Burastero[3], V. Iadisernia[3], G. Franceschi[3], M. Faltoni[3], S. Volpi[3], A. Mazzocchi[3], C. Mussini[2,3], G. Sebastiani[4], S.Calza[2], P. Raggi[5], G. Guaraldi[1,3]

[1]University of Modena and Reggio Emilia, Modena, Italy, [2]University of Brescia, Brescia, Italy, [3]Azienda Ospedaliero-Universitaria, Policlinico of Modena, Modena, Italy, [4]McGill University Health Centre, Montreal, Canada, [5]University of Alberta, Edmonton, Canada

Objective: It has recently been suggested that the definition of non-alcoholic fatty liver disease (NAFLD) be changed to Metabolic Associated FLD (MAFLD) to better reflect the complex metabolic aspects of this syndrome. We compared the ability of MAFLD and NAFLD to correctly identify high cardiovascular (CV) risk, sub-clinical atherosclerosis or a history of major adverse CV events (MACE) in patients living with HIV (PWH).
Methods: Single center, cross-sectional study of PWH on stable ART. NAFLD was diagnosed by transient liver elastography; published criteria were used to diagnose MAFLD (JHepatol.2020;73(1):202-209). Four mutually exclusive groups were considered: low (<7.5%) vs high (>7.5%) ASCVD risk, subclinical CVD (carotid IMT ≥1 mm and/or coronary calcium score >100), and prior CVEs. The association of NAFLD and MAFLD with the CVD risk groups was explored via a multinominal model adjusted for age, sex, liver fibrosis, HIV duration, nadir CD4 and current CD4 cell count. Prediction accuracy was also considered to compare the predictive role of NAFLD and MAFLD. Random forest, Extreme Gradient Boosting and Support Vector Machine were also applied and compared to multinomial regression for the accuracy in predicting CVD.
Results: We included 1249 PWH (mean age 55 years, 74% men, median HIV duration 24 years). Prevalence of overweight/obesity and diabetes was 40% and 18%. Prevalence of NAFLD and MAFLD and overlapping groups are shown in Figure 1A. Figure 1B shows distribution of NAFLD/MAFLD in the 4 patient categories (p-for-trend <0.001). Both MAFLD and NAFLD were significantly associated with an increased CV risk, subclinical CVD and major adverse CV event compared to the reference level (ASCVD<7.5%) (all p-values <0.001; Figure 2). When we considered the predictive role of NAFLD and MAFLD on CVD we observed a relatively low but similar accuracy (67% and 68% respectively). However, when we collapsed the CVD outcomes in low/high risk reducing class imbalance, we observed a much higher accuracy but still similar for NAFLD and MAFLD (87% and 86% respectively). Random forest, Extreme Gradient Boosting and Support Vector Machine showed similar performances in predicting the CVD outcomes.
Conclusions: NAFLD and MAFLD perform equally in detecting CVD or its risk. The proposed change in terminology may not help to identify PWH requiring enhanced surveillance and preventative interventions for cardiovascular disease.

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Diabetes, cardiovascular diseases and STIs. A wide range of comorbidities

OC 45 SYPHILIS INFECTION AND RE-INFECTION IN PLWH AND PREP USERS: NEW INSIGHTS INTO EPIDEMIC DYNAMICS

R. Rossotti[1,5], D. Tesoro[2,5], L. Gazzola[2], A. Tavelli[3], A. De Bona[2,5], V. Licari[4], F. D'Amico[1], C. Baiguera[1], D. Calzavara[5], N.B. Bana[1], V. Ferrara[5], R. Repossi[5], M. Cernuschi[5,6], M. Puoti[1,4], A. d'Arminio Monforte[2,7]

[1]Department of Infectious Diseases, ASST Grande Ospedale Metropolitano Niguarda, Milan, [2]Department of Infectious Diseases, ASST Santi Paolo e Carlo, Milan, [3]ICONA Foundation, Milan, [4]University of Milano-Bicocca, Milan, [5]Milano Checkpoint, Milan, [6]Unit of Infectious Diseases, IRCCS San Raffaele Scientific Institute, Milan, [7]University of Milano, Milan

Background: Syphilis is currently on the rise in many western countries. The rate of transmission might peak to 60% per sexual act depending on clinical stage. The probability of transmission differs according to the susceptibility of the exposed partner: literature suggests that people living with HIV (PLWH) have a risk to acquire the infection 3 times higher than the general population. Aim of this study is to evaluate incidence and factors associated to syphilis infection/re-infection in two cohorts of PLWH and PrEP users.

Material and methods: This retrospective analysis included all PLWH and PrEP users attending two tertiary hospitals who performed at least two serologic tests for syphilis from February 2019 to May 2021. Median and interquartile range (IQR) for continuous variables, absolute and relative values for categorical variables were used. Nonparametric tests were applied to compare variables. Incidence rates were assessed in the overall populations and in MSM. Cox regression analysis was performed to test factors associated to syphilis infection in MSM only.

Results: The analysis included 1,848 individuals: 1,567 (85%) PLWH and 281 (15%) PrEP users. PLWH were older, more frequently of foreign origin, and with a smaller percentage of males and MSM (Figure, section A). A similar proportion of PLWH and PrEP users had a previous syphilis infection (37% vs 36%, p=0.600). PrEP users were tested more frequently (3.6 vs 2.0 per 100 PYFU, p<0.001). Over a median follow up of 1.3 (IQR 0.7-1.8) years, 114 syphilis cases (39 new infections, 75 re-infections) were observed. Incidence of new infections was higher in PrEP users compared to PLWH (8.2 vs 2.0 per 100 PYFU, IRR 4.1, 95% CI 1.9-8.2, p<0.001) also restricting to MSM (8.6 vs 4.0 per 100 PYFU, IRR 2.1, 95% CI 1.0-4.5, p=0.040). Incidence of re-infection was higher but similar in PrEP users and PLWH (11.8 vs 8.2 per 100 PYFU, IRR 1.4, 95% CI 0.7-2.8, p=0.289) even restricting to MSM (10.8 vs 7.8 per 100 PYFU, IRR 1.4, 95% CI 0.6-2.9, p=0.373). Factors associated to new infection were younger age, PrEP use and the number of serologic tests performed (B) while no factors emerged for re-infections (C).

Conclusions: In STI epidemiology, core population is defined as the group with R0 >1 and a consequent major risk of epidemic spread. Bridging population represents a link group that connects core to the general population. These data suggest that PLWH and PrEP users with a previous syphilitic episode in our setting embody the core group with no distinctive defining risk factors. A different subgroup of PLWH and above all of PrEP users — mainly MSM — corresponds to our bridging population. HIV infection does not represent per se a risk factor to acquire syphilis: risky sexual behavior is the major driver for the spread. Intensive testing (and treating) hinders the bridging; thus, it could be the most effective tool to contain the epidemic.

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Immunological efficacy of SARS-CoV-2 vaccine II

OC 46 MONITORING SALIVA AND PLASMA NEUTRALIZING ACTIVITY INDUCED BY THE ADMINISTRATION OF A THIRD BNT162B2 VACCINE DOSE

M. Garziano[1,2], O. Utyro[3], S. Strizzi[1], C. Vanetti[1], I. Saulle[1], C. Conforti[1], F. Cicilano[1], M. Clerici[1,2], M. Biasin[1]

[1]Department of Biomedical and Clinical Sciences "L. Sacco", University of Milan, Milan, Italy, [2]Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy, [3]Department of Medical surgical and experimental sciences University of Sassari

Background: BNT162b2 COVID-19 vaccine is known to induce neutralizing antibodies in serum protecting against severe COVID19. However, it has not been investigated if, in the oral mucosa, which represents the primary route of viral entry: i) it could generate specific immunity; ii) if such immunity is boosted by SARS-CoV-2 infection; iii) how long it is maintained overtime iii) if it is protective even against new emerging variants of concern.
Material and Methods: Neutralizing activity (NA) against the "wild type" SARS-CoV-2 lineage B.1 (EU), Delta (B.1.617.2) and Omicron (B.1.1.529) strains was measured in plasma and saliva samples from uninfected SARS-CoV-2 vaccinated (SV, n°=55) and subjects who were infected before vaccination (SIV, n°=29), after 2 (SIV2, n°=16) or 3 (SIV3, n°=16) vaccine doses.
Sampling was performed immediately before the administration of the third vaccine dose (T0), 15 days (T1) and 3 months (T2) post the third dose (SV and SIV) or post infection (SIV2 and SIV3).
Results: In all the enrolled groups NA in plasma and saliva: i) was higher against EU compared to the Delta and mainly the Omicron variant at all-time points; ii) it was boosted by the administration of the third dose (T1); iii) it declined over time, though being detectable in almost all subjects at T2.
By comparing SV and SIV at T0 we observed a significantly higher NA in both plasma and saliva against all variants except Omicron in saliva; such difference was maintained at both T1 and T2, though it was no longer statistically significant.
At T2, in plasma, a higher NA against the Delta and Omicron variant was detected in SIV2 and SIV3 respectively, suggesting they were infected by different strains. Finally, in both saliva and plasma infection after 3 vaccine doses (SIV3) further boosted NA against the Delta and Omicron variant.
Conclusions: Our results suggest that previous infection increases humoral immune response, as SIV subjects show higher protection at both systemic and mucosal level at all time points. Notably, through NA assay we can discriminate the variant responsible for the infection. The monitoring of NA through time, together with the analyses of SARS-CoV-2 specific T cell response will be key to comprehend who and when would benefit from the administration of a 4th vaccine dose.

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Immunological efficacy of SARS-CoV-2 vaccine II

OC 47 LOWER NEUTRALIZATION LEVEL AGAINST SARS-COV-2 OMICRON (BA.1) VARIANT THAN AGAINST REFERENCE STRAIN AFTER A THIRD DOSE OF MRNA VACCINE IN PLWH

A. Vergori[1], A. Cozzi Lepri[2], G. Matusali[3], F. Colavita[3], S. Cicalini[1], P. Galli[4], A.R. Garbuglia[3], M. Fusto[1], V. Puro[5], E. Girardi[6], F. Vaia[7], A. Antinori[1,4]

[1]HIV/AIDS Unit, National Institute for Infectious Diseases L.Spallanzani, IRCCS, Rome, Italy, [2]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, UCL, London, UK, [3]Virology Unit, National Institute for Infectious Diseases L.Spallanzani, IRCCS, Rome, Italy, [4]Health Direction,National Institute for Infectious Diseases L.Spallanzani, IRCCS, Rome, Italy, [5]Risk Management Unit, National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy, [6]Scientific Direction, National Institute for Infectious Diseases L.Spallanzani, IRCCS, Rome, Italy, [7]General Direction, National Institute for Infectious Diseases L.Spallanzani, IRCCS, Rome, Italy

Background: Aim was to measure neutralizing antibodies levels against SARS-CoV-2 Omicron (BA.1) variant in serum samples obtained from vaccinated PLWH and healthcare workers (HCW), and compare them to those against the Wuhan-D614G (W-D614G) strain, before and after the third dose of a mRNA vaccine.

Methods: A sample of PLWH receiving care at our Institute and a control group of HCWs who received a full cycle of three doses of mRNA vaccine were included in this analysis. PLWH were stratified according to their CD4 count nadir (<350 vs. >350 cells/mm3). The low nadir group was further stratified according to the current CD4 count (>200/mm3, CD4 201-500/mm3 and >500 cells/mm3). All participants received either an additional 3rd dose (full dose at least 28 days after the 2nd, PLWH, low nadir group) or a booster dose of vaccine (booster at least 5 months after the 2nd , high nadir and HCW groups). Neutralizing antibodies titres (nAbsT) were assessed by micro-neutralization assay for W-D614G and the BA.1, before and after the third dose (after 15 days in PLWH, after 30 days in HCW). nAbsT were categorized as undetectable if <1:10. Mean levels of nAbsT to BA.1 vs W-D614G (in the log2 scale) were compared within and across groups using truncated linear regression models.

Results: We included 106 PLWH, 81 in low CD4 nadir group [27 (33%) with current CD4 count <200/mm3, 29 (36%) with CD4 between 201-500/mm3 and 25 (31%) withCD4>500/mm3], 25 in the high nadir group and 28 HCWs, for a total of 134 participants (Table 1). Before the 3rd dose, the proportion of participants with undetectable nAbsT against BA.1 was 88% in PLWH low nadir group, 80% in high nadir group and 100% in HCW . After the 3rd dose, 9 (11%) among PLWH with low nadir group, none in high nadir group and 1 (4%) among HCW have undetectable nAbsT. After the 3rd dose, the mean log2 nAbsT against BA.1 in the HCW and PLWH with high nadir was lower than that seen against W-D614G [6.1 log2 (±1.8) vs. 7.9 (±1.1) and 6.4 (±1.3) vs. 8.6 (±0.8)], respectively (Figure 1A). However, by fitting a truncated linear regression we found no evidence for a different level of nAbsT neutralization by BA.1 vs. W-D614G between PLWH with high CD4 nadir and HCW [0.40 (-1.64, 2.43); p=0.703, Table 2). In contrast, in PLWH with low CD4 nadir the mean log2 difference between nAbsT against BA.1 and W-D614G was smaller in those with current CD4 201-500 vs. those with CD4 <200 cells/mm3 [-0.80 (-1.52, -0.08); p=0.029] (Figure 1B, Table 2).

Conclusion: Overall, our results show that a primary 2-dose vaccination cycle induces poor nAbsT against the BA.1 variant, regardless of HIV status. After the 3rd dose, with one additional or a booster, nAbsT against BA.1 increased in all participants, although to a lower level than that seen for the original W-D614G strain. In PLWH with a CD4 nadir <200 cells/mm3, current CD4 count might play a role in diversifying the level of SARS-CoV-2 neutralization.

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Immunological efficacy of SARS-CoV-2 vaccine II

OC 48 T-CELL RESPONSES TO SARS-COV-2 SPIKE PROTEIN AFTER 3 DOSES OF BNT162B2 MRNA VACCINATION IN HEALTHY INDIVIDUALS, CROSS-RECOGNIZE ALPHA, DELTA AND OMICRON VARIANTS OF CONCERN

M. Iannetta, A. Di Lorenzo, A. Imeneo, A. Lodi, L. Ferrari, I. Fato, B. Massa, P.G. Pace, I. Spalliera, P. Vitale, B. Rossi, T. Mulas, L. Campogiani, L. Coppola, M. Compagno, V. Malagnino, E. Teti, M. Andreoni, L. Sarmati

Department of System Medicine Tor Vergata University, Rome

The emergence of SARS-CoV-2 variants of concern (VOC) is one of the most important issues in the COVID-19 pandemic. VOC may compromise the efficacy of the currently administered vaccines. Although several studies have investigated the effect of SARS-CoV-2 mutations on antibody neutralizing activity, little is known about T-cell immunity. Antigenic drift can potentially lead to a reduced T-cell specific immunity and, consequently, more severe disease manifestations.

Healthy donors (HD) with no history of SARS-CoV-2 infection were included in the study. Epidemiological and clinical data were recorded in an ad hoc database. Anti-Spike (S) and Anti-Nucleoprotein (N), T-cell responses to Spike and Nucleoprotein peptide libraries were assessed before and two months after BNT162b2 third dose, while T-cell responses to Spike peptides related to Alpha (A), Delta (D) and Omicron (O) VOC were assessed 3 months after BNT162b2 third dose. Briefly, Anti-S and Anti-N antibodies were assessed with The Elecsys immunoassay (Roche Diagnostics). T-cell responses were assessed with an in-house Interferon (IFN)-γ release assay (IGRA), after overnight stimulation of heparin whole blood with pools of lyophilized peptides (PepTivator SARS-CoV-2 Prot_S, Prot_S1, Prot_N, and Prot_S Alpha, Prot_S Delta, Prot_S Omicron mutational and reference pool, from Miltenyi). For each stimulation a negative and positive control were included. IFN-γ production was assessed with a commercial enzyme linked immunosorbent assay (ELISA). Data are shown as median [interquartile range]. Statistical analysis was performed with GraphPad Prism.

Ten HD (6M and 4F), with median age of 41 [31-48] years, were enrolled. Anti-N antibodies were negative before and 2 months after BNT162b2 third dose. Anti-S antibody titres significantly increased after BNT162b2 third dose (p=0.002), while IFN-γ production upon S+S1 (ancestral) peptide pool stimulation was unchanged before and after BNT162b2 third dose. After a median of 89 [87-92] days after BNT162b2 third dose, T-cell response to SARS-CoV -2 A, D and O VOC were assessed, showing significantly reduced IFN-γ production for the mutational pool of A VOC Spike compared to the reference pool (p=0.004). No differences were observed for D and O VOC. Reduced IFN-γ production by T-cells was observed after stimulation with A VOC compared to O VOC Spike mutational pool (p=0.04), while no differences were observed after stimulation with the corresponding reference pools (Figure).

Specific T-cell responses to A, D and O VOC can be detected in healthy individuals, without previous SARS-CoV-2 infection, who had received three doses of BNT162b2 mRNA vaccine. T cell responses seem to remain stable before and after BNT162b2 mRNA vaccine third dose, while Anti-S antibody titer are significantly increased. T-cell cross reactivity through different VOC can explain the ability of mRNA vaccines to prevent severe COVID-19.

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Immunological efficacy of SARS-CoV-2 vaccine II

OC 49 CD4 CELL COUNT IS CRITICAL FOR SPECIFIC T CELL-MEDIATED RESPONSE IN PLWH BEFORE AND AFTER THIRD DOSE OF COVID-19 VACCINE

E. Tortellini[1], M.A. Zingaropoli[1], G. Mancarella[1,2], R. Marocco[2], A. Carraro[1,2], M. Jhamour[2], V. Perri[1], M. Guardiani[1], F. Dominelli[1], A. Napoli[3], A. Gaeta[1], F. Mengoni[1], P. Zuccalà[2], V. Belvisi[2], B. Kertusha[1,2], A. Parente[1,2], C. Del Borgo[2], V. Vullo[1], M.R. Ciardi[1], C.M. Mastroianni[1], M. Lichtner[1,2] and LATINA COVID-19 Group

[1]Department of Public Health and Infectious Diseases, Sapienza University of Rome, [2]Infectious Diseases Unit, SM Goretti Hospital, Sapienza University of Rome, Latina, [3]Department of Molecular Medicine, Sapienza University of Rome

Background: Immunogenicity of a third dose of COVID-19 vaccine needs to be addressed, particularly in people living with HIV (PLWH). The aim of the study was to investigate specific B and T cell response before and after the third dose of mRNABNT162b2 (Comirnaty®) vaccine.

Materials and Methods: B and T cell responses were evaluated in PLWH at two time points: before (T0) and after 2 months from the administration of the third dose (T1). By intracellular cytokine flow cytometry assay, upon S peptide libraries stimulation in peripheral blood mononuclear cells, we identified T cells producing any of IFN-γorIL -2orTNF-α as "activated T cells". Similarly, we classed polyfunctional T cells those simultaneously producing all 3 cytokines (IFN-γ+IL-2+TNF-α+ T cells). PLWH were stratified according to CD4 T cell count as well as according to B cell response into responders (R) and non-responders (NR) and the differences in the % of "activated" and polyfunctional T cells between them were evaluated.

Results: Thirty-one PLWH (23 male/8 female, median age [IQR] of 62 [49-68] years, median CD4 T cell count [IQR] 557 [367-719] cells/μl) were enrolled between September 2021 and February 2022. All PLWH were on successful antiretroviral therapy (ART).

Overall, 84% (26/31) and 94% (29/31) of PLWH showed detectable levels of anti-S antibodies at T0 and T1, respectively. The longitudinal evaluation showed a significant increase at T1 (median [IQR] values: 2380 [1585 -7463] and 182 [104-481] BAU/ml, respectively, p<0.0001).

At T0, stratifying PLWH according to CD4 T cell count, higher % of "activated T cells" in PLWH with >250 cells/μl compared to those with <250 cells/μl was observed (CD4: 2.2 [0.7-6.3] and 0.4 [0.2-0.8], respectively, p=0.0139; CD8: 1.7 [0.5-5.4] and 0.2 [0.1-0.6], respectively, p=0.0012) as well as higher % of polyfunctional T cells (CD4: 0.4 [0.01-0.1] and 0.0 [0.0-0.04], respectively, p=0.0513; CD8: 0.1 [0.0-0.2] and 0.0 [0.0-0.04], respectively, p=0.0641), although not statistically significant. Moreover, higher % of "activated T cells" in R group compared to NR one was observed (CD4: 2.0 [0.7-5.9] and 0.4 [0.2-0.7], respectively, p=0.0131; CD8: 1.7 [0.5-5.0] and 0.1 [0.1-0.4], respectively, p=0.0024).

Positive correlations between CD4 T cell count and the % of "activated T cells" (CD4: ρ=0.5779 p=0.0013; CD8: ρ=0.6360 p=0.0003) as well as between CD4 T cell count and the % of polyfunctional CD4 T cells (ρ=0.4159 p=0.0277) were observed.

Finally, the longitudinal evaluation of % of "activated" and polyfunctional T cells did not show any significant difference.

Conclusions: In ART treated PLWH a specific antibody response was present in most of the participants already after the second dose, but the third boosted dose increased the rate of response. A higher T cell response was found in PLWH with >250 CD4 cell count as well as in R group. Our preliminary data underlines the role of CD4 cell as a key factor in the vaccine effectiveness in PLWH.

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Dual therapy in naive and switched PLWH

OC 50 ADHERENCE RATES AND FORGIVENESS TO UNCOMPLETE ADHERENCE TO 3TC/DTG

F. Maggiolo[1], D. Valenti[1,2], R. Teocchi[3], L. Comi[1], E. Di Filippo[1]

[1]UOC Infectious Diseases, [2]FROM foundation, [3]Informatics department, ASST Papa Giovanni XXII, Bergamo Italy

Background: When applied to ART, forgiveness refers to the ability of a given regimen to maintain complete viral suppression despite a documented imperfect adherence. In contrast with most pharmacological parameters, forgiveness lacks an established, quantitative measure, but, despite this, the medical community has embraced the concept that some regimens are more forgiving than others, basing on this assumption therapeutic choices that are made every days in clinics. We explored forgiveness of lamivudine/dolutegravir (3TC/DTG).

Methods: In this retrospective study pharmacy drug refills were used to calculate PDC as a proxy of adherence. PDC is the number of days with medication available divided by the number of days in a specified time interval. If excess medication is collected or refills are made early, the excess is applied toward subsequent absences of drugs. Finally, we evaluated forgiveness defined as the sensitive therapeutic success (e.g. selected HIV-RNA threshold) achieved rate under a given level of imperfect adherence. Three different virologic cut-offs were used: target not detected (TND), that is a value of HIV-RNA current standard methods do not detect; HIV-RNA < 50 copies/ml as the gold standard to define therapeutic efficacy; HIV-RNA < 200 copies/ml as the value that prevents HIV transmission by sexual contacts. A probit model was applied to verify the impact of baseline variables and adherence on the virologic outcomes.

Results: 240 adult PLWH were included, 75% were males with a median age of 52 years (IQR 43-58). The median follow-up of the cohort under 3TC/DTG was very long, 819 days (IQR 450-1459) with some PLWH followed for more of 5 years for a total of 681 patient/years. Adherence was very high with a median of 99% (IQR 95-100%). Consequently, the virologic response was sustained: 38.3% of PLWH had HIV-RNA TND throughout the study period; 83.8% showed constant HIV RNA < 50 copies/ml and 95.8% of subjects had HIV-RNA always < 200 copies/ml (U=U level). However, a PDC < 80% was invariably associated to a negative virologic response and the virologic outcome was linearly related to PDC up to 90%. At this level we observed a plateau (figure). Probit analysis confirmed these findings as adherence was the only variable strictly associated to the possibility to obtain and maintain an HIV-RNA < 50 copies/ml or < 200 copies/ml differentiating non-responders from patients with eventual sporadic low-level viral blips. Adherence in non-responders was very low (median 78%; IQR 63 -93%) compared to PLWH showing constant control of HIV replication (median 98%; IQR 97-98%) (figure).

Conclusions: Adherence dynamics under 3TC/DTG indicate that forgiveness for this regimen is not high and that an adherence level equal or greater than 90% is required for long-term success. However, median adherence levels to this regimen are extremely high (99%) with only a few patients showing insufficient adherence.

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Dual therapy in naive and switched PLWH

OC 51 12-MONTH IMMUNOLOGICAL CHANGES IN PATIENTS RANDOMIZED TO SWITCH EITHER TO BIC/TAF/FTC OR DTG/3TC (DEBATE STUDY)

A. Cossarizza[1], M. Mattioli[1], A. Paolini[1], A. Neroni[1], S. De Biasi[1], D. Lo Tartaro[1], R. Borella[1], L. Fidanza[1], L. Gibellini[1], B. Beghetto[2], E. Roncaglia[2], G. Nardini[2], M. Menozzi[2], G. Cuomo[2], M. Di Gaetano[2], G. Orlando[2], V. Borghi[2], C. Mussini[1,2]

[1]University of Modena and Reggio Emilia, School of Medicine, [2]AOU Policlinico di Modena

Background: Dolutegravir-lamivudine (DTG/3TC) is recommended either as initial or switch regimen by international guidelines; nevertheless, data on inflammation after switching to this regimen mostly come from observational studies. The aim of the present study was to evaluate, in a randomized longitudinal study, the immunological impact of switching to DTG/3TC or to bictegravir/TAF/FTC (BIC).

Methods: Open-label, prospective, randomized trial enrolling 66 patients on a triple-drug regimen and with a stable (>12 months) undetectable HIV RNA. Blood collection was performed in participants treated with BIC (group A, n=33) or DTG/3TC (n=33) who were longitudinally studied at time 0, after 6 (T6) and after 12 months (T12). We characterized peripheral blood mononuclear cells, including T lymphocytes (interrogated at the single cell level by using 15 markers), B cells (8 markers) and monocytes (6 markers). Statistical analysis was performed by paired or unpaired Student's t test.

Results: We studied 33 participants on DTG/3TC and 30/33 on BIC (1 discontinued for rash, 1 for lymphatic leukemia and 1 sample could not be analysed for technical reasons). No significant changes were found between groups in the absolute number and percentage of whole CD3+, CD4+ or CD8+ T cells, CD4/CD8 ratio or B lymphocytes. Significant differences were present in CD4+, with the DTG/3TC group showed a more marked increase with time in transitional memory lymphocytes (T0 vs. T 6: p=0.0022; T0 vs. T12: p<0.0001), terminally differentiated T cells (T0 vs. T12: p=0.0007) and cells with markers of exhaustion such as CD57 and PD-1 (To vs. T12: p=0.0004). Activated CD4+ T cells were more represented in BIC group (T0 vs. T12: p=0.0367). Then, at T12, both groups slightly increased the proportions of T stem cell memory lymphocytes and of regulatory T cells.
Activated CD8+ T cells expressing HLA-DR and CD38 increased similarly in both groups, while those with markers of exhaustion were more represented in DTG/3TC group (T0 vs. T6: p=0.0029; T0 vs. T12: p=0.0426; p=0.0260 between groups at T12). No main modifications were seen in B cell populations, but a slight decrease of cells expressing markers of exhaustion was observed in both groups. Total monocyte number and percentage did not change with time in both groups, but classical monocytes (CD14++CD16-) increased in BIC group (T0 vs. T6: p=0.009; p=0.0028 between groups at T6), while nonclassical monocytes (CD14+CD16++) increased with time in DTG/3TC group (T0 vs. T6: p=0.0002; T0 vs. T12: p=0.0195).

Conclusion: In this randomized study, switch to DTG/3TC was linked after 12 months to an increase both in CD4 + and CD8+ T lymphocytes with markers related to terminal differentiation or exhaustion, and in nonclassical monocytes, a population of cells that has been recently associated with endothelial dysfunction. Functional studies are in progress to better characterize our findings.

Dual therapy in naive and switched PLWH

OC 52 SWITCH TO DORAVIRINE WITH DOLUTEGRAVIR DUAL REGIMEN COMPARED TO OTHER DUAL DOLUTEGRAVIR-BASED REGIMES IN CLINICAL PRACTICE: A 96-WEEK ANALYSIS

R. Rossotti[1], F. D'Amico[1], A. Nava[2], A. Raimondi[1], D. Fanti[2], N.B. Bana[1], E. Inglese[2], L.G. Chianura[1], M.C. Moioli[1], C. Vismara[2], M. Puoti[1]

[1]Department of Infectious Diseases, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy, [2]Chemical-Clinical and Microbiological Analyses, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy

Background: The switch to a dolutegravir (DTG)-based regimen, in combination with either lamivudine (3TC) or rilpivirine (RPV), has been extensively studied in experienced subjects. The availability of a new drug as doravirine (DOR), characterized by a different resistance mutational pathway, allowed clinicians to prescribe another dual regimen also in individuals who are not eligible to 3TC or RPV. Aims of this study are to describe how these dual regimens are prescribed in clinical practice, the rate of treatment withdrawal, the rate of virological failure and the rate of target not-detected (TND) maintenance over time.

Material and methods. This retrospective, monocentric analysis included all subjects who started a DTG-based dual regimen from 2015. Demographic, clinical and virologic data were collected form hospital electronic patient and laboratory records. Virologic failure was defined as two consecutive detectable (>20 copies/mL) viral loads.

Descriptive statistics (median and interquartile range [IQR] for continuous variables, absolute and relative [%] values for categorical variables) and non-parametric tests (one-way ANOVA for continuous and Pearson Chi-square for categorical variables) to compare the groups were applied. Kaplan Meier probability curves and Cox regression models for regimens durability were used.

Results. The study enrolled 671 subjects, mainly men (73.5%) with a median age of 52 (IQR 41-58) years. Table 1 shows that the 3 groups were not homogeneous: DOR arm included older subjects with a longer infection and a higher prevalence of previous AIDS-defining events, who have been exposed to more antiretroviral regimes, who have developed more resistance-associated mutations (RAMs), and with a worse baseline virologic control.

Over a cumulative follow up of 64,298 weeks, 27 discontinuations were registered (4.0%). In the multivariate Cox model, after adjusting for length of infection, baselined viral load, number of previous regimens, CD4/CD8 ratio and presence of RAMs, only RPV use remained significantly associated to regimen withdrawal (aHR 2.89, 95% CI 1.21 -6.94, p=0.017).

Figure 1 shows virological control evolution over time: from week 48 onwards no more difference among treatment arms was observed. The maintenance of TND during the follow up was higher with 3TC (71.1%) and RPV (70.6%) compared to DOR (50.0%), p=0.012. The rate of protocol-defined virological failure was not different across the 3 groups (1.8% with 3TC, 2.52% with RPV, 4.35% with DOR, p=0.493).

Discussion. All DTG-based dual regimens showed good virologic control and high durability. The DOR+DTG combination proved to be an effective therapeutic option even in difficult to treat individuals.

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Dual therapy in naive and switched PLWH

OC 53 CLINICAL AND VIROLOGICAL CHARACTERISTICS OF PEOPLE LIVING WITH HIV WHO FAIL TO MAINTAIN VIROLOGICAL SUPPRESSION AFTER SWITCHING TO DOLUTEGRAVIR-BASED TWO DRUG REGIMENS. RESULTS FROM THE PROSPECTIVE OBSERVATIONAL ARCA COHORT

L. Taramasso[1], R. Gagliardini[2], C. Sepulcri[3], A. Shallvari[4], W. Gennari[5], F. Lombardi[6], S. Di Giambenedetto[6,7], F. Maggiolo[8], I. Vicenti[9], V. Borghi[10], V. Micheli[11], D. Francisci[12], E. Pontali[13], S. Rusconi[14], R. Maserati[15], P. Laghetti[16], B. Bruzzone[17], S.T. Kiros[18], A. Di Biagio[1,3], ARCA collaborative group

[1]Infectious Disease Clinic, IRCCS Policlinico San Martino Hospital, Genoa, Italy, [2]HIV/AIDS Unit, National Institute for Infectious Diseases, Lazzaro Spallanzani IRCCS, Rome, Italy, [3]Department of Health Sciences (DISSAL), University of Genoa, Genoa, Italy, [4]InformaPRO S.r.l., Rome, Italy, [5]Clinical Microbiology, Ospedale Civile di Baggiovara-Policilinico di Modena, Modena, Italy, [6]Infectious Diseases Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy, [7]Department of Safety and Bioethics, Catholic University of the Sacred Heart, Rome, Italy, [8]Infectious Disease Unit, ASST Papa Giovanni XXIII, Bergamo, Italy, [9]Department of Medical Biotechnologies, University of Siena, Siena, Italy, [10]Clinica Malattie infettive, Azienda Ospedaliero Universitaria di Modena, [11]Laboratory of Clinical Microbiology, Virology and Bioemergencies, ASST Fatebenefratelli Sacco L. Sacco Hospital, Milan, Italy, [12]Department of Medicine and Surgery, Clinic of Infectious Diseases, "Santa Maria della Misericordia" Hospital, University of Perugia, Perugia, Italy, [13]Department of Infectious Diseases, Galliera Hospital, Genoa, Italy, [14]Infectious Disease Unit, ASST Ovest Milanese, Legnano (MI), Italy; Department of Biomedical and Clinical Sciences DIBIC L. Sacco, University of Milan, Milan, Italy, [15]Dipartimento Scienze mediche e malattie infettive, Fondazione IRCCS Policlinico "San Matteo", Pavia, Italy, [16]Clinic of Infectious Diseases, University Hospital Policlinico, University of Bari, Bari, Italy, [17]Hygiene Unit, IRCCS AOU San Martino-IST, Genoa, Italy, [18]Infectious Disease Unit, Department of Experimental and Clinical Medicine, University of Florence, Firenze, Italy

Background: After having demonstrated their non-inferiority when compared to three-drug regimens in large trials, dolutegravir (DTG)-based 2-drug regimens (2DR) are being increasingly used in treatment experienced patients in switching strategies. Real-world data on patients experiencing virological failure (VF) or blips (VB) under 2DR are still scant, also due to the very low incidence of the phenomenon. The aim of this study is to describe the clinical and virological characteristics of a multicenter cohort of people living with HIV (PWH) who experienced VF or VB after being switched to 2DR with DTG+ lamivudine (3TC) or DTG+ rilpivirine (RPV).

Methods: Descriptive analysis of VF (single HIV RNA >200 copies/mL or confirmed HIV RNA >50 copies/mL) and VB (single HIV RNA ranging between 51 and 200 copies/mL) and of pre-existing and emerging resistance mutations (RAMs) in PWH under 2DR with DTG+3TC or DTG+RPV.

Results: A total of 1,860 PWH from 16 Italian centers participating in ARCA database were included. All were on 2DR with either DTG+3TC (n=1,368, 74%) or DTG+RPV (n= 492, 26%). A total of 89 PWH (4.8%) experienced at least one VF or VB. Clinical and viro-immunological characteristics of PWH on 2DR regimen are outlined in Table. Most were male (61%, n=54), with unprotected sex as a risk factor for HIV infection (64%, n=57). Mean age was 51.7 (±11.85) years and mean BMI was 24.4 (±4.4) kg/m2. Study participants had a median of 6 (IQR 3-10) previous regimens and 1 (IQR 0-3) previous VF in anamnesis, [1 (IQR 0-2) in PLWH on DTG+3TC and 2 (IQR 0-3) on DTG+RPV, p=0.032]. Sixty PWH (67%) had subtype B, 12 (13%) had circulating recombinant forms (CRFs) and 17 (19%) did not have a reported subtype.

VF/VB occurred in 65 (4.7%, 1.30 per 100 PYFU) PWH on DTG+3TC and in 24 (4.8%, 1.50 per 100 PYFU) on DTG+RPV, for a total of 89 VF/VB events. Mean time to VF/VB was 536.9 (±406) days. Among PWH with a VF/VB while on DTG-2DR, at least a previous GRT was available for 70 (79%). Cumulative GRT evaluation revealed 16.3% (n=8) pre-existing RAMs to 3TC among PWH on DTG+3TC, and 21% (n=5) RAMs to RPV in those of DTG +RPV. No RAMs to DTG were present in either regimen. Post-failure GRT was performed in 6 PWH, with no occurrence of new emerging RAMs to 3TC or RPV or DTG.

Considering only VF, 54 events occurred during the study period, 40 (2.9%, 0.8 per 100 PYFU) in DTG+3TC and 14 (2.8%, 0.9 per 100 PYFU) in DTG+RPV. 12.5% had RAMs to 3TC (n=5) and 35.7% to RPV (n=5) in the two groups of treatment, respectively.

VB before VF were present in 15% of failures events (n=6) for DTG+3TC regimen and in 21% (n=3) for DTG+RPV regimen.

Conclusions: In ARCA cohort, almost 5% of patients switched to DTG-based 2DR experienced a VF/VB, with a similar prevalence between DTG+3TC and DTG+RPV regimens, without any newly emerging RAMs.

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Mental health and predictors of AIDS and non-AIDS defining co-pathologies

OC 54 RELATION BETWEEN GENETIC POLYMORPHISMS OR VARIANTS AND COGNITIVE IMPAIRMENT IN A GROUP OF HIV-INFECTED PEOPLE

M. Degli Antoni[1], I. Zanella[2], E. Zacchi[2], C. Fornari[1], B. Fumarola[1], E. Focà[1], F. Castelli[1], E. Quiros-Roldan[1]

[1]University Department of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili di Brescia, Brescia, [2]Department of Molecular and Translational Medicine, University of Brescia and Clinical Chemistry Laboratory, Diagnostic Department, ASST Spedali Civili di Brescia, Brescia

Antiretroviral therapy (ART) had mitigated the prevalence of neurocognitive impairment in people living with HIV (PLWH), however the HIV-associated neurocognitive disorders (HAND) remain high. Cognitive decline in PLWH may be affected by HIV-induced inflammation, lifestyle, long-term effects of ART and age-associated comorbidities. The role of genetics in the susceptibility to HAND is still unclear. Nucleotide expansions in C9orf72 gene, H63D gene variant in HFE and APOE variants are linked with the onset of neuroinflammation processes. Little is known about the association between these genetic variants and HAND.

We explored the possible relations among variants in 3 genes involved in inflammation and neurodegenerative disorders (APOE: ε2/ε3/ε4; HFE: H63D; C9ORF72: hexanucleotide expansions ≥ 9 repeats), cognitive/functional impairment (Mini Mental State Examination MMSE, Clock Drawing Test CDT, Short Physical Performance Battery SPPB), comorbidities and HIV-related variables in a cohort of > 50 years old PLWH with at least 10 years efficient ART. We performed Kruskal-Wallis test and the Fisher's exact test; Spearman's correlations were calculated to analyze the associations between the neuropsychological tests scores, the HIV-related values and medical history. Three multiple regressions models were performed to assess the association between all variables.

A total of 60 patients, 45 male (75%) and 15 female (25%), participated to the study. The prevalence of polymorphisms was the same of general population. The most common polymorphisms were H63D in HFE (28.3% with a single allele) and APOEε4 (16.7%). Only 8 patients (13.3%) had the expansion of C9ORF gene. We also found several associations: those patients with at least a single allele in APOEε3 showed higher CDT score ($p = .019$), while those with APOEε4 variant had lower CDT score ($p = .068$). Moreover, higher score in CDT was found in patients with higher years of illness ($p = .055$). Higher CD4 count was associated with better performance in SPPB ($p = .053$) and with the expansion of C9orf ($p = .032$). Cardiovascular disease was associated to APOEε4 ($p = .05$) and hypertriglyceridemia was linked to H63D in HFE gene ($p = .023$). At last, lower CD8 zenith value was associated with the presence of an allele in APOEε2 ($p = .01$). From the regression analysis, we observed that CDT score is positively associated with APOEε3 [2.1; 95% CI (0.01-0.8); $p = .045$].

This exploratory study displays genetic polymorphisms were not linked to motor impairment, while APOEε3 variant was associated to higher executive functions in PLWH. Moreover, APOEε4 seems to be a protective factor for cardiovascular disease while H63D can be a risk factor for hypertriglyceridemia. These data suggest that in PWH on efficient ART cognitive abilities and physical performances may be partly associated with comorbidities and genetic background. Further investigations are needed to confirm these findings.

Mental health and predictors of AIDS and non-AIDS defining co-pathologies

OC 55 A HIGHER CPE SCORE IN PLWH WITH HAND SWITCHED TO A LESS NEUROTOXIC REGIMEN IS ASSOCIATED TO IMPROVED MEMORY TEST (MARAND-X STUDY)

A. Lazzaro[1], D. Vai[2], A. Barco[3], G. Stroffolini[4,5], V. Pirriatore[6], G. Guastamacchia[2], M. Nigra[7], V. Ghisetti[8], M.C. Tettoni[4], M. Trunfio[4], A. Trentalange[4], S. Bonora[4], G. Di Perri[4], A. Calcagno[4]

[1]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Policlinico Umberto I of Rome, Roma Italy, [2]Unit of Neurology, Maria Vittoria Hospital, ASL Città di Torino, Turin, Italy, [3]Infectious Diseases Unit, Ospedale Maggiore della Carità, Novara, Italy, [4]Unit of Infectious Diseases, Department of Medical Sciences, University of Turin, Turin, Italy [5]Department of Infectious-Tropical Diseases and Microbiology, IRCCS Sacro Cuore Don Calabria Hospital, Negrar, Italy, [6]SC Tropical and Infectious Disease ASL Città di Torino, [7]Biochemistry and Immunology Laboratory, Maria Vittoria Hospital, ASL "Città di Torino", Turin, Italy, [8]Microbiology and Molcular Biology Laboratory, Amedeo di Savoia Hospitasl, ASL Città di Torino, Turin, Italy

Background: HIV-associated neurocognitive disorders (HAND) pathogenesis is incompletely understood and antiretroviral (ARV) neurotoxicity has been suggested as a potential mechanism. ARV intensification based on central nervous system (CNS) penetration effectiveness (CPE) score (measuring the drug ability to enter the CNS) has shown cognitive improvements among people living with HIV (PLWH) treated with intensified ARVs with increased CPE score ≥3 and total ARV regimen CPE score ≥9. We designed a pilot, randomized, prospective, single-blind clinical trial to assess changes in neurocognitive function in PLWH with HAND randomized to a less neurotoxic ARV regimen (darunavir/cobicistat, maraviroc, emtricitabine: "MARAND", with a CPE score of 9), or to continue their treatment.

Method: PLWH were screened from clinical records and subsequently studied with an array of 23 neuropsychological (NPS) tests and lumbar puncture: only PLWH with HAND, on efavirenz/darunavir-free ARV regimens, with R5-tropic infection susceptible to MARAND and HIV-RNA <50 copies/mL on both plasma and CSF were enrolled. After 1:1 randomization, NPS tests were repeated after 24 weeks. Using published normative data, NPS raw scores were converted to demographically corrected T-scores to minimize the age, education, sex, and ethnicity influence. Data are expressed as median (interquartile range). Longitudinal pair-wise comparison between baseline (BL) and week 24 (w24) was assessed by the paired Wilcoxon test for; p-value <.05 was considered statistically significant, with FDR correction for multiple comparisons. Planned sample size was 76.

Results: The study was terminated for slow accrual when 38 participants were enrolled and 28 completed the follow-up. Male (75%) and European ancestry (89%) were prevalent: median age was 56 years (7.5); median CD4 + count was 706 cell/μL (413). Baseline characteristics were similar between study arms.

Longitudinal analysis showed a significant improvement from BL to w24 only in the MARAND arm for the "complex attention and processing speed"-assessing test Digit Span Backward test (DSB) (p .04), and the "learning and long-term memory"-assessing tests Immediate (IFCSR) and Delayed (DFCSR) Free and Cued Selective Reminding tests (p .02 and .04, respectively).

To assess whether the improvement was linked to MARAND arm itself or to ARV intensification with increased CPE scoring =3, we repeated the longitudinal analysis stratifying for CPE score increase =3 from previous ARV regimen to MARAND. We detected a significant improvement in the DBS and IFCSR only in PLWH within the MARAND arm with a CPE score =3, as shown in figure 1.

Conclusion: In this small but well controlled study the use of less neurotoxic ARV showed no major beneficial effect over unchanged ARV regimen. The beneficial effects observed in the memory domain appeared to be linked to a CPE score increase of at least 3, similarly to what was previously shown in other non-controlled studies.

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Mental health and predictors of AIDS and non-AIDS defining co-pathologies

OC 56 PRE-ART PLATELET-TO-LYMPHOCYTE RATIO AND THE RISK OF SERIOUS NON-AIDS-EVENTS, AIDS-EVENTS AND MORTALITY IN PLWH STARTING FIRST-LINE ART

P. Saltini[1,2,3], A. Cozzi-Lepri[4], G. Bozzi[1], G. Marchetti[5], L. Taramasso[6], S. Mazzanti[7], V. Rizzo[8], A. Antinori[9], C. Mussini[10], A. Gori[1,2,3], A. D'Arminio Monforte[5], A. Bandera[1,2,3]

[1]Infectious Diseases Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy, [2]Department of Pathophysiology and Transplantation, University of Milano, Milano, Italy, [3]Centre for Multidisciplinary Research in Health Science (MACH), University of Milano, Milano, Italy, [4]Institute for Global Health UCL, University College London, London, UK, [5]Clinic of Infectious Diseases, San Paolo Hospital, ASST Santi Paolo e Carlo, Department of Health Sciences, University of Milan, Italy, [6]Infectious Diseases Unit, San Martino Policlinico Hospital, IRCCS for Oncology and Neuroscience, Genoa, Italy, [7]Infectious Diseases Clinic, Ospedali Riuniti Umberto I, Ancona, Torrette, Italy, [8]Immunodeficiency and Gender Related Infectious Diseases Unit, Department of Infectious Disease and Infectious Emergencies, AORN dei Colli, P.O. Cotugno, Naples, Italy, [9]Istituto Nazionale per le Malattie Infettive Lazzaro Spallanzani IRCCS, Rome, Italy, [10]Clinic of Infectious Diseases, University of Modena, Modena, Italy

Background: Among people living with HIV (PLWH) on effective antiretroviral therapy (ART), serious non-AIDS events (SNAEs) have become the major cause of morbidity and mortality and linked to systemic inflammation. Neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and lymphocyte-to-monocyte ratio (LMR) were shown to be good indicators of inflammation and prognostic factors for different conditions in the general population but similar association analyses conducted in PLWH are sparse.

Methods: PLWH starting first line ART (baseline) between 1997-2021 enrolled in the ICONA Foundation Study cohort with a measure of the NL, PL and LM ratios over the 6 months before ART initiation were included. PLR, NLR and LMR values were divided in 3 subgroups based on the tertiles of the baseline distribution (T1, T2, T3). PLWH's characteristics at baseline were compared across the tertile groups using chi-square and Mann-Whitney test. The association between baseline PLR, NLR and LMR and the risk of SNAEs and death, AIDS events and all-cause mortality were tested using Kaplan-Meier and Cox proportional hazard models adjusting for a priori identified confounding factors (age, CD4 count, VL, HCV status and year of starting ART).

Results: We included 9,248 pts in the PLR analysis, 8,727 pts in the NLR analysis and 1,090 pts in the LMR analysis. Exact values of the tertiles for the considered ratios are shown in Tables/Figure. Participants were mainly males, 43% MSM, aged 38 years, with a median baseline CD4 count of 330/mmc. Baseline PLR was significantly associated with age, female gender, mode of HIV transmission, nationality, AIDS diagnosis, hepatitis coinfection (HBV and HCV), current and nadir CD4 count, CD8 count, smoking and lower time from HIV diagnosis (Table 1).

After a median (IQR) follow-up of 5.0 (2.2-8.7) years, 489 SNAEs, 390 AIDS-events and 371 deaths were observed. By 15 years from starting ART, the risk of SNAE or death was 23% in PLWH with PLR<T1 vs. 18% in those with PLR=T2 vs 19% in those with PLR>T3 (Table 2, p=0.01). This difference was strongly significant and confirmed for SNAEs or death and all-cause mortality after the adjustment (Figure 1).

Similarly, in the unadjusted analysis, there was a difference in risk of SNAE/death across tertiles of NLR and LMR (Table 2, log-rank p<0.0001 and p<0.0001, respectively). However, none of these associations retained statistical significance after controlling for age, CD4 count, VL, HCV status and year of starting ART. Results were similar for the other two endpoints.

Conclusions: Our data show that in PLWH starting a first-line ART, baseline PLR is a strong predictor of the risk of SNAEs, and mortality independently of key confounding factors. Because the biomarker is derived from common blood parameters routinely collected in the clinics, its use should be encouraged to identify and carefully manage PLWH who are at increased risk of poor long-term clinical outcomes.

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Mental health and predictors of AIDS and non-AIDS defining co-pathologies

OC 57 ASSOCIATION BETWEEN HIV-1 DNA AND CLINICAL OUTCOME IN PEOPLE LIVING WITH HIV

M. Bottanelli[1], D. Ceccarelli[2], R. Lolatto[2], L. Galli[2], M. Guffanti[2], R. Dell'Acqua[2], G. Ponta[1], G. Mori[1], A. Castagna[1,2], C. Muccini[1,2]

[1]School of Medicine and Surgery, Vita Salute San Raffaele University, Milan, Italy, [2]Infectious Diseases Unit, San Raffaele Scientific Institute, Milan, Italy

Background: Total HIV-1 DNA is the most widely used marker for exploring HIV reservoir and has proved to be predictive of lower CD4 count and higher levels of HIV-1 RNA. Our aim is to evaluate if HIV-1 DNA may be associated with the occurrence of cardiovascular (CV) events and mortality.

Material and Methods: Retrospective study on adult people living with HIV (PLWH) for at least 10 years (yrs) since the start of antiretroviral therapy (ART) and 5 yrs from the first HIV-1 DNA determination. Total HIV-1 DNA was quantified in peripheral blood mononuclear cells (PBMC) by Real Time PCR (ABI Prism 7900).

Patients' characteristics were reported as median (interquartile range, IQR) or frequency (%).

Characteristics in PLWH with HIV-1 DNA ≥100 copies (cp)/106PBMC or HIV-1 DNA <100 cp/106PBMC were compared using the Chi-square/Fisher's exact test or the Wilcoxon rank-sum test.

Both survival and CV events probability were estimated by Kaplan-Meier (KM) curves.

Multivariable Cox proportional hazard model was applied to assess risk factors for CV events or mortality; adjusted hazard ratio (AHR) with the respective 95% confidence intervals (95%CI) are reported.

Results: We evaluated 749 PLWH: 606 (80.9%) with HIV-1 DNA ≥100 cp/106PBMC and 143 (19.1%) with HIV-1 DNA <100 cp/106PBMC. Median age was 47 (43-52) yrs and 575 (76.8%) were male; median yrs of HIV and ART were greater in PLWH with HIV-1 DNA ≥100 cp/106PBMC compared to PLWH with HIV-1 DNA <100 cp/106PBMC [17 (11-21) vs. 12 (6-18) yrs, p<0.001 and 14 (8-16) vs. 9 (4-15) yrs, p<0.001, respectively].

Overall, 541/749 (71.8%) PLWH had HIV-1 RNA <50 cp/mL, 113/749 (15.1%) HIV-1 RNA ≥50 cp/mL and 95/749 (12.7%) did not have a paired HIV-1 RNA at HIV-1 DNA determination; in the group of HIV-DNA ≥100 cp/106PBMC, PLWH were 435/606 (71.8%), 99/606 (16.3%) and 72/606 (11.9%), respectively, while in the group of HIV-1 DNA <100 cp/106PBMC, PLWH were 106/143 (74.1%), 14/143 (9.8%) and 23/143 (16.1%), respectively (p=0.083).

After the first HIV-1 DNA determination, CV events occurred in 33/606 (6.4%) PLWH with HIV-DNA ≥100 cp/106PBMC and in 3/143 (2.2%) PLWH with HIV-1 DNA <100 cp/106PBMC (p=0.088); death was reported in 23/606 (3.8%) in the first group and no cases (0/143, 0%) in the second group (p=0.013).

Higher probabilities of CV events and death were observed in PLWH with HIV-1 DNA ≥100 cp/106PBMC and HIV -1 RNA ≥50 cp/mL (p=0.05) (Figure).

After adjusting for HIV-1 RNA and CD4/CD8, the risk of CV events or death was higher in older PLWH (HR=1.07, 95%CI: 1.04-1.10, p<0.001) with a longer exposure to ART (HR=1.06, 95%CI: 1.00-1.12, p=0.044) while HIV-1 DNA >100 cp/106PBMC was only marginally associated with this composite outcome (HR=0.37, 95%CI: 0.15 -1.21, p=0.10).

Conclusion: In our cohort, the probability of occurrence of CV events or mortality is higher in PLWH with HIV-DNA ≥100 cp/106PBMC. Further larger studies are needed to validate HIV-1 DNA as a prognostic marker for these clinical outcomes.

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Complexities of SARS-CoV-2 infection

OC 58 PREVALENCE AND EPIDEMIOLOGICAL, CLINICAL AND MICROBIOLOGICAL CHARACTERISTICS OF BACTERIAL INFECTIONS IN A LARGE COHORT OF PATIENTS ADMITTED FOR COVID-19 IN CAMPANIA: A MULTICENTRE COHORT STUDY

L. Onorato[1], M. Palamone[1], P. Maggi[2], F.G. Numis[3], I. Gentile[4], V. Sangiovanni[5], V. Esposito[6], R. Punzi[7], G. Calabria[8], C. Rescigno[9], A. Salomone Megna[10], A. Masullo[11], E. Manzillo[12], G. Russo[13], R. Parrella[14], G. Dell'Aquila[15], M. Gambardella[16], A. Ponticiello[17], M. Pisaturo[1], N. Coppola[1], on behalf of CoviCam group

[1]Infectious Diseases, Department of Mental Health and Public Medicine, University of Campania "L. Vanvitelli", Napoli, Italy, [2]Infectious Diseases Unit, A.O. S Anna e S Sebastiano Caserta, Italy, [3]Emergency Department, PO Santa Maria delle Grazie, Pozzuoli, Italy, [4]Infectious Diseases Unit; University Federico II, Naples, Italy, [5]Third Infectious Diseases Unit, AORN dei Colli, P.O. Cotugno, Naples, Italy, [6]IV Infectious Diseases Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [7]Hepatic Infectious Disease Unit, AORN dei Colli, PO Cotugno, Naples, Italy, [8]IX Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [9]First Infectious Diseases Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [10]Infectious Diseeases Unit, A.O. San Pio, PO Rummo, Benevento, Italy, [11]Infectious disease unit, A.O. San Giovanni di Dio e Ruggi D'Aragona Salerno, Italy, [12]VIII Infectious Diseases Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [13]Infectious Diseases Unit, Ospedale Maria S.S. Addolorata di Eboli, ASL Salerno, Italy, [14]Respiratory Infectious Diseases Unit, AORN dei Colli, PO Cotugno, Naples, Italy, [15]Infectious Diseases Unit, AO Avellino, Italy, [16]Infectious Diseeases Unit, PO S. Luca, Vallo della Lucania, ASL Salerno, Italy, [17]Pneumology Unit, AORN Caserta, Italy

Background: Despite several data demonstrating a limited prevalence of bacterial coinfection or superinfection in patients hospitalized for COVID-19, a large number of subjects receive antibiotic prescriptions during illness. The aim of this study was to evaluate the prevalence and clinical characteristics of bacterial infections among a large cohort of COVID-19 patients and to identify the independent predictors of infection.

Methods: All consecutive patients admitted with a diagnosis of COVID-19 to one of the 10 centers participating in the study from March 2020 to November 2021 were included in the analysis. All subjects showing a clinical presentation consistent with a bacterial infection, with a microbiological confirmation and/or a procalcitonin value >1 ng/ml were considered as having a coinfection (if present at admission) or a superinfection (if acquired after at least 48 hours of hospital stay). Independent predictors of infection were identified through logistic regression analysis.

Results: During the study period, 1993 patients were enrolled. The subjects had a mean age of 62.2 (+16) years, and 61.5% were male. The most frequent comorbidities included cardiovascular diseases (27.9% of patients), diabetes (20.4%), chronic pulmonary diseases (10.4%), and chronic kidney diseases (8.7%); 46.4% of patients presented a sever or critical disease. Forty-two patients (2.1%) presented a microbiologically documented infection, including 17 coinfection and 25 superinfection, while 264 patients (13.2%) had a peak procalcitonin value >1 ng/ml. The remaining 1686 subjects showed no evidence of bacterial infection. A total of 416 patients (20.8%) were treated with a macrolide, while 488 subjects (24.5%) received a different antibacterial treatment. The overall mortality rate was 10.4%. Patients who developed a bacterial infection presented a higher prevalence of cardiovascular diseases (p=0.028), chronic kidney (p<0.001) and liver diseases (p<0.001), and diabetes (p=0.006) as compared to those without infection but required less frequently supplemental oxygen therapy (<0.001) (table 1). However, hospital mortality was similar between the two groups. Finally, patients with bacterial infections had higher creatinine values (p<0.001) and received more frequently corticosteroid treatment (p<0.001). At multivariate logistic regression analysis, diabetes mellitus (OR 3.5, 95% CI 1.01-12.6, p=0.048) and clinical severity (OR 3.3, 95% CI 1.15-9.57) were identified as independent predictors of bacterial infections.

Conclusions: A 15.5% of bacterial coinfections or superinfections were observed in our large cohort of patients admitted for SARS-CoV-2 pneumonia in 10 centers of Campania region. Diabetes mellitus and clinical severity were identified as independent predictors of bacterial infections. Approximately 37% of patients showing no evidence of bacterial infection received an antimicrobial treatment.

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Complexities of SARS-CoV-2 infection

OC 59 EVALUATION OF SARS-COV-2 REINFECTION RISK DURING THE DIFFERENT COVID-19 VARIANTS' SPREAD

S. Leone, A. Agresta, G. De Carli, C. De Santis, M.C. Fusco, V. Vantaggio, M. D'Amato, G. Pitti, E. Girardi, F. Vairo

National Institute for Infectious Diseases "L.Spallanzani" IRCCS

Background: A better understanding of dynamic of SARS-CoV-2 reinfection during the different phase of the pandemic and associated risk factors and outcome is important to drive pharmaceutical and non-pharmaceutical measures. We conducted a retrospective cohort study to assess the dynamic, determinants and outcome of COVID-19 reinfection.

Material and Methods: Reinfections were identified based on RT-PC tests collected by Lazio regional integrated surveillance system platform and defined as 2 positive RT-PC tests at least 90 days apart. Daily individuals eligible for reinfection (at least 90 days after the primary infection) were assessed from the date of the spread of the Alpha variant (Jan 1,2021) until the end of the study (Jan 24,2022). A mixed-effects negative binomial regression was used to derive reinfection incidence rate ratios (IRR) for the different phases of Covid-19 pandemic: Alpha (Jan 1,2021 to Jul 18,2021) as reference, Delta (Jul 19,2021 to Dec 5,2021) and Omicron (Dec 6,2021 to Jan 24,2022). The model was adjusted for the following covariates: age group, sex, healthcare workers (HCWs), time since primary infection, vaccination status and Covid-19 incidence. Clinical status and outcomes were evaluated in a subset of reported reinfection cases. Statistical analyses were performed using R software.

Results: A total of 216474 patients with SARS-Cov-2 primary infection met our inclusion criteria. Reinfection was identified in 5818 individuals (2.7%). According to the different phases of pandemic, 806 reinfection (13.9%) occurred in the Alpha phase, 773 (13.3%) in the Delta phase and 4239 (72.9%) in the Omicron phase. 3131 (53.8%) occurred between 9 and 15 months following primary infection. Compared with Alpha phase, we found that the adjusted risk of reinfection was reduced by 32% (IRR:0.68 $p<0.001$) in the Delta phase. The risk of reinfection in the Omicron phase was 6.19 times higher than Alpha phase ($p<0.001$), 4.58 times higher than Delta phase ($p<0.001$). The risk of reinfection was more pronounced in females (IRR:1.11;$p=0.003$), in HCWs (IRR:2.53; $p<0.001$) and increased with time since primary infection (i.e. 15 months after primary infection IRR:1.98;$p<0.001$). The reinfection risk reduction was estimated to be 43% ($p<0.001$) in patients who had received at least 1 dose of vaccine within 120 days. Those who had received at least 1 dose since more than 120 days had the same reinfection risk of unvaccinated(Tab.1). In our analysis, reinfections were more likely to be asymptomatic($p<0.001$), less likely to require hospitalization($p<0.001$) and to result in death($p<0.001$).

Conclusions: Our results suggest clear evidence to increased risk of reinfection in the Omicron phase. Additionally, we observed a reduction in the protective effect of vaccine against infection after 120 days since receipt of any dose after primary infection and a less severe clinical manifestations with lower rates of hospitalization.

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Complexities of SARS-CoV-2 infection

OC 60 PRE-EXISTENT SOCIO-ECONOMIC STATUS AND ITS ROLE IN PASC SYNDROME: RESULTS FROM THE VASCO STUDY (VARIABILI SOCIOECONOMICHE E COVID-19), ON THE "SURVIVING-COVID" COHORT, FROM BERGAMO (ITALY)

S.V. Benatti[1], S. Venturelli[1], R. Buzzetti[2], F. Binda[1], L. Soavi[1], L. Belotti[1], A.M. Biffi[1], M.S. Spada[1], M. Casati[1], M. Rizzi[1]

[1]ASST Papa Giovanni XXIII, Bergamo, [2]Clinical Epidemiologist, freelance, Bergamo

Background: Socio-economic disadvantage is associated to higher risks of contagion and mortality by COVID-19, according to various reports, from different countries. No association between pre-existent socio-economic status (SES) and Post-acute Sequelae of COVID-19 (PASC) has been documented, so far. VASCO study aimed to evaluate the impact of SES on PASC in the "Surviving COVID" cohort, seen at Papa Giovanni XXIII Hospital in Bergamo in the aftermath of the first epidemic wave.

Methods: All adults discharged from the Emergency Department or after admission to our hospital, between February 20th and September 20th 2020, for any condition possibly related to SARS-CoV-2 infection, were proposed to receive a multidisciplinary follow-up. This included pulmonary function test with diffusion, psychological evaluation with quality of life assessment (SF-36, IES-R), and clinical evaluation of persisting symptoms (fatigue, dyspnoea, chest pain, myalgia and palpitations). A self-administered Socio-Economical Questionnaire allowed to estimate their SES, according to a 9-class model developed by ISTAT in 2017. To comply with the definition of PASC given by NICE, we excluded those patients, who had a follow-up appointment before 12 weeks from symptoms onset, and those who experienced any complication in the acute phase, (possibly responsible for symptoms persistence).

The endpoints were: persistence of physical symptoms, reduced DLCO and pathologic scores in SF-36 or IES-R. Several analyses were performed with multiple logistic regression models to identify factors independently related to the outcome variables. Goodness of fit was assessed by the Hosmer-Lemeshow test.

Results: We included 825 patients. After a median time from symptom onset to follow-up visit of 143 days (IQR 115-171), 40% (95% C.I. 36.6 to 43.3) still complained of symptoms, among which fatigue in 248 (30.1% - 95% C. I. 26.9 to 33.2) and dyspnoea in 126 (15,3% - 95% C.I. 26.9 to 33.2). DLCO was less than 80% of expected in 147 (18% - 95% C.I. 12,8 to 17,7) and IES-R identified 256 patients (31% - 95% C.I. 27.9 to 34.2) with COVID-19-related traumatic aspects. SF-36 showed major abnormalities in the Physical Role Limitation (65% - 95% C.I. 61.7 to 68.3) and Emotional Role Limitation (30% - 95% C.I. 26.9 to 33.1) items

In the multiple analysis, SES correlated with the SF-36 items for Physical Activity, General Health Perception, Physical Role Limitation and Bodily Pain, with low class predicting pathologic scores (Figure 1). No such correlation was found with physical symptoms, DLCO reduction, or SF-36 items for Social Activity, Emotional Role Limitation, Vitality and Mental Health Perception.

Conclusions: In a large, hospital-based, directly interviewed cohort, from a single center, in the first COVID-19 epidemic wave, low social status is associated with a harder experience of recovery, but not with psychological disturbances, physical symptoms persistence, or DLCO reduction.

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Complexities of SARS-CoV-2 infection

OC 61 DEPRESSIVE SYMPTOMS AMONG COVID-19 SURVIVED PATIENTS ONE YEAR AFTER HOSPITAL DISCHARGE: PREVALENCE AND FACTORS ASSOCIATED

P. Vassalini[1], R. Serra[2], L. Tarsitani[2], G. Ceccarelli[1], A.E. Koukopoulos[2], C. Borrazzo[1], C. Di Nicolantonio[2], C. Tosato[1], F. Cherubini[1], F. Alessandri[3], C.M. Mastroianni[1], G. d'Ettorre[1]

[1]Department of Public Health and Infectious Diseases, Policlinico Umberto I, Sapienza University of Rome, Rome, Italy, [2]Department of Human Neurosciences, Policlinico Umberto I, Sapienza University of Rome, Rome, Italy, [3]Intensive Care Unit, Department of General and Specialist Surgery "Paride Stefanini", Policlinico Umberto I, Sapienza University of Rome, Rome, Italy

Background: People affected by coronavirus disease 2019 (COVID-19) experience long-lasting sustained mental disorders and neuropsychiatric consequences. Specifically, depressive disorder shows high incidence and may lead to chronic impairment and reduction of the quality of life. In this study we aim to assess the prevalence of depressive symptoms and related risk factors at 12-months after discharge to home care from the hospitalization for SARS-CoV-2 infection.
Methods: Patients were recruited among those admitted to the Division of Infectious Diseases, Umberto I "Sapienza" University Hospital of Rome. As a part of a larger project on long term neuropsychiatric disorders in COVID-19, patients were contacted by clinical raters by telephone after three, six and twelve months after hospital discharge, and Patient Health Questionnaire-9 (PHQ-9) was administered. PHQ-9 is a validated screening tool for assessing the presence and severity of depression. Multivariate logistic regression models were used to analyse risk factors for the development of depressive symptoms.
Results: Of 109 participants, 22% (N = 24) received a PHQ-9-based diagnosis of depression. Pre-existing mental disorders ($p = 0.027$), chronic pulmonary disease ($p < 0.001$), presence of a family cluster of SARS-CoV-2 infection ($p = 0.011$) and to be unemployed or fired during the pandemic ($p = 0.018$) were found to be significant risk factors for developing depression. Variables indicating a more severe disease (ie, duration of hospitalisation, ICU treatment), age or gender were not associated to depressive symptoms.
Conclusions: A large proportion of COVID-19 patients experience some discomfort due to depressive symptoms after hospitalizatio. Pre-existing mental disorders and presence of chronic pulmonary diseases were already established as risk factors for depression in our previous findings at three and six months after discarge, persisting after one year. Furthermore, the employment status and the presence of a SARS-CoV-2 family cluster as risk factors for developing depressive symptoms underline the critical impact of the pandemic from a social point of view. Clinicians should consider screening for depression in follow-up control visits for COVID-19 patients.

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Insights on epidemiological and clinical management of hepatitis viruses

OC 62 SERUM HBSAG AND HIGHLY-SENSITIVE HBV-DNA QUANTIFICATION CAN PREDICT HBSAG LOSS AFTER NUCLEO(S)TIDE ANALOGUE SYSTEMATIC DISCONTINUATION IN NON-CIRRHOTIC PATIENTS WITH CHRONIC HEPATITIS B

L. Piermatteo[1], R. Salpini[1], S. D'Anna[1], A.F. Guerra[2], G. Tomassoli[2], G. Abbati[2], A. Pietrangelo[2], P. Ventura[2], V. Svicher[1,3]

[1]Department of Experimental Medicine, University of Rome "Tor Vergata, [2]Internal Medicine and Centre for Hemochromatosis, University Hospital of Modena, University of Modena and Reggio Emilia, Italy, [3]Department of Biology, University of Rome "Tor Vergata"

Background: Systematic discontinuation of nucleo(s)tide analogue (NA) treatment in selected non-cirrhotic Chronic Hepatitis B (CHB) patients may promote sustained serological and virological off-treatment response. Nevertheless, this approach often leads to biochemical and virological relapse, which may result in life-threatening liver failure. Therefore, in order to ensure a safe treatment discontinuation, reliable predictors of post-NAs remission are needed.
In this light, we aimed to define predictive parameters of virological response after NAs systematic discontinuation and their association with HBsAg loss or HBsAg levels < 100 IU/ml, known to be predictive of HBsAg loss.
Material and Methods: 38 non-cirrhotic CHB patients, with complete virological suppression (for at least 4 years), were prospectively monitored after suspending NA treatment for a median (IQR) time of 16 (10 - 19) months. For each patient, a plasma sample at suspension date (baseline) was collected and used for highly-sensitive serum HBV-DNA quantification by droplet digital PCR (ddPCR). HBsAg levels were quantified through ARCHITECT HBsAg assay at BL, every 2 weeks from suspension in the first month, monthly until the sixth month and then every 3 months hereinafter, in order to assess the achievement of HBsAg < 100 IU/ml or HBsAg loss.
Results: At baseline, ddPCR revealed that 28 (73.7 %) patients still had detectable serum HBV-DNA (median [IQR] 5 [2 - 11] IU/mL), while 10 (26.3 %) were completely negative to HBV-DNA. After NA discontinuation, 7 (18.4 %) patients achieved HBsAg < 100 IU/mL (median [IQR]: 43 [35 - 53] IU/ml) and 8 (21.1 %) HBsAg loss at last follow-up. As expected, patients achieving HBsAg loss had lower HBsAg levels at baseline (140 [70 - 480] IU/ml in patients achieving vs 1162 [439 - 3135] in those not achieving HBsAg loss, p = 0.014).
Notably, the negativity to HBV-DNA by ddPCR at baseline strongly correlated with the achievement of HBsAg < 100 IU/mL or HBsAg loss after NA discontinuation (outcome observed in 70% [7 / 10] with vs 28.6 % [8 / 28] without negative HBV-DNA at baseline; OR [95 % CI]: 5.8 [1.3 - 23.6], p = 0.03). Even more, the combination of HBsAg < 500 IU/mL and the negativity to ddPCR HBV-DNA at baseline was the best predictor for achieving HBsAg < 100 IU/mL or HBsAg loss (outcome observed in 85.7 % with vs 27.6 % without this combination; OR [95 % CI]: 15.8 (1.6 - 152.2; p = 0.008; PPV = 86 %; NPV = 72 %).
Conclusions: In the setting of systematic discontinuation of nucleo(s)tide analogue, the detection of residual HBV replicative activity by innovative and highly-sensitive ddPCR assay can be an useful tool for the identification of patients eligible to a safe NA discontinuation and thus more prone to achieve HBV functional cure.

Insights on epidemiological and clinical management of hepatitis viruses

OC 63 HEPATITIS D VIRUS INFECTION IN A LARGE COHORT OF IMMIGRANTS IN SOUTHERN ITALY A MULTICENTER, PROSPECTIVE STUDY

E. Cordua[1], M. Pisaturo[1,2,7], L. Alessio[2,7], M. Starace[1], A. Di Fraia[1], C. Monari[2,7], L. Onorato[2,7], C. Sagnelli[1,2,5], S. De Pascalis[2], L. Gualdieri[6], C. Minichini[1], G. Di Caprio[3,4], L. Occhiello[1,6], G. Scotto[8], M. Macera[2,7], N. Coppola[1,2]

[1]Department of Mental and Physical Health and Preventive Medicine, Infectious Diseases section, University of Campania Luigi Vanvitelli, Naples, [2]L. Vanvitelli University Hospital, Naples, [3]UOC of Infectious Diseases, AORN Sant'Anna and San Sebastiano, Caserta, [4]"Abraham's Tent" Reception Center, Caserta, [5]Missionary Sisters of Charity Center, Naples, [6]Center for the Protection of Immigrant Health, Naples, [7]Social center "ex-canapificio", Caserta, [8]UOC of Infectious Diseases, Foggia

Background: aim of our study was to evaluate the demographic and virological characteristics of HDV infection in a cohort of immigrants living in Southern Italy.

Methods: Between January 2012 and February 2020 all immigrants attending one of the 5 first- level centers in Southern Italy were enrolled and screened for HBsAg, the HBsAg-positive for anti-Delta and if positive, for HDV-RNA and HDV genotype.

The data relating to the epidemiological characteristics were collected in an electronic database.

Results: Of the 3,521 immigrants observed in the study period, 3,417 (97.0%) agreed to be screened; they were mainly males (61%), with a median age of 27 years (IQR 8-74) and came prevalently (58%) from sub-Saharan Africa (table 1)

Of the 3,417 patients enrolled, 243 (7%) subjects were HBsAg-positive, and of those, 8 (3%) were anti-Delta-positive.

Table 2 showed the epidemiological and virological characteristics of the 243 HBsAg positive patients based on serum HDV status. There was no difference in gender prevalence between the anti-Delta-negative vs -positive subjects (94% vs 87.5%; p=0.4), nor in median age [26.5 (IQR=32-21) vs 21.5 (IQR=30.5 - 19.25); p=0.18], nor in the area of origin: there was a higher prevalence of subjects from sub-Saharan Africa in both groups (88% vs. 100% p=0.3). The average of the months of stay in Italy was higher in anti-HDV-positive subjects (22±37.7 vs. 7 ±8.2 months), but with no significance to the statistical analysis (p=0.2). The most frequent risk factors were unprotected sexual intercourse and intramuscular therapy, but with no statistical difference between the two groups (62% vs. 50%, p=0.4; and 59% vs. 62.5%, p=0.8, respectively).

HBV DNA was more frequently positive in 143 (81%) of the 235 HBsAg-positive/anti-Delta- negative subjects and in 3 (37%) of the 8 HBAg and anti-Delta-positive (p=0.0001); HBV load was similar in the two groups (Table 2). As regards the HBV genotype, identified only in HBsAg-positive subjects, genotype E was the most prevalent, then genotype D and A, and finally genotype C (Table 2). In no anti-Delta-positive subject was the HBV genotype identified because they were HBV DNA-negative or at a low viral load. All anti-Delta-positive subjects were evaluated for serum HDV-RNA and HDV genotype. Only one patient resulted positive for HDV-RNA, genotype 1. This patient was a 46-year-old, had HDV viremia of 7,050 IU/mL and an ultrasound diagnosis of compensated cirrhosis. In May 2016 he started therapy with pegylated interferon, interrupted in November 2016 because of thrombocytopenia and started therapy with entecavir 1 mg/die.

None of the enrolled patients was aware of their serological status.

Conclusions: There are few data that characterize HDV infection in an immigrant population, therefore we believe that screening procedures should be implemented in this category of subjects

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Insights on epidemiological and clinical management of hepatitis viruses

OC 64 REACTIVATION OF HEPATITIS B VIRUS IS A FREQUENT EVENT IN ANTI-HBC-POSITIVE/HBSAG-NEGATIVE HIV-INFECTED PATIENTS SWITCHING TO TENOFOVIR SPARING THERAPY AS REVEALED BY HIGHLY SENSITIVE HBV ASSAYS

R. Salpini[1], S. D'Anna[1], M. Alkhatib[1], L. Piermatteo[1], A. Tavelli[2], E. Quiros[3], A. Cingolani[4], C. Papalini[5], S. Carrara[6], V. Malagnino[7], M. Puoti[8], L. Sarmati[7], A. d'Arminio Monforte[9], F. Ceccherini Silberstein[1], V. Svicher[1] for the Icona Foundation Study Group

[1]Department of Experimental Medicine, University of Rome Tor Vergata, Rome, Italy, [2]ICONA Foundation, [3]University Division of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili, Brescia, Italy, [4]Unit of Infectious Diseases, Fondazione Policlinico Universitario A. Gemelli-Università Cattolica Del Sacro Cuore, Rome, Italy, [5]Infectious Diseases Clinic, Department of Medicine, University of Perugia, Perugia, Italy, [6]Microbiology Biobank and Cell Factory Unit, National Institute for Infectious Diseases "Lazzaro Spallanzani', Rome, Italy, [7]Unit of Infectious Diseases, University Hospital Tor Vergata, Rome, Italy, [8]Dipartimento Medicina e Chirurgia, Università degli studi di Milano Bicocca, Milan, Italy, 9[C]linic of Infectious Diseases, ASST Santi Paolo e Carlo, Department of Health Sciences, University of Milan, Italy

Background: Tenofovir-sparing antiretroviral therapy (ART) is increasingly used in the setting of HIV-infection, raising the issue to properly identify those anti-HBc-positive/HBsAg-negative patients who can safely suspend this drug. Here, we aim to unravel HBV replication kinetics after tenofovir withdrawal in anti-HBc-positive/HBsAg-negative HIV-infected patients.

Methods: This study includes 101 HIV-infected patients from ICoNA cohort, all anti-HBc-positive/HBsAg-negative and mostly Anti-HBs-positive (71%; median (IQR): 69 (10-932)mIU/ml]. All patients were treated with TDF/TAF-containing ART for >12 months and switched to TDF/TAF-sparing ART, including LAM in 73 patients and no-active HBV drugs in 28 patients. At switching (T0), 98% of patients has undetectable HIV-RNA.

For each patient, a plasma sample is analyzed at T0 and during the first 12 months of TDF/TAF-sparing ART (T1). HBV-reactivation (HBV-R) during TDF/TAF-sparing ART is defined as HBV-DNA>1IU/ml in patients with negative HBV-DNA at T0 or >2-fold increase in HBV-DNA from T0 to T1. HBV-DNA and -RNA are quantified by highly sensitive droplet digital PCR (LLOD:1IU/ml) and anti-HBc by Fujirebio (anti-HBc>15COI indicating active HBV reservoir based on Salpini,2020). Factors associated with HBV-R are assessed by multivariate analysis.

Results: At T0, despite TDF/TAF therapy, 34 (33.7%) patients have detectable HBV-DNA (median[IQR]: 2[1-5] IU/ml). Among the remaining 67 patients, 9% has detectable HBV-RNA (median[IQR]:6[5-7]IU/ml) and anti-HBc>15COI, indicating a transcriptionally active cccDNA. Notably, an active HBV replication at T0 is found more frequently in patients with low-level anti-HBs (42% of patients with vs 22.7% without Anti-HBs<100 IU/ml has detectable HBV-DNA, p=0.04).

At T1, after TDF/TAF withdrawal, HBV-R occurs in 40 (39.6%) patients (median[IQR] HBV-DNA: 4[2-13]IU/ml) with no difference between LAM- vs no LAM-group (42.5% vs 32.1%, P=0.3). Among HBV-R cases, 32.5% has HBV-DNA>10IU/ml (median[IQR]: 31[15-73]IU/ml) and 25% has ALT>40U/L.

Notably, HBV-R is confirmed in 77% of patients with an additional sample available during TDF/TAF-sparing ART (median [IQR] HBV-DNA:24[13-31]IU/ml), supporting persistent HBV replication.

Finally, nadir CD4+T cell count<100cells/ul is the only factor significantly associated with a higher risk to develop HBV-R (OR: 5.3 [1.6-17.4], p=0.007), after correcting for patients' demographics, viro-immunological parameters and ART duration.

Conclusion: A conspicuous fraction of HIV-infected anti-HBc-positive/HBsAg-negative patients has an active intrahepatic reservoir that can predispose to HBV-reactivation under suboptimal/absent pharmacological pressure. The status of HIV-driven immunecompromission can exacerbate this phenomenon. Highly sensitive and accurate assays to measure HBV replicative activity are crucial for a proper management of HIV-infected anti-HBc-positive/HBsAg-negative patients that are candidate to TDF/TAF-sparing regimen.

Insights on epidemiological and clinical management of hepatitis viruses

OC 65 HEPATITIS C TESTING, LINKAGE TO CARE AND TREATMENT DURING COVID-19 ERA IN A NORTH-EAST ITALIAN HOSPITAL: WHAT CAN WE STILL NEED TO DO TO IMPROVE ELIMINATION?

E. Garlatti Costa[1], M. Da Re[2], D. Villalta[2], M. Tonizzo[1]

[1]SC Medicina Interna, Azienda sanitaria Friuli Occidentale, Pordenone, [2]SSD Immunologia Allergologia, Azienda sanitaria Friuli Occidentale, Pordenone

Background and Aims: The WHO has launched a global programme to achieve HCV elimination targets for 2030. HCV testing is the first tool to diagnose hepatitis C in the subgroup of submerged people with HCV infection who are unaware of their condition. In Italy, HCV is currently tested through the detection of HCV antibodies (anti-HCV) and, second, among those who are anti-HCV positive, active HCV infection is confirmed by another blood specimen for HCV-RNA PCR. Linkage to care of patients with hepatitis C is necessary to start antiviral treatment. COVID-19 has resulted in many hepatitis elimination programs slowing or stopping altogether. Friuli Venezia Giulia (Italy) was most affected by this latest outbreak. Our aim is to assess the impact of pandemic COVID-19 on HCV testing, linkage to care and treatment in the Hub Hospital of Pordenone (Friuli Venezia Giulia) comparing 2019, 2020 and 2021.

Method: We retrospectively collected anti-HCV and HCV-RNA RT-PCR results from 01.01.2019 to 31.12.2021. Laboratory tests were divided according to referrer. Anti-HCV assays were performed using CLIA ADVIA-Centaur (Siemens Healthineers) while HCV-RNA RT-PCR was detected using COBAS 6800 (Roche) (Sensitivity 15 UI/ml). We considered patients with hepatitis C (HCV-RNA PCR positive) and we registered if they were linked to care and treated with DAAs.

Results: 14.221, 12.628 and 11.580 subjects were tested for HCV infection respectively in 2019, 2020 and 2021 with anti-HCV positivity of 2.4% (350/14.221) in 2019; 2.9% (374/12.628) in 2020 and 2.6% (309/11.580) in 2021. We noted 320 patients with hepatitis C in 2019 (2.2%), 222 in 2020 (1.7%) and 180 in 2021 (1.5%). In 2019, testing site was out-of-hospital setting for 5.907 subjects, in-hospital setting for 7.899 patients, Addiction Centers (Ser.T) for 163 and prison for 252. 4.999 and 4.368 outpatients were tested respectively in 2020 and in 2021, 7.208 and 7.048 hospitalized patients were tested in 2020 and in 2021; 180 and 122 subjects attending Addiction Centers were screened in 2020 and in 2021. 241 and 41 inmates were screened in 2020 and in 2021. In our hospital, we treated 246 patients of 320 (76.8%) in 2019, 156 of 222 (70.2%) in 2020 and 130 of 180 (72.2%) in 2021.

Conclusion: Following the COVID-19 outbreak, hepatitis C testing in Pordenone has gradually decreased by 18.5% (14.221 in 2019 compared to 11.580 in 2021). A drop of 43.7% in viremic patients and a decline of testing in prison were showed. A bad linkage to care and a decrease of treatments were noted. According to our data, interventions to improve HCV screening in key frail populations are urgently needed. Screening in hospitalized patients planning HCV free hospital should be considered too. An integrated simplifed network for testing and treatment between Hepatologysts and General Practitioners should be created. Laboratory-based HCV reflex testing is necessary to optimize linkage to care/treatment.

COVID-19: treatment strategies I

OP 1 REAL-LIFE DATA ON EARLY TREATMENT WITH ANTIVIRALS IN OUTPATIENTS WITH MILD COVID-19 SYMPTOMS

A. Rugova[1], G. Ghilardi[2], G. Lapadula[1,2], N. Squillace[1], A. Cappelletti[1], F. Sabbatini[1], A. Ranzani[1], M. Rossi[1], F. Iannuzzi[1], E. Pollastri[1], P. Columpsi[1], L. Bisi[1], E. Colella[1], S. Limonta[1], I. De Benedetto[1], N. Corti[1,2], G.M. Migliorino[1], S. Foresti[1], A. Soria[1], P. Bonfanti[1,2]

[1]Clinic of Infectious Diseases San Gerardo Hospital ASST Monza, Monza, [2]School of Medicine and Surgery University of Milano-Bicocca, Monza

Introduction: In clinical trials, early treatment with antivirals, either intravenous (remdesivir [REM]) or oral (nirmatrelvir/ritonavir [PAX]), reduced COVID-19 hospitalization rate in patients at risk of clinical progression. Real-life data are still limited.

Methods: Data on all the consecutive COVID-19 outpatients who received early treatment with antivirals in Infectious Disease Unit of San Gerardo Hospital were collected. Follow-up was assessed by phone call at least 10 days after treatment. Differences between treatment groups were assessed by t test or chi-square test, as appropriate. Logistic regression analysis was performed to determine risk factors for hospitalization.

Results: Among 114 outpatients (51 [45%] women) treated during the period January-March 2022, 59 (52%) received REM and 55 (48%) PAX. Table 1 shows differences between the two groups: as compared to PAX, REM recipients were younger, had more often an active onco-hematological disease, received treatment a bit later from the onset of symptoms.

After a median (IQR) follow-up of 38 (18-67) days, 10 hospitalizations were recorded (mean [IQR] time to hospitalization 9.5 [6-14] days): 9 (15%) in REM and 1 (2%) in PAX recipients (p=0.011). One patient, hospitalized for COVID-19-related respiratory failure 31 days after receiving REM, died 2 days later. Clinical worsening of COVID-19 was deemed to be the reason for hospitalization in 6 out of 9 REM recipients and 0 out of 1 PAX recipients. Mean time to symptoms resolution was shorter for PAX than for REM recipients: 6.2 (SD: 6) vs 9.2 (SD: 9.5) days, respectively (p=0.038). In a logistic regression analysis, adjusted for age, days since symptoms onset, presence of onco-hematological disease and type of antiviral, only active onco-hematological malignancy independently predicted hospitalization (Odds Ratio [OR] 9.53 95% Confidence Intervals [CI] 1.81-50.05 p=0.008), while a trend was observed for use of REM vs PAX (OR 6.99 95% CI 0.79-61.66 p=0.080).

Conclusions: Early treatment with antivirals in patients at high risk of COVID-19 progression in a real-life setting resulted in a hospitalization rate of 8.8%, with a pronounced difference in favor of PAX. Symptoms resolution was also shorter in PAX than in REM recipients. Data should be interpreted cautiously as REM recipients were more often suffering of onco-hematological malignancy, therefore more prone to clinical progression for a more fragile condition at baseline.

Further larger studies aimed at comparing the efficacy of different antiviral early treatments for preventing COVID -19 worsening in real life settings could help physicians in choosing the more appropriate treatment in this common clinical situation.

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OP 2 EFFICACY OF LICENSED MONOCLONAL ANTIBODIES AND ANTIVIRAL AGENTS AGAINST THE SARS-COV-2 OMICRON SUB-LINEAGES BA.1 AND BA.2 AND DELTA SUB-LINEAGE AY.4.2

L. Fiaschi[1], F. Dragoni[1], E. Schiaroli[2], A. Bergna[3], B. Rossetti[4], F. Giammarino[1], C. Biba[1], A. Gidari[2], A. Lai[3], C. Nencioni[4], D. Francisci[2], M. Zazzi[1], I. Vicenti[1]

[1]Department of Medical Biotechnologies, University of Siena, Siena, Italy, [2]Department of Medicine and Surgery, Clinic of Infectious Diseases, University of Perugia, Perugia, Italy, [3]Department of Biomedical and Clinical Sciences L. Sacco, University of Milan, Milan, Italy, [4]Infectious Disease Department, USL SUDEST, Toscana, Misericordia Hospital, Grosseto, Italy

Background: Newly emerging SARS-CoV-2 variants have the potential to escape monoclonal antibodies (mAbs) and antiviral drugs. We assessed the ex vivo inhibition of omicron and delta sub-lineages by sera obtained from patients treated with licensed mAb preparations including bamlanivimab/etesevimab (LYC), casirivimab/imdevimab (REG) and sotrovimab (SOT). In addition, we assessed the in vitro susceptibility of the same variants to remdesivir (RMD), nirmatrelvir (NRM) and EIDD-1931, the active form of molnupiravir (EIDD-1931).

Materials and Methods: Of 30 patients treated with mAbs (14 males, 59±18 years) one was asymptomatic while the others had mild symptoms. Patients were treated with LYC (n=10), REG (n=10), or SOT (n=10), 3.5±1.7 days from diagnosis. To test mAb activity, paired sera were obtained before (baseline) and 1 hour post mAb infusion and used in a live virus neutralization assay in VERO E6 cells with automated cell viability readout. To assess antiviral drug activity, viral isolates were used at MOI 0.005 to infect VERO E6 cells treated with 0.5 μM of P-GP inhibitor (CP-100356) and with decreasing concentrations of RMD, EIDD-1931 and NRM. Challenge viruses included the B.1 wild type (WT), delta, delta sub-lineage AY.4.2, omicron BA.1 and BA.2. Neutralizing antibody titers (ID50) and drug activity (IC50) were defined as the reciprocal value of the serum dilution and as the drug concentration, respectively, showing 50% protection of virus-induced cytopathic effect.

Results: All pre-infusion sera were negative for SARS-CoV-2 NtAb activity. In post-infusion sera REG, LYC and SOT showed activity against the WT (19,814 [17,459-23,471]; 6,792 [4,736-8,328] and 456 [259-592] ID50), the delta (58,858 [41,585-79,971]; 12,145 [10,840-18,667] and 1,023 [798-1,134] ID50) and the AY.4.2 (58,602 [42,941-82,960]; 11,067 [10,757-12,614] and 1,333 [708-1,714] ID50).

Notably, SOT was the only active treatment against the BA.1 (216 [118-233] ID50) while the BA.2 was neutralized by REG (185 [120-211] ID50) and SOT (9 [5-20] ID50) but not by LYC (Figure 1). No significant inter-variant IC50 differences were observed for EIDD-1931 (1.5 ±0.1/0.9±0.1/0.7±0.3/0.8±0.3/0.8±0.1 μM for WT/delta/AY.4.2.1/BA.1/BA.2 respectively); NRM (0.04±0.02/0.06±0.01/0.07±0.03/0.02±0.01/0.04±0.01 μM) or RMD (0.1±0.04/0.1±0.1/0.1±0.03/ 0.1±0.1/0.1±0.01).

Conclusions: Although designed based on the ancestral virus, licensed mAbs retain activity against the main delta variant and its sublineage AY.4.2, which has been circulating in Italy. The BA.1 and BA.2 variants fully escape the LYC cocktail, while REG retains partial activity only against BA.2 with a fold-change decrease (FCD) of 131±45 with respect to WT. Interestingly, SOT retains significant activity against BA.1 (2.8±1 FCD) and BA.2 (23±9 FC on the 5 paired sera with measurable activity). Since omicron has rapidly replaced past variants, the mAbs arsenal should be updated accordingly. By contrast, currently approved antiviral drugs are not affected by SARS-CoV-2 variability at this time.

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OP 3 SARILUMAB PLUS STANDARD OF CARE VERSUS STANDARD OF CARE FOR THE TREATMENT OF SEVERE COVID-19: A PHASE 3, RANDOMIZED, OPEN-LABELED, MULTI-CENTER STUDY (ESCAPE STUDY)

I. Mastrorosa[1], R. Gagliardini[1], F.V. Segala[2], A. Mondi[1], P. Lorenzini[1], C. Cerva[1], E. Taddei[2], F. Bai[3], M. Negri 2, C. Pinnetti[1], S. Cicalini[1], R. Murri[2], V. Mazzotta[1], M. Camici[1], S. Mosti[1], T. Bini[3], A. Beccacece[1], E. Milozzi[1], M. Iannetta[4], M. Fusto[1], M.M. Plazzi[1], M. Lichtner[5], M. Fantoni[2], M. Andreoni[4], L. Sarmati[4], R. Cauda[2], E. Nicastri[1], A. D'Arminio Monforte[3], F. Palmieri[1], A. Cingolani[2], A. Antinori[1]

[1]Lazzaro Spallanzani National Institute for Infectious Diseases, Rome, Italy, [2]Fondazione Policlinico A. Gemelli IRCCS- Università Cattolica S. Cuore, Rome, Italy, [3]Azienda Ospedaliera San Paolo, Milan, Italy, [4]University of Rome Tor Vergata, Rome, Italy, [5]Sapienza University of Rome, Italy, Polo Pontino

Background: Sarilumab is considered as an alternative to tocilizumab in the treatment of severe COVID-19. However, there are less robust evidences for its efficacy. Aim was to evaluate the efficacy of sarilumab, combined with standard of care (SOC), in patients affected by severe COVID-19 pneumonia.

Methods: Open-label, phase 3, randomized trial assessing clinical efficacy and safety of intravenous sarilumab in patients with severe COVID-19, at 5 clinical centers in Italy. We included hospitalized patients with SARS-CoV-2 infection and pneumonia, in severe or critical condition (excluding mechanically ventilated). Patients were randomized 2:1 to receive sarilumab 400 mg plus SOC (arm A) or to continue SOC (arm B). The primary endpoint was time to clinical improvement of 2 points on a 7-point category ordinal scale, ranging from 1 (discharged with resumption of normal activities) to 7 (death). Patients were stratified according to baseline disease severity (PaO2/FiO2 ratio < or ≥ 200 mmHg), C reactive protein (CRP < or ≥ 7 mg/dL) and lymphocytes count (< or ≥ 870/mmc). The key secondary endpoint was time to death. Adverse events (AEs) and secondary infections were evaluated as safety outcomes. We used Kaplan Meier method and log-rank test to compare the primary outcome between the two arms, and Cox regression stratified by clinical center to estimate the hazard ratio (HR) of primary endpoint.

Results: Of 191 patients screened, 176 were assigned to arm A (121) and B (55). A similar proportion of patients was treated with steroids and remdesivir. 58/121 (48%) patients underwent to a second dose of sarilumab 12 hours after the first dose. Median time to clinical improvement was 13 days (95%CI 11-15) in arm A and 14 (12-21) in arm B, log-rank p=0.504. At day 30, no significant differences in the primary endpoint were found between the arms (88% [95% CI 81-94] in arm A vs 85% [74-93], HR 1.08 [0.8-1.6] in arm B; log-rank p=0.50). After stratifying for inflammatory parameters, the probability of improvement seemed greater in arm A than B, for the strata with CRP <7 mg/dL (88% [95% CI 77-96] vs 79% [63- 91], HR 1.55 [0.9-2.6]; log-rank p=0.049) and with lymphocytes <870/mmc (90% [79-96]) vs (73% [55-89], HR 1.53 [0.9-2.7]; log-rank p=0.058). There were no significant differences in death probability and in the rates of AEs, serious AEs and secondary infections. See figure for Kaplan Meier survival curves.

Conclusions: In our population, efficacy of sarilumab in patients with severe COVID-19 was not demonstrated, even if some benefits were shown in those treated at an early stage of the disease with lower inflammatory burden. The low rate of concomitant corticosteroid use among the study participants, could partially explain our results. Further trials are needed for identifying targeted subgroups in order to maximize benefit of this treatment.

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COVID-19: treatment strategies I

OP 4 SAFETY AND EFFICACY OF ANTIVIRAL AGENTS IN SARS-COV-2 INFECTED PATIENTS: A REAL-LIFE EXPERIENCE

A. De Vito, A. Colpani, A. Bitti, V. Manca, B. Zauli, M.C. Meloni, M. Fois, L. Denti, S. Bacciu, C. Marcia, I. Maida, S. Babudieri, G. Madeddu

Unit of Infectious Diseases, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy

Introduction: Since the start of the pandemic, several treatments have been proposed against SARS-CoV-2 infection. Currently, three antiviral agents have been approved by the Italian Medicine Agency (AIFA) for patients with noneed for oxygen therapy: molnupiravir, nirmatrelvir/ritonavir(r), and remdesivir (three days courses). Therefore, we aimed to evaluate the efficacy and safety of these three different agents.

Methods: We conducted a retrospective cohort study including all people treated with molnupiravir, nirmatrelvir/r or remdesivir between the 10th of January and the 20th of March 2022 at the University Hospital of Sassari, Italy. According to AIFA indications, treatment was prescribed in patients with recent symptoms onset (≤five days), no need for oxygen supplementation, and at risk for disease progression.

Results: We included 225 people with a mean age of 69.7±16.0 years; 22 (9.7%) patients experienced disease progression during the follow-up. Factors associated with disease progression were being older, having a higher comorbidity burden, hospital-acquired infection, and dyspnea at baseline. The main characteristics are summarized in Table 1.

Among 225, 188 (83.6%) patients were treated with molnupiravir, 15 (6.7%) with nirmatrelvir/r, and 22 (9.8%) with remdesivir. Patients treated with nirmatrelvir/r were younger and had a lower comorbidity burden. More than half of people treated with remdesivir acquired SARS-CoV-2 infection during the hospital stay. Patients' characteristics by antiretroviral agents are summarized in Table 2.

In the multivariate analysis, older age and dyspnea at symptoms' onset were associated with an increased risk of progression. On the contrary, early treatment (defined as the start of treatment within three days since symptoms' onset) and outpatient treatment were associated with a reduced risk of disease progression (Table 3).

Overall, 16 adverse events were reported, 12 (6.4%) in people treated with molnupiravir, three (20%) in people treated with nirmatrelvir/r, and one (4.6%) in people treated with remdesivir. However, these led to treatment discontinuation only in three cases (two rashes and one transaminases increase) (Figure 1).

Conclusions: Our results confirm the efficacy and safety of antiviral treatment for SARS-CoV-2 infection in a real-life setting and showed a risk of disease progression <10%. Of note, our cases were older and had a higher comorbidity burden when compared to those enrolled in clinical trials. Regarding timing, our data support the crucial role of early treatment start.

COVID-19: treatment strategies I

OP 5 EFFICACY OF EARLY ANTIVIRAL THERAPIES AMONG HIGH-RISK PATIENTS WITH MILD TO MODERATE COVID-19

S. Amadasi[1], M. Degli Antoni[1], P. Grechi[2], A. Tregambe[2], S. Arsuffi[1], F. Pennati[1], M.A. Forleo[1], F. Castelli[1], E. Quiros-Roldan[1]

[1]Department of Clinical and Experimental Sciences, Unit of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili di Brescia, Brescia, [2]Unit of Infectious and Tropical Diseases, ASST Spedali Civili di Brescia, Brescia

Background: Patients with comorbidities such as obesity, oncohematological disease, chronic kidney disease, cardiovascular disease, Chronic Obstructive Pulmonary Disease (COPD), immunodeficiencies and diabetes have an increased risk of progression to severe COVID-19. In December 2021 Italian Medical Agency (Agenzia Italiana del Farmaco, AIFA) authorized the emergency use of oral antiviral molnupiravir and remdesivir for early treatment of patients with mild-to-moderate COVID-19 at high-risk for progression. In January 2022 a combination of another oral antiviral, nirmatrelvir, plus ritonavir, was approved. We aim to describe characteristics and outcomes of patients treated with remdesivir, molnupiravir and nirmatrelvir/ritonavir.

Material and Methods: We conducted a retrospective observational study including patients who started an antiviral therapy with remdesivir, molnupiravir or nirmatrelvir/ritonavir from 1st January until 15th March 2022. We evaluated efficacy of these therapies (in terms of persistence of symptoms, time to negativization, hospitalization and death) after one day, one month and three months.

Results: We treated 140 patients, 35 with remdesivir, 57 with molnupiravir and 48 with nirmatrelvir/ritonavir. Median age was 58, 68 were males (48.6%). Ten patients (7%) had not received any dose of vaccine, while 102 patients (72.9%) were fully vaccinated. Main risk factors for progression to severe COVID-19 were cardiological disease, obesity and immunodeficiencies (Table 1). The majority of patients reported complete resolution of symptoms 24 hours after having started antiviral therapy (68.6% in the remdesivir group, 79% in the molnupiravir group and 62.4% in the nirmatrelvir/ritonavir group). More than half patients treated with molnupiravir and nirmatrelvir/ritonavir (62% and 56.8% respectively) had a nasopharyngeal swab negativization between 7 and 14 days, while 65.7% of patients treated with remdesivir obtained negativization after more than 14 days. During the follow-up period, no patient died, one patient treated with molnupiravir was hospitalized 24 hours after the beginning of antiviral therapy (Table 2). This patient was a 83 year-old-man, fully vaccinated, affected by cardiovascular and hematological disease and the admitting diagnosis was acute heart failure. No therapies have been interrupted because of side effects. Remdesivir and molnupiravir were very well tolerated, whereas 8 patients treated with nirmatrelvir/ritonavir (16.7%) developped mild gastrointestinal symptoms (dysgeusia and diarrhoea).

Conclusions: Progression of disease is very uncommon in patients treated with early antiviral therapies. In our case series no patient died or was hospitalized for COVID-19. Further studies are necessary to compare the evolution of disease between patients who were treated and patients who were not treated with antivirals to understand the real efficacy of these early therapies.

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COVID-19: treatment strategies I

OP 6 REAL LIFE EXPERIENCE ON THE USE OF ANTI-SARS-COV-2 MONOCLONAL ANTIBODIES TO PREVENT COVID-19 PROGRESSION AMONG INPATIENTS AND OUTPATIENTS: A MONOCENTRIC EXPERIENCE

C. Leanza[1], S. Di Bari[1], N. Perrotta[2], L.A. Fiorito[2], R. Gentile[3], V. Cioffi[2], G. Casini[2], F. Cogliati Dezza[1], D. Fago[1], C. Ajassa[1], G. Iaiani[1], R. Lobello[2], E.M. Proli[2], C.M. Mastroianni[1], G. Russo[1]

[1]Infectious Diseases Unit, AOU Policlinico Umberto 1st Sapienza University, Rome, Italy, [2]Pharmacy, AOU Policlinico Umberto 1st, Rome, Italy, [3]Pharmacy, G. D'annunzio University, Chieti Pescara, Italy

Background: Different studies showed that monoclonal antibodies against the spike protein of SARS-CoV-2 are effective in reducing the risk of disease progression (1-3), although more evidences are needing (4), above all on the efficacy to different viral variants (5). Thus, real-life data are needing in order to confirm the efficacy of this treatment to prevent severe COVID-19.

Material and Methods: We performed a real-life, retrospective, monocentric study on SARS-CoV-2 symptomatic outpatients and inpatients receiving monoclonal antibodies from March 2021 to January 2022. All patients received available monoclonal antibodies (bamlanivimab-etesevimab or casirivimab-indevimab or sotrovimab) according to the dominant known circulating viral variant (6). All patients fulfilled criteria for severe COVID-19 progression established by the Italian Pharmaceutic Agency (AIFA) (7). Mortality, timing of viral clearance and safety were evaluated in all patients with completed data.

Results: A total of 114 hospitalized (median age 68 years, 38.6% female) and 327 non hospitalized (median age 61 years, 39.4% female) patients were included in this study. The vaccination status was known for all participants: 50% (n=57; 40% of them within < 4 months) and 58.7% (n=192; 56% of them within < 4 months) were vaccinated against SARS-CoV-2 among inpatients and outpatients respectively. The main comorbidities were cardiovascular diseases (CVDs) (57%) and Diabetes (21%) among inpatients; CVDs (32.4%) and immunodeficiency (24.7%) among outpatients.

Among inpatients, the majority (n=74, 64.9%) had as cause of hospitalization COVID-19, the remaining (n=40, 35.1%) became infected during hospital stay. The overall mortality among inpatients was 15.7% (n=18/114), being 13.5% (n=10/74) among those admitted because of COVID-19, and 20% (n=8/40) among those becoming infected during their hospital stay for other underlying diseases. The median length of hospital stay was 18 days - being longer (30.9 days) among those who developed COVID-19 during their hospital stay for other underlying medical conditions – and the median time to virologic clearance was 24 days.

Among outpatients, only 7 (2.1%) individuals showed worsening of clinical symptoms requiring admission to hospital but all fully recovered, and the median time to virologic clearance was 17 days. No deaths were reported among outpatients.

Concerning the safety of anti-SARS-CoV-2 monoclonal antibodies, adverse events were reported in 7% and 14% of inpatients and outpatients respectively, with reversible fever being the most common reported event.

Conclusions: In order to better asses the efficacy of different anti-SARS-CoV-2 monoclonal antibodies, further studies taking in account the dominant circulating viral variants and comparison to control groups are needing. Overall, our real-life experience shows that monoclonal antibodies are safe and play an important role to prevent COVID-19 progression, mainly among outpatients.

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COVID-19: treatment strategies II

OP 7 USE OF SOTROVIMAB IN A COHORT OF PREGNANT WOMEN WITH A HIGH RISK OF COVID 19 PROGRESSION: A SINGLE-CENTER EXPERIENCE

L. Frallonardo[1], A. Vimercati[2], R. Novara[1], D.F. Bavaro[1], G. Brindicci[1], C.R. Santoro[1], I. Ferrante[2], G. Chiarello[2], C. Lepera[2], M. Mongelli[2], R. Cicinelli[2], F. Di Gennaro[1], E. Cicinelli[2], A. Saracino[1]

[1]Clinic of Infectious Diseases, University of "Aldo Moro", Department of Biomedical Sciences and Human Oncology, Bari, Italy, [2]Clinic of Obstetrics & Gynaecology, University of "Aldo Moro", Department of Biomedical Sciences and Human Oncology, Bari, Italy

Background: Neutralizing monoclonal antibodies (mAbs) have been shown to reduce disease progression in patients with SARS CoV2 infection, particularly in subjects with predisposing underlying conditions, including pregnancy. Unfortunately, there is no literature on the use of Sotrovimab in pregnant women. Herein we present a case series of pregnant women who received mAbs with Sotrovimab following the Italian Drug Agency (AIFA) indications.

Methods: Since February 1st, 2022, all pregnant women - regardless of gestational age - admitted to Obstetrics and Gynaecology of Policlinico Hospital, University of Bari with a positive nasopharyngeal NAAT for SARS-CoV2 were screened against the AIFA indication for Sotrovimab and, if eligible, were proposed for treatment. The study was approved by the local Ethics Commitee. All women who consented to the administration of Sotrovimab were enrolled in the study and followed until delivery. Data on COVID-19, pregnancy, delivery, newborn status and adverse events were collected. Preliminary data of patients enrolled until April 5, 2022, are presented.

Result: From February 1 to April 5, 45 pregnant women were screened. 38 patients were eligible, 13 of them (29%) denied their consent, in 15 cases (33%) the drug was temporarily unavailable and the remaining 10 (22%) patients were treated with Sotrovimab. Out of these ten patients (median age: 33ys), 6 (60%) were in the 3rd and 4 (40%) in the 2nd trimester of pregnancy, respectively. Risk factors for disease progression were obesity (n.5), hematological disease (n.2), hypertension (n.1), and autoimmune disease (n.1) (Table 1). None of the ten patients experienced adverse reactions due to Sotrovimab and all had a good clinical outcome not requiring either oxygen therapy or admission to Intensive Care Unit. Furthermore, evaluating the pre- and post-infusion clinical status and the haematochemical profile, a reduction in D-dimers ($p<0.01$) and an increase in SARS CoV2 antibodies ($p<0.01$) during the 72 hours following the infusion were observed. In addition, 5 out of 10 women have given birth to date and all newborns were in generally good conditions, with normal birth weight and SARS CoV2 negative.

Conclusions: Our data, to our knowledge the first on the use of Sotrovimab in pregnant women, showed a good safety and efficacy drug profile, highlighting a potential crucial role of this strategy in preventing COVID-19 disease progression.

COVID-19: treatment strategies II

OP 8 REMDESIVIR DOES NOT INFLUENCE SARS-COV-2 RNA VIRAL LOAD KINETICS IN NASOPHARYNGEAL SWAB SPECIMENS OF COVID-19 HOSPITALIZED PATIENTS: A REAL-LIFE EXPERIENCE

L. Campogiani[1,2], M. Iannetta[1,2], A. Di Lorenzo[1,2], M. Zordan[1,2], L. Coppola[1,2], M. Compagno[1,2], V. Malagnino[1,2], E. Teti[1,2], M. Andreoni[1,2], L. Sarmati[1,2]

[1]Department of System Medicine, Tor Vergata University, Rome, Italy, [2]Infectious Disease Clinic, Policlinico Tor Vergata, Rome Italy

Background: Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) causes coronavirus disease 2019 (COVID-19). Viral nucleic acid detection by reverse transcription polymerase chain reaction (RT-PCR) on a nasopharyngeal (NPh) swab is the diagnostic gold standard, and the cycle threshold (Ct) can be used as a proxy of viral load. Remdesivir demonstrated inhibition of SARS-CoV-2 replication in vitro, receiving an emergency approval for COVID-19 treatment.

Aim of this study was to evaluate the effect of remdesivir on SARS-CoV-2 viral decay on NPh swab, through Ct variation analysis over time, in a real-life setting.

Methods: Adult patients, hospitalized at the Infectious Diseases clinic of Policlinico Tor Vergata, Rome (Italy) from March 5th to July 30th 2020 and from September 2nd to December 31st 2020, with a positive RT-PCR for SARS-CoV-2 on a NPh swab, were included in a retrospective single-center study. Ct values obtained from RT-PCR targeting Envelope (E), Nucleocapsid (N) and RNA-dependent RNA-Polymerase (RdRP) genes of SARS-CoV-2, on the first NPh swab performed on admission (T0) and after 7 days (± 2 days) (T7), were considered.

Results: 513 patients were evaluated. 266 patients had a NPh swab performed at T0 and T7 with Ct values reported for each of the three genes. 13 patients were excluded, because they received with IL-6 inhibitors. Final population consisted of 253 individuals (Table 1).

67 patients received lopinavir/ or darunavir/ritonavir (PI group), 123 received remdesivir (R group) and 63 received no antiviral treatment (NT group). No significant differences were recorded in time from symptoms' onset to T0 NPh swab collection, amongst the three treatment groups (Table 1). Median Ct values of the N gene were significantly lower on both T0 and T7 NPh swabs in the remdesivir group (T0 $p<0.001$; T7: $p=0.019$). No significant differences over time were noted in the Ct variation (T7-T0) of any of the analyzed genes, throughout the three groups (figure 1A).

Given the greater percentage of severe patients in the remdesivir group, additional delta Ct analysis were performed separately for non-severe and severe patients: no significant differences over time were noted in the Ct variation (T7-T0) of any of the analyzed genes, throughout the three treatment groups (table 2A and 2B).

When stratified by outcome, in survivors and non-survivors, median Ct values of the E, N and RdRP genes were significantly lower in the non-survivors group compared to survivors at both T0 and T7 ($p<0.01$). Ct variation was significantly reduced in the non-survivors group compared to survivors (delta Ct E gene $p=0.084$; delta Ct N gene $p=0.050$; delta Ct RdRP gene $p=0.018$) (Figure 1B)

Conclusions: Although SARS-CoV-2 RNA decay on NPh swab was slower in COVID-19 patients with a poorer outcome, no differences were observed in NPh swab viral decay after stratification according to the antiviral regimen received (either remdesivir or protease inhibitors, or no antivirals).

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COVID-19: treatment strategies II

OP 9 ANTI-SPIKE MONOCLONAL ANTIBODIES TO PREVENT HOSPITALIZATION IN MILD COVID-19: PRELIMINARY DATA OF AN ONGOING LARGE OBSERVATIONAL MULTICENTER STUDY (CONDIVIDIAMO)

A. Soria[1], G. Ghilardi[2], F. Graziano[3], S.V. Benatti[4], G. Lapadula[1,2], A. Ferraresi[5], P. Brambilla[5], D. Pocaterra[6], M.E. Quiros Roldan[7], M. Franzetti[8], L. Bradanini[9], A. Cappelletti[1], A. Rugova[1], ML. Borghesi[1], S. Piconi[9], S. Rusconi[8,10], F. Castelli[7], P. Morelli[6], A. Pan[5], M. Rizzi[4], S. Galimberti[3], M.G. Valsecchi[3], P. Bonfanti[1,2]

[1]San Gerardo Hospital ASST Monza, Monza, [2]School of Medicine and Surgery University of Milano-Bicocca, Monza, [3]Bicocca Bioinformatics Biostatistics and Bioimaging Center B4 School of Medicine and Surgery University of Milano-Bicocca, Monza, [4]ASST Papa Giovanni XXIII, Bergamo, [5]ASST Cremona, Cremona, [6]Humanitas Clinical and Research Center, Milan, [7]ASST Spedali Civili University of Brescia, Brescia, [8]Legnano Hospital ASST Ovest Milanese, Legnano, [9]ASST A Manzoni, Lecco, [10]DIBIC "Luigi Sacco" Università degli Studi di Milano, Milan

Introduction: Anti-SARS-CoV-2 monoclonal antibodies (mAbs) reduce COVID-19 hospitalizations and deaths in clinical trials, but appropriate use in the real life, logistically complex, is yet to be described.
Methods: CONDIVIDIAMO is a multicenter observational study enrolling patients treated with mAbs in Lombardy. All patients were followed for 28 days since mAbs treatment. Among those treated as outpatients, rates of death, hospitalization or emergency room visit were evaluated. Characteristics of those who were/were not hospitalized within 28 days of treatment were compared by Mann-Whitney U test for continuous data and χ^2 test for categorical data. Moreover, the outcome of inpatients receiving mAbs as part of the anti-SARS-CoV-2 treatment during hospitalization was described.
Results: Since March 2021, in 7 centers, 464 subjects received mAbs as outpatients: 216 (46.6%) bamlanivimab (206 in combination with etesevimab), 85 (18.3%) casirivimab/imdevimab, 163 (35.1%) sotrovimab. Median (IQR) age was 67 (54-75) years, 192 (41%) were women. All patients had at least 1 risk factor for COVID-19 progression, the most common being age >65 years (214 [46%]), cardiovascular disease (156 [34%]), immunodeficiency (154 [33%]) and obesity (97 [21%]). 313 patients (67.4%) had received at least 1 shot of COVID -19 vaccination before mAbs treatment. The median (IQR) time between onset of symptoms and mAbs receipt was 4 (3-6) days.
After 28-day follow-up, 21 subjects were hospitalized (cumulative 28-day incidence 5.5%, 95%CI 3.1-7.8), of whom 1 had died. The median (IQR) time to hospitalization was 5 (2-7) days. Table 1 shows the characteristics of the patients according to hospitalization outcome by 28 days. Hospitalized patients had higher prevalence of diabetes, received more frequently casirivimab/imdevimab and less frequently sotrovimab, had more frequently 3 or more risk factors for clinical progression, received mAbs earlier in the study than those who were not hospitalized. Time between symptoms and mAbs receipt did not seem to influence outcome: the proportion of hospitalization in patients receiving mAbs within or after 3 days from onset of symptoms were 6.3% (10/158) and 4.4% (11/249), respectively.
In the sub-study of 86 hospitalized patients who received mAbs as part of anti-SARS-CoV-2 treatment, 3 (3.5%) died after a median (IQR) of 8 (6-9.5) days and the remaining have been discharged alive after a median (IQR) of 11 (8-16) days.
Discussion: Hospitalization rate in mAbs recipients with mild COVID-19 in a large real-life cohort was generally low, although higher than what seen in clinical trials, probably because of a higher age and comorbidity in real world than in controlled clinical trials. Patients who progressed to hospitalization despite mAbs had a higher morbidity burden. Differences between mAbs could be influenced by many factors, notably the calendar period and the shift of SARS-CoV-2 variants, thus they should be interpreted cautiously.

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COVID-19: treatment strategies II

OP 10 EARLY USE OF SHORT-COURSE REMDESIVIR AND MONOCLONAL ANTIBODIES MAY REDUCE THE RISK OF DISEASE PROGRESSION IN HOSPITALIZED PATIENTS WITH COVID-19: A SINGLE CENTER RETROSPECTIVE STUDY

D.F. Bavaro[1], L. Diella[1], A. Belati[1], G. Brindicci[1], F. Balena[1], D. Fiordelisi[1], M.F. Mariani[1], F. Signorile[1], G. Metrangolo[1], L. De Santis[1], V. Spada[1], M. Camporeale[1], A. Dargenio[1], G. Nicoletta[2], F. Di Gennaro[1], M. Dell'Aera[2], A. Saracino[1]

[1]Clinic of Infectious Diseases, University Hospital of Bari, Bari, Italy, [2]Hospital Pharmacy Department, University Hospital of Bari, Bari, Italy

Introduction: Recent data suggest that a three-day short-course remdesivir (sc-REM) and monoclonal antibodies (mAbs) may reduce the risk of hospitalization when administered in outpatients with mild-moderate COVID-19. However, data are conflicting about their in-hospital use during the early stage of disease.
Accordingly, the aim of this study was to assess the efficacy of mAbs and sc-REM as adjunctive therapies compared to the standard of care for preventing the COVID-19 disease progression in the hospital setting.
Methods: Since November 01st 2022, the use of mAbs (Casirivimab/Imdevimab until 15th December, and Sotrovimab thereafter) and sc-REM (since January 12th, 2022) were included in our internal protocol for hospitalized patients. Particularly, sc-REM was prescribed to all subjects without need of oxygen therapy and presence of risk factors for severe COVID-19, while mAbs were given in case of lack of vaccination or absence of IgG anti-SARS-CoV2. In case of severe immune-compromission, or multiple risk factors in subjects with negative serology, the combination therapy was suggested.
All consecutive patients treated at our Unit for COVID-19 since July 1st, 2021, to March 15th, 2022, were retrospectively enrolled.The primary endpoint was disease progression to severe COVID-19 (P/F < 200). Secondary endpoints were the overall in-hospital mortality and incidence of adverse events.
Results: A total of 331 subjects were included; median (q1-q3) age was 71 (51 - 80) years, males in 52% of cases. During hospitalization, 78 (23%) of them developed a severe COVID-19 (see Table 1). All cause in-hospital mortality was 14%, significantly more frequent in those with disease progression (36% vs 7%, p <.001). No severe adverse events were recorded with antivirals or mAbs.
By performing a univariate and multivariate logistic regression, independent predictors of disease progression were age (aOR=1.03, 95%CI=1.01-1.05, p<.001) and severe secondary infections during hospitalization (aOR=3.61, 95%CI=1.49-8.74, p=.004), while being fully vaccinated (aOR=0.08, 95%CI=0.04-0.16, p<.001) and receiving sc-REM (aOR=0.35, 95%CI=0.15-0.83, p=.017) were protective.
Interestingly, by repeating the same analysis on the subgroup of patients with lack/uncomplete vaccination or use of anti-CD20 for hematologic malignancies (Table 2), age was confirmed as the only independent predictor of disease progression, while both antiviral therapy and mAbs resulted protective. In particular, the analysis showed that, in this setting, combination therapy was the most effective strategy (aOR=0.26, 95%CI=0.09-0.80, p=.032).
Conclusions: The early use of sc-REM may reduce the risk of severe lung failure also in subjects hospitalized with COVID-19. Importantly, in those with lack/uncomplete vaccination or use of anti-CD20 for hematologic malignancies both mAbs and sc-REM may be beneficial, particularly if used in combination.

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COVID-19: treatment strategies II

OP 11 CONTINUOUS POSITIVE AIRWAY PRESSURE IN SARS-COV-2 ASSOCIATED ACUTE RESPIRATORY DISTRESS SYNDROME: TIMING TO MAXIMIZE RESULTS

R. Nevola[1,3], A. Russo[2], S. Scuotto[2], S. Imbriani[1], C. Aprea[1], M. Abitabile[1], D. Beccia[1], C. Brin[1], C. Carusone[1], F. Cinone[1], G. Cirigliano[1], S. Colantuoni[1], D. Cozzolino[1], G.Cuomo[1], M. Del Core[1], K. Gjeloshi[1], A. Marrone[1], G. Medicamento[1], L. Meo[1], F. Nappo[1], A. Padula[1], P.C. Pafundi[1], R. Ranieri[1], C. Ricozzi[1], L. Rinaldi[1], C.P. Romano[1], R. Ruocco[1], C. Ruosi[1], A. Salvati[2], F.C. Sasso[1], A. Sellitto[1], P. Sommese[1], A. Villani[1], N. Coppola[2], L.E. Adinolfi[1]

[1]Internal Medicine Unit, Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Naples, Italy, [2]Infectious Diseases Unit, Department of Mental Health and Public Medicine, University of Campania "Luigi Vanvitelli", Naples, Italy, [3]Internal Medicine and Hepatology Unit, Betania Evangelical Hospital, Naples, Italy

Background: Acute respiratory distress syndrome (ARDS) is one of the most severe complications of SARS-CoV -2 infection. Although not universally accepted, CPAP has proven efficacy in the management of SARS-CoV-2-related ARDS, but the most appropriate timing for start CPAP is unknown.
Methods: We conducted a prospective multicentre study including all patients with moderate to severe SARS-CoV -2-related ARDS. Of 512 patients admitted, 128 underwent CPAP and divided into two groups according to the severity of ARDS (assessed by PaO2/FiO2-P/F) at which CPAP was started: moderate ARDS if 100>P/F≤200, severe ARDS if P/F≤100. Patients underwent CPAP in a moderate stage were divided into two subgroups: 150>P/F≤200 and 100>P/F≤150. The outcomes were: in-hospital mortality, oro-tracheal intubation (OTI) and days of hospitalization.
Results: Patients underwent CPAP in a moderate stage had a significantly lower in-hospital mortality rate (13,4% vs 29,0%,p=0,044) and days of hospitalization (14 vs 15 days,p=0.038) than patients underwent CPAP in a severe stage. In contrast, early CPAP (P/F 151-200) didn't demonstrate significant differences in outcomes compared to treatment starting when P/F range was 101-150. In multivariate analysis, predictors of NIV failure were: age and need for continuous ventilation.
Conclusions: Starting CPAP in a moderate stage of ARDS results in significant reduction in in-hospital mortality rate and in days of hospitalization compared to a late start in a severe stage. Early CPAP (P/F>150) doesn't lead to a significant reduction in mortality rate and OTI, potentially resulting in ventilator-associate lung injury and increasing costs. Advanced age and need for continuous ventilation are independent predictors of NIV failure.

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COVID-19: treatment strategies II

OP 12 EPCOT: AN OPEN-LABEL, CONTROLLED, RANDOMIZED CLINICAL TRIAL ON THE EFFICACY OF EARLY PRONE-POSITIONING IN PATIENTS WITH MILD PNEUMONIA DUE TO SARS-COV-2

M. Fezzi[1], G. Lapadula[1,2], L. Antolini[1], A. Soria[2], A. Rugova[2], M. Rossi[2], L. Bisi[2], F. Sabbatini[2], A. Cappelletti[2], S. Limonta[2], A. Ranzani[2], I. De Benedetto[2], N. Corti[1,2], P. Bonfanti1[,2]

[1]Università degli Studi di Milano Bicocca - Dipartimento di Medicina e Chirurgia, Monza, [2]ASST Monza Ospedale San Gerardo, Monza

Background: Prone positioning (PP) is widely recognized as an effective treatment for Acute Respiratory Distress Syndrome patients requiring mechanical ventilation (MV). However, few studies have so far explored its use in awake, spontaneously-breathing patients with Covid-19 pneumonia.

Materials and Methods: In an open-label randomized controlled trial, we enrolled adult patients hospitalized due to Covid-19 pneumonia, defined as a positive molecular test for SARS-CoV-2 RNA and at least one among the following: (i) radiological evidence of pneumonia, (ii) room air arterial oxygen tension <80 mmHg or peripheral saturation (SpO2) <94%, (iii) need for oxygen supplementation. Need for MV, non-invasive ventilation (NIV), PaO2/FiO2 ratio <200 and any contraindication to PP were exclusion criteria.

Patients were randomized 1:1 to awake PP (≥3 hours twice daily) on top of standard of care versus standard of care only (controls). Time to the primary composite outcome including death, need for NIV or MV was compared between groups by a survival analysis. Event rates were calculated and compared by an exponential survival model. Using the same methods, time to oxygen weaning was also explored.

Results: Among 54 enrolled patients, 25 were adjudicated to PP and 29 to the control group. The mean age was 59.4 years (SD 15.6); 33 (61%) were male, 26 (48%) were vaccinated against Covid-19 with at least one dose. The most common comorbidities were hypertension (28%), history of solid or hematological malignancy (13% and 9%) and iatrogenic immunosuppression (18%). The mean time since symptom's onset was 8.6 days (SD 3.6). Suboptimal adherence to adjudicated treatment was observed: at follow-up, only 56%, 60% and 54% of patients randomized to PP maintained it for ≥3 hours on day 1, 3 and 7, compared to 0%, 8% and 6.7% in the control group.

On day 28, 50 patients (93%) were discharged alive, 2 had died and 2 were still hospitalized; 10 (19%) of them had required NIV and 3 (6%) MV.

In an intention to treat analysis (Fig.1A), 10/25 (40.0%) patients in PP group experienced the primary composite outcome versus 3/29 controls (10.3%), accounting for an incidence of 44.6 (95% CI 23.9-82.9) vs. 8.3 (95% CI 2.69-25.8) events per 100 person-weeks of observation (P=0.001). In the as-treated analysis, which included in the PP group only patients who actually maintained PP, no difference was found between the two groups (P=0.525, Fig.1B).

No differences were found between the two groups regarding time to oxygen weaning, either in the intention to treat analysis (P=0.387, Fig.2A) or in the as-treated analysis (P=0.594, Fig.2B).

Conclusions: We observed no evidence of any clinically significant beneficial effects of PP in awake patients with mild Covid-19 pneumonia. Given the small sample size and the incomplete adherence to PP, further analyses are warranted.

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Treatment of naive PLWH: current strategies and rapid start of ART

OP 13 REASONS FOR CHOOSING DRV/COB/FTC/TAF IN ART-NAÏVE AND ART-EXPERIENCED PATIENTS: DATA FROM THE ICONA COHORT

A. Tavelli[1], D. Tomasoni[2], N. Gianotti[3], R. Gagliardini[4], E. Bruzzesi[3], P. Milini[5], B. Menzaghi[6], G. Lapadula[7], P. Cinque[8], L. Taramasso[9], A. Antinori[4], A. d'Arminio Monforte[2]

[1]ICONA Foundation, Milan, Italy, [2]Clinic of Infectious and Tropical Diseases, ASST Santi Paolo e Carlo, Department of Health Sciences, University of Milan, Milan, Italy, [3]Department of Infectious Diseases, IRCCS San Raffaele Scientific Institute, Milan, Italy, [4]National Institute for Infectious Diseases "L. Spallanzani" IRCCS, Rome, Italy, [5]Infectious Diseases Unit, Macerata Hospital, Macerata, Italy, [6]Unit of Infectious Diseases, ASST della Valle Olona, Busto Arsizio Hospital, Busto Arsizio, Italy, [7]Clinic of Infectious Diseases, San Gerardo Hospital - ASST Monza, University of Milano-Bicocca, Monza, Italy, [8]Department of Infectious Diseases, IRCCS San Raffaele Scientific Institute, San Raffaele Vita-Salute University, Milan, Italy, [9]Infectious Diseases Unit, Ospedale Policlinico San Martino-IRCCS, Genoa, Italy

Background: Despite the preferential use of unboosted INSTI drugs, darunavir (DRV) is still recommended in all major guidelines and widely used. This study provides insight into the characteristics of People Living with HIV (PLWH) who started darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) in a real-world setting.
Materials and Methods: Observational study using data from the multicentre Italian ICONA Cohort starting from January 2017. PLWH who started from ART-naive D/C/F/TAF, 3TC/DTG, FTC/TAF/INSTI or FTC/TAF/RPV regimen or PLWH who switched from any other regimen to D/C/F/TAF were included, regardless of HIV-RNA and the type of regimen (single and multi-tablet). The objective was to evaluate predictors of starting D/C/F/TAF from ART-naïve vs several comparator groups (1. FTC/TAF/INSTI; 2. FTC/TAF/RPV; 3. 3TC/DTG) or switching to D/C/F/TAF for the first time from another non boosted-DRV (b-DRV) based regimen. Unadjusted and adjusted logistic regression models were constructed to identify factors associated with the probability of starting from naive D/C/F/TAF vs. other considered regimens. In the ART-experienced group, a comparison between subjects with or without a b-DRV regimen before the switch was performed. Unadjusted and adjusted logistic regression models were fitted to identify factors associated with the switch to D/C/F/TAF without previous exposure to b-DRV.
Results: 2050 ART-naïve subjects were included, of which 289 (14%) started D/C/F/TAF, 158 FTC/TAF/RPV (7.7%), 238 3TC/DTG (11.6%) and finally 1365 FTC/TAF/INSTI (66.6%). Main patients' characteristics are shown in Table 1. Predictors of starting D/C/F/TAF over 2DR INSTI-based, FTC/TAF/INSTI-based or FTC/TAF/RPV are shown on Table 2; AIDS diagnosis at presentation, high HIV-RNA load and low CD4 count (<200 cells/mmc) are some of the most common independent predictors. Compared to FTC/TAF/RPV and 3TC/DTG the D/C/F/TAF had a higher probability of being started in a 'rapid-ART' timeframe. 685 PLWH switched for the first time to D/C/F/TAF, 34% in the STR formulation; 80% of subjects were male, median age was 47 years (37-54), 78% Italian, 42% heterosexual and 39% MSM. Median CD4 cell count was 568 cells/mmc (358-793) and 20% had HIV-RNA >50 copies/ml at switch. 212 PLWH (31%) did not have b-DRV in the previous regimen. In the adjusted logistic regression model, independent predictors of switching to D/C/F/TAF from non b-DRV regimen were recent calendar year of switch, female sex, non-Italian, HIV-RNA > 50 copies/ml at switch, a higher number of previous virological failure and serum glucose > 100 mg/dL (Table 3).
Conclusions: The well-known potency and high genetic barrier of b-DRV make D/C/F/TAF one of the main choices for ART-start in advance naïve and highly viraemic patients. In patients switching from non b-DRV regimen, D/C/F/TAF is considered a valid option in subjects with a long history of ART, previous virological failures, or current failure at switch.
The study was partially funded by an unrestricted research grant from Janssen

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Treatment of naive PLWH: current strategies and rapid start of ART

OP 14 BLOOD TELOMERE LENGTH IN TREATMENT-NAIVE HIV-INFECTED ADULTS STARTING DOLUTEGRAVIR PLUS LAMIVUDINE VERSUS TRIPLE REGIMEN WITH TWO NUCLEOSIDES

F. Lombardi[1], A. Sanfilippo[2], M. Fabbiani[3], A. Borghetti[1], A. Ciccullo[4], S. Di Giambenedetto[1,2]

[1]Fondazione Policlinico Universitario A. Gemelli IRCCS, UOC Malattie Infettive, Roma, Italia, [2]Università Cattolica del Sacro Cuore, Dipartimento di Sicurezza e Bioetica, Roma Italia, [3]UOC Malattie Infettive e Tropicali, Azienda Ospedaliero-Universitaria Senese, Siena, Italia, [4]Unità di Malattie infettive, Ospedale San Salvatore, L'Aquila, Italia

Background: People living with HIV (PLWH) show shorter blood telomere length (BTL) and this determines an accelerated or accentuated aging and increased risk of age-associated diseases compared with HIV-negative people. Mechanisms that contribute to BTL shortening in PLWH may include uncontrolled viral replication, which is associated with sustained immune activation and immunosenescence and the inhibition of telomerase by HIV proteins. Antiretroviral therapy (ART) partially reverses HIV-associated immunosenescence. Initial control of HIV replication translates into an increase in naive and central memory cells that have longer telomeres. On the other hand tenofovir (TDF/TAF) and abacavir (ABC), 2 recommended nucleos(t)ide reverse transcriptase inhibitors (N(t)RTIs), are able to inhibit human telomerase.

Objectives: To assess the impact on the BTL in treatment-naive PLWH who start either a dual therapy with one NRTI, lamivudine (3TC), and one integrase inhibitor, dolutegravir (DTG) or triple standard therapy with two NRTIs, one of which is TDF/TAF or ABC, plus a third anchor drug.

Patients and methods: This was a prospective, longitudinal study. We enrolled treatment-naive HIV patients who started at baseline (BL) dual therapy (DT group) or triple therapy (TT group). Relative BTL was assessed by a monochrome multiplex qPCR at BL, at virological success (VS), defined as achievement of HIV-RNA<50copies/mL, and week 48 (W48). GLM repeated measures ANOVA was used to compare the BTL over the study period within and between two groups. To explore variables associated with BL BTL regression analysis was performed.

Results: We enrolled 19 patients in each group; mostly males (86.8%), median age was 37 years (IQR 28-50). As compared to TT, patients in DT were younger (p=0.028), with higher CD4 cell count (p=0.023), higher CD4/CD8 ratio (p=0.001) and lower HIV-RNA load (p=0.020). In TT, 37% of patients had an AIDS event. At BL, the mean of BTL was significantly higher in the DT respect to TT group: 1.01 (95%CI 0.87-1.14) and 0.84 (95%CI 0.78-0.90) (p=0.021). Median time to reach VS was similar between groups (49 in DT vs 83 days in TT, p=0.480). Frequency of patients with undetectable viremia was equal between groups, about 50% at VS and 80% at W48. CD4 remained markedly higher in DT group at VS and W48. Overall, no variation in BTL over time in the two groups was observed (DT p=0.747 and TT p=0.171). The BTL trend was also comparable between groups (p=0.694). By regression analysis, BL BTL was associated with younger age (-0.006 95%CI -0.011/-0.0003, p=0.038).

Conclusions: In this clinical practice setting, treatment-naive patients who started either dual regimen with one NRTI or triple standard therapy did not show any significant change in BTL over 48 weeks. These data suggest that starting ART, regardless of triple or dual regimen, mainly determines the effective control of viral replication without any tangible impact on the BTL in the short term.

Treatment of naive PLWH: current strategies and rapid start of ART

OP 15 BIC/FTC/TAF IN ART-NAÏVE KEY POPULATIONS: REAL-LIFE DATA FROM THE ICONA COHORT

A. Tavelli[1], G. Marchetti[2], A. Vergori[3], E. Quiros-Roldan[4], V. Malagnino[5], F. Vichi[6], M. Lichtner[7], S. Nozza[8], R. Rossotti[9], L. Sarmati[5], A. Antinori[3], A. d'Arminio Monforte[2]

[1]Icona Foundation, Milan, Italy, [2]Department of Health Sciences, Clinic of Infectious Diseases, 'San Paolo' Hospital, University of Milan, Milan, Italy, [3]Clinical Department, HIV/AIDS Unit, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Roma, Italy, [4]Department of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili of Brescia, Brescia, Italy, [5]Unit of Clinical Infectious Disease, Department of System Medicine, Tor Vergata University, Rome, Italy, [6]Infectious Diseases Unit 1, Santa Maria Annunziata Hospital, Azienda USL Toscana Centro, Florence, Italy, [7]Infectious Diseases Unit, Santa Maria Goretti Hospital, Sapienza University of Rome, Latina, Italy, [8]Infectious Diseases Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy, [9]Department of Infectious Diseases Unit, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy

Background: Real world data are scarce on several key population starting a first line regimen with bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF). The aim of this study is to evaluate the effectiveness of BIC/FTC/TAF in ART-naïve people living with HIV (PLWH), focusing on the subgroups of female, late-presenters, PLWH with advanced HIV disease and PLWH >50 years.

Methods: Observational study on ART-naïve PLWH, enrolled in Icona who started BIC/FTC/TAF (Jun 2016 -Dec 2021). Primary endpoint: treatment failure (TF) i.e. virological failure (2 consecutive HIV-RNA > 200 cps/ml or 1 HIV-RNA>1000 cps/ml >6 months from start) or discontinuation (TD) of BIC/FTC/TAF for any reason. Secondary objectives: i) TD for any reason (TD); ii) TD for toxicity/intolerance (TDT); iii) TD for simplification (TDS).

Standard survival analysis (Kaplan–Meier curves and log-rank test) were used. Unadjusted and adjusted hazard ratios (HR) of TF were estimated by Cox regression according to the different exposures of interest: age (≥50 years old); sex; late presenters (<350 cell/mm3 or AIDS); PLWH with advanced HIV disease (CD4<200 cell/mm3 or AIDS).

Results: 416 ART-naïve patients started BIC/FTC/TAF (Table 1): 124 patients >=50 years (29.8%), 73 females (17.5%), 242 late presenters (58.1%) and 169 had advanced HIV disease (40.6%).

Over a median follow-up of 0.9 years (IQR 0.4-1.2), 51/416 PLWH had TF (12.2%), including 7 VF and 44 TD. The 1-year probability of TF was 11.0% (95%CI 7.9-15.1), (details in Table 2A). In the Cox regression models adjusted for confounders, none of the exposure groups analyzed have been found to be associated with a higher risk of TF (Table 3A).

45/416 PLWH had TD (10.8%). 16 PLWH discontinued for toxicity/intolerance (3.8%), 15 for simplification (3.6%), 4 for failure (1.0%), 1 for patient's decision (0.2%) and 9 (2.2%) for other reasons (5 for enrolment in RCT and 4 unknown). The most used ARV regimens after discontinuation were the DTG-based dual regimens (n=23).

The 1-year KM probabilities of discontinuing BIC/FTC/TAF for any reason, toxicity/intolerance or simplification are shown on Table 2B,2C,2D. By multivariate Cox analysis, none of the exposure groups were associated with the risk of the TD endpoints.

Conclusions: First line therapy with BIC/FTC/TAF demonstrated high effectiveness in a real world setting (11.0% TF at 1-year). This was also confirmed, although limited by the number of events, in populations at risk of lower response to therapy, I.e. older individuals, females, and severely immunosupressed individuals.

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Treatment of naive PLWH: current strategies and rapid start of ART

OP 16 A PILOT STUDY OF THE IMPACT OF A RAPID ART INITIATION IN ADVANCED HIV DISEASE

M. Camici, R. Gagliardini, S. Lanini, S. Ottou, A. Mondi, M.M. Plazzi, C. Pinnetti, A. Vergori, E. Grilli, F. De Zottis , I. Mastrorosa, V. Mazzotta, J. Paulicelli, R. Bellagamba, S.Cicalini, A. Antinori

HIV/AIDS Clinical Unit, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy

Background: Rapid ART initiation is important in patients with advanced HIV disease because of their high morbidity and mortality.

Material and Methods: Pilot, single-center, single-arm, prospective, phase IV, clinical trial conducted in a tertiary care Italian hospital from 1.05.2020 to 31.12.2021. 30 ART-naïve participants, presenting at HIV-1 diagnosis with advanced disease described as the presence of an AIDS-defining condition and/or CD4 cell count <200 cells/μL, were enrolled. Exclusion criteria were: CrCl <30 mL/min, severe hepatic impairment, active tuberculosis (TB), cryptococcosis, pregnancy or breastfeeding and systemic cancer chemotherapy. Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) 50/200/25 mg was started within 7 days of HIV diagnosis. The primary endpoint was time-to-clinical or virologic failure (VF) (ITT analysis). Safety and feasibility were assessed as well.

Results: Among 116 new HIV diagnoses at INMI Spallanzani, 40 (34%) had advanced HIV disease. 30 fulfilled eligibility criteria and were enrolled. 16.7% were female, 90% white, median age 45yrs (38-58), 43% presented with CDC stage C disease, CD4 cell count was 90 cells/μL (39-147), CD4/CD8 0.14 (0.09-0.24), HIV RNA log10 cp/ml 6.0 (5.4-6.4), HIV DNA log10 cp/106 PBMC 4.1 (3.8-4.4), 40% of patients had ≥ 1 comorbidity. Proportion of participants with HIV RNA <50 cp/mL was 9/30 (30%) at w4, 19/30 (63%) at w12, 24/30 (80%) at w24, 23/30 (77%) at w36 and 27/30 (90%) at w48. No viral rebound was observed. Proportion of patients with CD4 >200 cells/μL was 2/30 (7%) at BL, 14/30 (47%) at w4, 18/29 (60%) at w12, 17/30 (57%) at w24, 22/30 (73%) at w 36 and 24/30 (80%) al w 48. CD4/CD8 improved (p<0.001) and HIV-DNA decreased during study period (p<0.001). The estimated glomerular filtration rate, by MDRD, decreased slightly (p<0.001), while BMI increased from 22.7 to 24.8 (p<0.001) (Figure 1).

There were no ART discontinuations due to toxicity or VF. Overall 6 SAEs have occurred (3 unrelated, 3 potentially related to B/F/TAF): participant 1 had seizure (w4 and w12) and PML with IRIS (w5); participant 2 had Pneumocystis pneumonia with IRIS (w4) and pneumomediastinum (w5); participant 3 was admitted for clinical worsening (w1) and acute appendicitis associated with disseminated TB and IRIS (w2) that required ART switch. There were no ART modifications based on review of baseline genotype (no NRTI mutations, 3 accessory INSTI mutations [E157Q, G163K, L74I]).

Conclusions: Our results support the efficacy, safety and feasibility of a rapid start strategy with B/F/TAF in patients with advanced HIV.

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Treatment of naive PLWH: current strategies and rapid start of ART

OP 17 RAPID ART INITIATION IN A SINGLE-CENTER ITALIAN COHORT: AN OBSERVATIONAL ANALYSIS

R. Pincino[1,3], L. Taramasso[2], M. Berruti[1], G. Cenderello[1], M. Bassetti[2,3], A. Di Biagio[2,3]

[1]Infectious diseases unit, Borea Hospital, ASL-1 Imperiese, Sanremo, Italy, [2]Infectious diseases unit, Policlinico San Martino Hospital, Genoa, Italy, [3]Health and science department, Genoa University, Genoa, Italy

Background: Rapid initiation of antiretroviral therapy (ART) strategy is increasing global interest because of its positive impact on both people living with HIV (PWH) and the community. The aim of this study is to assess predictors of virological suppression and adverse outcomes in a cohort of newly diagnosed PWH, comparing rapid and standard ART initiation.

Methods: Observational, single center, retrospective study, including all PWH who started ART during the period January 2018 – December 2021. Exclusion criteria were insufficient virological follow-up and transfer to other center before 24 weeks follow-up.

The study population was divided into two groups: rapid ART, defined as ART start on the same day of diagnosis/referral to HIV clinic or up to 4 days later, and standard ART, defined as ART start > 4 days after diagnosis/referral. Predictors of rapid ART, virological suppression, defined as HIV RNA < 50 copies/mL at week 24, and of adverse outcome, a composite of lack of virological suppression, loss to follow up and death within 24 weeks, were analyzed using a binomial regression model.

Results: 120 PWH were enrolled, 39 (32.5%) in rapid ART and 81 (67.5%) in standard ART; baseline characteristics of the two groups are shown in table 1. Over the study period we observed a decrease in the use of standard ART strategies, with 20 (24.7%) PWH starting ART more than 4 days after HIV diagnosis/referral in 2021 compared to 30 (37.0%) in 2018. 118 PWH (98.3%) started an ART regimen containing an integrase inhibitor (INSTI), 102 of which (86.4%) were second generation INSTI. Four PLWH (3.3%) started a two-drug ART regimen containing dolutegravir. None presented significant resistance associated mutations (RAMs) for the chosen ART regimen at baseline genotypic resistance testing (GRT).

Fewer people in the rapid ART group (5.1%) started ART with known CD4+ count; nonetheless PLWH in the rapid ART group showed higher rates of virological suppression and lower rates of adverse outcome.

According to the multivariable analysis, having HIV RNA <50 copies/mL at 24 weeks was associated to rapid ART initiation (aOR 38.52, 95%CI 0.61-2418.03, p=0.080), while waiting for CD4+ count before ART start was a negative predictor of rapid ART (aOR 0.01, 95%CI 7.62 e-4-0.06, p < 0.001), Table 2.

Standard ART initiation was associated with lower probability of virological suppression (OR 0.16, p 0.080) and higher probability of adverse outcome (OR 3.43, p 0.061) when compared to rapid ART at univariate analysis, however, no statistical significance was reached at multivariate analysis.

AIDS diagnosis was the stronger predictor of lack of virological suppression (p=0.028) and of adverse outcome (p=0.033) at multivariate analysis (table 3 and 4).

Conclusion: According to our study rapid ART was not associated with worse outcomes at 24 weeks than standard ART, also showing a beneficial trend towards virological suppression and adverse outcomes.

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Treatment of naive PLWH: current strategies and rapid start of ART

OP 18 VIRO-IMMUNOLOGICAL EFFECTIVENESS OF DIFFERENT INTEGRASE STRAND-TRANSFER INHIBITOR-BASED ANTIRETROVIRAL THERAPY REGIMENS. A SINGLE CENTER RETROSPECTIVE STUDY

M. Ceccarelli[1,2,3], D. Scuderi[4], R. Bruno[1,3], G. Bruno[5], A. Marino[3,6], V. Moscatt[3,7], Y. Russotto[7], C. Micali[7], E. Venanzi Rullo[7], G. Nunnari[7], B. Santi Cacopardo[1], B.M. Celesia[3]

[1]Department of Clinical and Experimental Medicine, Unit of Infectious Diseases, University of Catania, Catania, Italy, [2]Department of Biomedical, Dental, Morphological and Functional Imaging Sciences, Unit of Infectious Diseases, University of Messina, Messina, Italy, [3]Unit of Infectious Diseases, ARNAS "Garibaldi", "Nesima" Hospital, Catania, Italy, [4]Unit of Infectious Diseases, "Cannizzaro" Hospital, Catania, Italy, [5]Department of Medical and Surgical Sciences, Unit of Infectious Diseases, "Magna Graecia" University of Catanzaro, Catanzaro, Italy, [6]Department of Biomedical and Biotechnological Sciences, Unit of Infectious Diseases, University of Catania, Catania, Italy, [7]Department of Clinical and Experimental Medicine, Unit of Infectious Diseases, University of Messina, Messina, Italy

Background: Low level viremia is a common feature during combined antiretroviral treatment. Integrase strand transfer inhibitors (INSTIs) are effective and well-tolerated, and they seem to have a higher impact than other regimens on markers of inflammation. This study is focused on finding correlations of the different INSTI-based regimens with LLV, and their effects on virologic and immunologic control of the infection.
Methods: Longitudinal retrospective study. We anonymously collected and analyzed data about People Living with HIV (PLWH) who started cART with an INSTI (RAL, EVG/c, DTG, BIC) during the period January 1st, 2009, and September 30th, 2021. Follow-up data were collected until March 31st, 2022.
Results: 411 PLWH were included in the study. 324 (78.8%) patients were male. Median age was 46.3 years (IQR 36.6-55.9). Median durability of INSTI drugs in naïve PLWH is 111 weeks (IQR 57-213), while in experienced PLWH is 168 weeks (IQR 91-253). Overall, 89 PLWH (21.6%) showed a detectable pVL between 20 and 50cps/mL after reaching TND during the period of follow-up. BIC shows a slower pVL decay than the other drugs in the class in PLWHs with a median baseline pVL>100,000 cps/mL, although there are no statistically significant differences with the other INSTIs (figure 1). Considering normal a value of CD4+ T-lymphocyte count above 500cells/μL, the PLWH included in our study who started with a value below 350cells/μL (median 220cells/μL) never reached normality within the two years of follow-up. In PLWHs starting the INSTI with a baseline CD4+/CD8 + ratio ≤0.5, there is no statistically significant difference between groups regarding the starting baseline CD4 +/CD8+ ratio (p=0.186). This difference is still not significant at 4 weeks (p=0.325), 16 weeks (p=0.771), 48 weeks (p=0.320) and 96 weeks (p=0.107).
Conclusions: 15 of the PLWH having LLV at baseline either failed the treatment or did not reach TND after the switch. Despite having similar viro-immunological characteristics at baseline, therapy is chosen considering the patient as a whole. As a matter of fact, in clinical practice EVG/c was chosen for PLWHs who have a better adherence, a better virologic and immunologic control and did not have any problems with taking their pills during a meal. INSTI-based treatments are effective in limiting the prevalence of LLV. In some cases, with a suboptimal treatment, LLV can evolve in virologic failure, even though this event is a rare complication nowadays. In some cases, even with an optimal treatment, LLV prevent the achievement of TND. Seen the effectiveness of INSTI-based treatments on controlling both the virus and the immune system, we recommend their utilization. However, we also recommend to closely monitor PLWHs showing a persistent LLV under treatment, and even to study the resistances present within the integrated HIV-DNA of these PLWHs. More studies are needed, especially prospective ones, to confirm our results.

Attach: https://www.icar2022.it/public/abstract/Attach_ABS_21.tiff

PrEP: real life experience

OP 19 PREP IN ITALY: HOW MANY PEOPLE ACCESS IT AND WHAT KIND OF SERVICES ARE OFFERED?

M. Stizioli[1], G.M. Corbelli[2], M. Falaguasta[1], E. Nittolo[1]

[1]PrEP in Italia, [2]Plus Roma

Background: No official statistic is until now available on people using pre-exposure prophylaxis (PrEP) in Italy or on modalities for accessing clinics where it is prescribed. The first survey of this kind was conducted in 2019 by Plus, network of LGBT people living with HIV.
Material and Methods: After three years, Plus, together with PrEP in Italy and in collaboration with INMI L. Spallanzani in Rome, conducted a new survey aimed at gathering data on PrEP centres and understanding how characteristics of people using PrEP changed. A questionnaire was sent out to 56 out of the 70 centres listed on the webpage www.prepinfo.it/chi-ti-segue (as per 14 of them, no email address was available, or they were only recently opened) in March and April 2022. The questionnaire addressed these topics: history of the PrEP centre, characteristics of users in care, HIV and STIs diagnosis both at baseline and during follow up, impact of COVID-19 on services, modalities and costs for accessing to services.
Results: The questionnaire was filled in by 28 centres, 13 located in the North, 11 in the Center, 4 in the South.
As per December 2021, 3641 people were in care for PrEP: a significant increase compared to 531 users in 2019. Most of them are MSM (3447 people, 94.6%; but they were 98% in 2019). There is a numeric increase in PrEP use among other demographic groups such as heterosexual cisgender men (80 in 2021, 7 in 2019), trans women (46 in 2021, 4 in 2019), cisgender women (22 in 2021, 4 in 2019) and intravenous drugs users (35 in 2021, 0 in 2019).
COVID-19 crisis had a great impact on access, causing temporary closure in 60% of centres.
Only in one clinic access is possible only with a prescription by a general practitioner. In 90% specific exemptions are in use to grant free infectious diseases visits. As per IST testing, proportion of centres where specific exemptions are used is lower (65.5%).
Costs for services vary greatly: users can spend up to 36€ for the initial infectious diseases visit, 20€ for the follow up visits, 80€ for IST tests, 15 for biochemical testing. Users can spend at each follow-up visit up to 90€.
21 HIV infections were diagnosed at baseline, 12 during follow-up. IST diagnosis at baseline and follow-up are presented in the attached table.
Conclusions: At our knowledge, this is the only national data gathering about PrEP use in Italy. Access to PrEP is still uneven on the Italian territory, with great disparities between North and South. People using PrEP are mostly MSM, despite some encouraging data among cisgender heterosexual men and trans women. Uniform implementation of PrEP services at the national level is therefore needed to facilitate access for all people who wish to use it and to obtain a greater impact on HIV epidemiology.

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PrEP: real life experience

OP 20 HIV PRE-EXPOSURE PROPHYLAXIS (PREP): THE EXPERIENCE OF THE OUTPATIENT CLINIC OF PERUGIA

G. Gamboni, C. Gabrielli, C. Papalini, C. Pallotto, G. De Socio, F. Paciosi, A. Zoffoli, S.Tordi, E. Schiaroli, D. Francisci

Department of Medicine and Surgery, Clinic of Infectious Diseases, "Santa Maria della Misericordia" Hospital, University of Perugia, Perugia, Italy

Background: The Pre-Exposure Prophylaxis (PrEP) has been already identified as a valid means able to guarantee a protection rate from HIV infection higher than 90%, when correctly taken. The aim of this study is to describe our experience of using PrEP.

Material and methods: We started PrEP in late 2019, creating during this period a dedicated outpatient clinic, even with all the limitations due to SARS-CoV2 pandemic. The first access to PrEP clinic is free, without booking, and includes counselling and prescription of tests considered useful. Follow up visits are booked according to an internal protocol, in agreement with ministerial and international indications. The drug supplying is done within the hospital, payed by the user and dispensed by the local pharmacy.

Results: During a 3 years period we had 61 contacts with people interested to use PrEP, of whom 54 received at least one prescription. The 83.3% of this sample attended the clinic between 2021 and 2022. Only three subjects started PrEP in 2019, were then followed by other centres, and came back to ours in 2021. Among the 54 people, 94.4% are males and 5.5% are transgender women. Nintytwo point six% are MSM and 7.4% bisexual men. Median age is 33 years (IQR 29.5-43.5), 87% are italians and 77% do not present any comorbidity. To evaluate the individual risk of exposition to infection we have used the DK Smith score which has been filled by half of these subjects, with a median score of 22 points (IQR 15-29.5). A previous STI has been reported by 68,5% of the interviewees; in 46% it was due to syphilis. Sixty % of people started a daily PrEP, 31.5% “on demand”, in the remaining cases the choice was not expressed at the prescription time. Only 2 patients out of 54 presented side effects so severe to suggest to suspend the drug. More in detail, one person had a rise of transaminase (>3 times normal value) and the other one had a deterioration of renal function, already compromised when therapy was started; for both of them this happened within the first month of dailytherapy. STI onset while taking PrEP was more frequently seen at 3 months from prophylaxis beginning, with a 25 % prevalence in people who had a 3 month control. During observation period we observed one seroconversion and only one subject used PEP at our centre. Among people who are still on follow up, at least 1/3 received HAV, HBV or HPV vaccination at the local outpatient clinics, as suggested.

Conclusions: During pandemic we observed an increasing request of PrEP use; most people came to our outpatient clinic through “word of mouth” thanks to a constant contact with local associations active in HIV prevention programs. The population we have studied, has many risk factors for HIV infection, the onset of STI during PrEP was high. These data prompt us to reflect on the impact that this new service could have on the whole activity of our centre and on the use of new and more effective transmission risk prevention strategies.

PrEP: real life experience

OP 21 IMPACT OF A PRE-EXPOSURE PROPHYLAXIS PROGRAM ON HIV AND OTHER SEXUALLY TRANSMITTED INFECTIONS OVER THE LAST THREE YEARS IN A THIRD LEVEL HOSPITAL: THE EXPERIENCE FROM PADUA

F. Barbaro, S. Cavinato, M. Mazzitelli, L. Sasset, D. Leoni, A. Cattelan

Unità Operativa Complessa Malattie Infettive e Tropicali, Azienda Ospedale Università Padova, Padova, Italy

Background: Solid data demonstrated how HIV pre-exposure prophylaxis (PrEP) became a cornerstone in protecting populations at risk of acquiring HIV by unprotected sex. Moreover, in PrEP centers patients are routinely offered the opportunity to be tested also for other sexually transmitted diseases (STDs). However, as shown by many published experiences, during COVID-19 pandemic the activities of centers providing PrEP have been dramatically reduced. The long-term effect on HIV and STDs prevention/transmission of the reduction of access or the suspension of PrEP services is still to be determined. Therefore, we aimed at describing our PrEP service experience and its clinical outcome (in terms of HIV and STDs acquisition) from January 2019 to March 2022.

Material and methods: We established a full service for PrEP prescription and STDs testing (HIV, Hepatitis A, B, C, syphilis, pharyngeal, urethral and rectal swabs every 3 or 4 months and safety bloods) in Padua Hospital in 2019. Access is warranted with no waiting list, with a dedicated phone line/email address, with then opportunity to perform both in person access and telemedicine assessment. We retrospectively collected data from medical health record of all subjects recruited in our PrEP program and assessed the rate of both HIV and STDs acquisition.

Results: Over the study period (January 2019-March 2022) 85 subjects (mean age 40 years) were recruited in our PrEP program, 83 (97.6%) men who have sex with men (MSM) and 2 women having a partner living with HIV on antiretroviral treatment. After PrEP prescription, 3 subjects discontinued PrEP: 1 for a skin rash, 1 for moving abroad, and 1 for no more need of it. While over the study period we did not observe any HIV infection, 35/85 patients (41,2%) have developed STDs, whose specific incidences are as follows: syphilis 10/85 pts. (11,8%), acute gonorrhea 13/85 pts (15,3%), chlamydia 7/85 pts (8,2%), mixed infection 3/85 pts (3,5%). All syphilis episodes were diagnosed in the early phase. Three subjects experienced multiple gonorrhea infections, but with no evidence of ceftriaxone resistance. All the diagnosed Chlamydia infections were asymptomatic. No acute viral hepatitis occurred during the study period.

Conclusions: In our experience PREP was clearly confirmed an extremely effective strategy to prevent HIV infection (0% infections over about 3 years). Despite the dramatic italian healthcare system strain due to COVID -19 pandemic, from February 2020 on patients have been guaranteed a regular access to our PrEP program, even in the most severe waves of the pandemic with telemedicine evaluations. We confirm a high PrEP patients request and participation rate. By contrast, a significant proportion of subjects experiences one or more STDs. However, our approach, with a systematic testing, allowed us to timely diagnose and treat them properly. The significant STDs incidence rate highlights the value of this screening, coupled to HIV testing, and suggests enhanced counseling on condom use.

PrEP: real life experience

OP 22 PRE-EXPOSURE PROPHYLAXIS (PREP) SERVICE IN BERGAMO: THREE-YEAR EXPERIENCE

S. Venturelli, F. Borghi, L. Baldassari, D. Ripamonti, F. Maggiolo, M. Rizzi

ASST Papa Giovanni XXIII, Bergamo

Background: Pre-Exposure Prophylaxis (PrEP) is an evidence-based and well-consolidated strategy of HIV prevention recommended by both EACS and SIMIT guidelines. Both the Italian National Prevention Plan and Regional Prevention Plan of Lombardy for years 2020-2025 declared the implementation of PrEP protocols as strategic objectives. The PrEP Service in Bergamo was set up in June 2018. The aim of this study is to review our three-year experience.

Methods: A retrospective study was performed, including all persons who initiated PrEP at our Centre, from June 2018 to March 2022. We collected data on demographics, past medical history (PMH), vaccination status, PrEP regimen, time of starting PrEP since first visit, PrEP side effects, previous STIs and incident STIs, previous Post-Exposure Prophylaxis (PEP) use and reasons for discontinuation. The PrEP Service was temporarily suspended in March-May 2020 due to the SARS-CoV-2 pandemic, although PrEP prescription was guaranteed to people already on treatment.

Results: A total of 108 individuals were enrolled, 98% male, 1% female and 1% transgender woman. Among male users 80% were MSM, 5% heterosexual and 15% bisexual. Median age was 35 years (20-63). 37% of persons came from provinces different from Bergamo. 70% of persons had no significant PMH. Previous PEP use was reported by 14% of users and 73 users (68%) reported past STIs with 48% of them with more than one (syphilis and urethral gonorrhoea were the most frequent). A total of 50%, 18% and 71% of attenders were not protected from HAV, HBV and HPV infection, respectively; if eligible, they were referred to our vaccination Service.

The enrolments gradually increased from 6 in 2018 to 22, 22 and 44 persons in 2019, 2020 and 2021, respectively. The run-rate of 2022 suggests a further increase (14 in the first trimester). New users reported they had received information about PrEP service by friends, healthcare workers and through internet searching in 36%, 29% and 35% of cases, respectively. Information from friends already on PrEP has increased over time. On-demand PrEP was prescribed to 62% of persons. A total of 21% of persons started PrEP on the same day of first visit, 35% within 7 days, 29% within 14 days and 15% within 3 months. Follow-up visits were planned every three or four months. Overall, 20 adverse events were reported during PrEP use (the most common was nausea) and 72 incident STIs were documented (mostly rectal chlamydia). PrEP was discontinued in 12 users (11%), only in 1 case due to side effect. No incident HIV infection was diagnosed.

Conclusions: Over the last three years, there was an increasing number of PrEP users at our service, with a high rate of retention. No HIV incident cases were reported in our cohort. We registered a high proportion of users coming from outside the Bergamo Province; this suggests that such prevention strategy might benefit from more extensive and geographically distributed services.

PrEP: real life experience

OP 23 HIV PRE-EXPOSURE PROPHYLAXIS IN A LARGE TEACHING HOSPITAL IN MILAN: THE CSL-PREP COHORT EXPERIENCE

A.R. Raccagni[1], R. Lolatto[2], L. Galli[2], F. Alberton[1], E. Bruzzesi[1], D. Canetti[2], M. Strano[1], M. Ripa[2], A. Castagna[1,2], S. Nozza[2]

[1]Vita-Salute San Raffaele University, Milan, Italy, [2]Infectious Diseases Unit IRCCS San Raffaele, Milan, italy

Background: Among PrEP users, high-risk sexual behaviors and sexually transmitted infections (STIs) are common. Aim of this study is to describe characteristics of a large cohort of PrEP users, who have sex with men (MSM) and to evaluate prevalence of STIs.

Materials and Methods: This is a cross-sectional study of a cohort of MSM receiving PrEP, followed at the Infectious Diseases Unit of IRCCS San Raffaele, Milan (CSL-PrEP Cohort), from May 2017-December 2021. All characteristics were collected at enrollment visit (baseline, BL) using self-completion questionnaires, with additional physician visits: previous STIs were also collected. STIs investigated at BL were syphilis, gonorrhea and chlamydia at urethral, rectal and pharyngeal sites. Associations between the number of partners in the previous 3 months, Smith DK index and chemsex with presence of STIs at BL was assessed by Chi-square/Fishers' exact-test; Cochran-Armitage test was used to assess linear trend in STIs prevalence over time.

Results: The cohort includes 503 MSM PrEP users: 253 (50%) daily-based, 250 (50%) event-based; 250 (50%) MSM had ≥1 previous STI while, at BL, ≥1 STI was diagnosed in 110 (22%) MSM; 213 (42%) were chemsex users. Individuals' characteristics are shown in Table1 and Figure1. Over the period 2017-2021, STIs prevalence before or after enrollment in the cohort is shown in Figure 2 [chlamydia: previous 32 (6%), BL 49 (10%); gonorrhea: previous 96 (19%), BL 37 (7%); syphilis: previous 133 (26%), BL 26 (5%)]. BL chlamydia proctitis (39, 8%) were more frequent than in the past (17, 3%); BL urethritis were 4 (1%), previous 13 (3%). BL gonorrhea proctitis were 23 (5%), previous 27 (5%); BL urethritis were 7 (1%), previous 62 (12%). HCV was detected in 3 MSM at BL vs 3 (1%) previous, no HAV and HBV at BL vs 36 (7%) and 11 (2%) previous; 49 (10%) had history of HPV and 15 (3%) of HSV. The number of partners was associated with BL chlamydia ($p<0.001$), BL gonorrhea ($p=0.048$) and BL syphilis ($p=0.003$); Smith DK index with BL chlamydia ($p=0.016$) and BL gonorrhea ($p=0.029$). No association was detected between chemsex and any BL STIs. Median BL AST (U/L: 28, IQR=22-33), ALT (U/L: 28, IQR=22-38) and creatinine (mg/dL: 1.01, IQR=0.94-1.11) levels were all within normal ranges allowing PrEP use. Four/503 individuals interrupted PrEP (2 event-based users for HIV-infection, 2 daily-based users for renal toxicity). HAV vaccine was administered in 113 MSM (22%), HPV in 168 (33%) and HBV in 37 (7%).

Conclusions: In our cohort most PrEP users were high-educated, Caucasian young adults, confirming a disproportionate access to PrEP. High-risk sexual behaviors and STIs were frequently observed; chemsex use was higher than reported in other cohorts. A similar event-based or daily PrEP use was observed. BL chlamydia prevalence was higher than in previous clinical history, possibly suggesting a lack of STIs screenings in asymptomatic MSM before access to PrEP, especially for proctitis.

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PrEP: real life experience

OP 24 THE ITALIAN EXPERIENCE OF PRE-EXPOSURE PROPHYLAXIS (PREP) USERS AND SERUM CREATININE VARIATION: A TWO CENTERS RETROSPECTIVE ANALYSIS

M. Menozzi[1], S. Volpi[1], G.J. Burastero[1], S. Colombaioni[1], B. Fontana[1], E. Martini[1], M. Martini Fasce[2], L. Labate[2], A. Di Biagio[3], C. Mussini[1]

[1]Infectious Disease Clinic, University Hospital of Modena, Italy, [2]Infectious Diseases Unit, Ospedale Policlinico San Martino IRCCS – Genoa, Italy, [3]Department of Health Sciences (DISSAL), University of Genoa – Genoa, Italy

Background: Pre-exposure prophylaxis (PrEP) is a strategy to prevent HIV infection in seronegative people. Tenofovir disoproxil/emtricitabine (TDF/FTC) is the only drug approved for this aim and tenofovir may be associated with increase of serum creatinine as a proxy of kidney failure. The aim of our study was to describe the characteristics of the population of PrEP users from two Italian centers, focusing on the modification of serum creatinine during years.

Material and Methods: Retrospective observational multicenter study was conducted reviewing data from two Italian university hospital of Modena and Genova, collected from January 2019 to March 2022. PrEP was dispensed as daily or on-demand regimen. Every three months serum creatinine levels, transaminase, phosphoremia and screening for sexually transmitted infections (STIs) were collected. Nephrotoxicity was defined as at least 20% increase in serum creatinine between basal and last follow-up detection. We divided population by age group at PrEP initiation (≤30 years-old, 31-50, >50). A descriptive analysis was performed using mean (standard deviations) and number (frequency) for continuous and categorical variables respectively. Comparisons were done with Mann-Whitney U test, ANOVA and Chi-square test according to variable distribution and type.

Results: We collected data of 133 PrEP users (tab 1): 127 were male (95,5%), 4 female (3%) and 2 male-to-female (1,5%), with a median age of 40,3 ± 10,7 years. Most of users were Italian (89,4%), men who have sex with men (MSM, 76,7%) and began to use PrEP in the age group 31-50 years (59,4%). According to PrEP initiation (tab 2), 30 people started it in 2019, 26 in 2020, 49 in 2021 and already 15 until March 2022. On-demand regimen was preferred by 36% of people, daily by 21,8%, while 19,6% declared to use both regimens. The main reason to begin was having at risk sexual intercourse (63,2%), followed by previous STIs (10,5%) and having a partner with HIV (6%). We traced the use of condom in 79 people, 55,7% declared an intermittent use and 11% admitted to never use it. We reported side effect in 18 people (13,5%): 10 reported gastrointestinal disorders (7,5%), 4 presented hepatic toxicity (3%), 4 nephrotoxicity (3%). Focusing on renal function, of the 78 people with available complete data, we observed mild variations in serum creatinine levels: only 4 users presented nephrotoxicity (tab 3). The maximum rise was of 0,88 ml/min (from 1,36 ml/min to 2,24 ml/min) in a user with lisinopril comedication, leading to PrEP stop only in this case. 3 out of these 4 people were using on-demand PrEP regimen and no differences were found according to age and sex.

Conclusions: Our PrEP cohort presented similar demographic characteristics to others from literature, except for higher mean age and female users' inclusion. The low nephrotoxicity prevalence confirm safety of TDF as a PrEP medication.

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Access to test and educational aspects

OP 25 HIV TESTING IN COMMUNITY-BASED CENTERS AND MSM PREMISES: DIFFERENT SETTINGS, SAME NEEDS

A. Bianchi[1,2], D. Zagato[1], D. Calzavara[2], R. Repossi[1,2], P. Testoni[1,2], A. Antonino[1,2], G. Fracca[1], F. Rossi[1,2], A.J. Gallucci[2,3], I. Gotti[2,4], N. Frattini[1,2], R. Rossotti[2,6], G. Pigliapochi[2], P. Russo[2,3], M. Albiani[2], M. Cernuschi[1,2,5]

[1]ASA Associazione Solidarietà AIDS Onlus, Milan, Italy, [2]Milano CheckPoint, Milan, Italy, [3]CIG Arcigay Milano, Milan, Italy, [4]Anlaids Sez. Lombarda, Milan, Italy, [5]San Raffaele Hospital, Milan, Italy, [6]ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy

Background: Testing in an informal setting is a useful strategy to achieve the 90-90-90 target. Since 2012 ASA Onlus provides once monthly rapid point-of-care HIV testing (POCT), in anonymity and free of charge to encourage widespread screening. Since 2016 ASA provides POCT in association with CIG Arcigay Milano also in MSM venues. From 2019 it is also possible to get tested once weekly at Milano Checkpoint. Aim of this analysis is to describe the sample for preventive intervention's evaluation and new infections early detection.

Methodology: Before testing, an HIV-skilled peer or psychologist conducts an informal counseling. If the POCT tests reactive, a counselor assists the person and newly-diagnosed individuals are directed to hospital clinics to confirmation positivity and to facilitate the retention in care. Risk behaviors (unprotected anal/vaginal/oral intercourse; chemsex; awareness of partner disclosure) are described. PrEP is also discussed. Peer-facilitated questionnaires are administered before testing: those collected from July 2021 to March 2022 have been analyzed. Psycho-socio-cultural characteristics of the sample have been correlated to risk behaviors.

Results: The study included 2 different samples: sample 1 (S1) was collected in ASA Onlus and Milano Checkpoint (N= 1055): males were 78%, frequently very young (31% were aged 18-25 years), MSM in 83% cases. In 73% they have been previously tested, 45% had a risky behavior, 10% had a diagnosis of STI in the previous 12 months, and 5% was on PrEP. 6 out of 1,055 POCT (0.6%) tested HIV positive. Sample 2 was collected in MSM venues (S2) (N= 378): males were 87%, in 86% of cases MSM. 79% were ever tested before, 50% had a risky behavior, 8% had a STI in the previous 12 months and only 3% was on PrEP. 5 out of 378 POCT (1.3%) tested HIV positive (p=0.150).

Samples were similar in relation of self-reported behavior (unprotected anal sex about 21%; unprotected oral sex about 37%). Most participants stated they know the partners with whom they have had unprotected sex: in S1, 22% did not know their HIV status, in S2 only 13% (p=0.013). Over 70% of the users had already been tested, about half a year earlier. In both samples, almost 60% of the respondents used condoms in the last intercourse (among women the use was lower). About 40% of participants were interested in PrEP. Substance use was reported by 5% (mostly men). The most frequently consumed drug was cocaine. Low uptake of Chemsex practices were referred in a small number, probably because of social desirability, a bias present in the assisted-administered questionnaires (in previous analyses, in community-based settings, chemsex was reported by 12%).

Conclusions: Given these findings, it is useful to continue to implement these actions. Even if in MSM venues there is a disclosure issue, spreading information on PrEP and other fundamental preventive tools, is essential to stop new HIV infections.

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Access to test and educational aspects

OP 26 HIV TESTING: ARE WE MISSING SOME OPPORTUNITIES?

M. Mazzitelli, L. Sasset, D. Leoni, F. Barbaro, A.M. Cattelan

Infectious and Tropical Diseases Unit, Azienda Ospedale Università Padova, Italy

HIV testing is one of the most important strategies in reducing the burden of HIV worldwide. However, it is estimated that still 20% are living with HIV without knowing it worldwide. In Italy, by the law n°35/1990 the detection of HIV infection must be carried out in a manner that does not allow identification of the person with absolute impossibility of reaching the identification of the persons concerned.

Objectives of this study was to assess proportion of subjects who tests positive for HIV infection but does not return to the center to collect and receive properly a diagnosis.

This is a retrospective study including all subjects who came for HIV testing at Infectious and Tropical Diseases Unit of Padua University Hospital from January 2012 to December 2021. For HIV screening we are used to perform the screening for HIV1-2 antibodies with a 3rd generation ELISA method, followed by a Western Blot (if the first one is positive), and HIV RNA quantification. We collected the number of tests performed by calendar year, the number of subjects who tested positive, the number of patients who did not show up to collect results. On the consent for testing, patient could disclose some demographics (such as age, gender, and Country); hence, we also collected this data whenever available.

Results: Over the study period, we performed 13,621 HIV tests, detecting 253 people with HIV (1.8%). Among these, 117 (46.2%) did not return to collect the result. Table 1 shows the numbers of tests, proportion of PLW who were diagnosed and people who did not show up by calendar year. We observed about the halving of number of tests during pandemic (2020-2021). Information for demographics and provenance was available from 2015 onwards. Median range of age for testing was from 31 up to 45 years. Reasons for HIV testing were unsafe sex (65 % cases), partner of HIV positive subject (0.3%), unknown (24%), IVDU (10.8 % cases). From 2015 to 2020, testing was performed in > 75% cases among males. Proportion of Italian people who came for testing decreased over years.

Discussion/conclusions: Our data alarmingly showed a high percentage of patients who tested positive do not return to the center to receive the diagnosis appropriately. We believe that the implementation of rapid HIV testing (results in 20 minutes or less) could be an effective method to increase the number of individuals who know their HIV status. In addition, numbers of both young people (age < 25 years) and women who came for testing in our center were too low. Information and education campaign aimed at improving HIV transmission and prevention knowledge targeted also to young people and female gender are needed to reduce social/behavioral barriers and encouragement for testing. This work presents however some limitations such as its retrospective nature, the fact that people could have disclosed or provided false information or that people were linked to care elsewhere). We lastly feel that HIV testing should be promoted among all subjects who present risky behaviors and normalized in different settings, in order both to favor new HIV diagnoses and to reduce the stigma surrounding the testing activities.

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Access to test and educational aspects

OP 27 POPULATION OF THE BERGAMO CHECK-POINT. A FIRST ANALYSIS OF COBATEST DATA

I. Mercurio[1], C. Pellegris[2], P. Meli[2], E. Zanetti[2], F. Maggiolo[3], F. Radici[4], R. Carissoli[4]

[1]Croce Rossa Italiana – Comitato di Bergamo, [2]Società Cooperativa Sociale Don Giuseppe Monticelli, [3]ASST Papa Giovanni XXIII, [4]Arcigay Bergamo Cives

Background: on March 19th, 2019, Bergamo has signed the Paris Declaration becoming a Fast Track City (FTC). In June 2020 the Check point was opened offering rapid tests for HIV, HCV and syphilis. Since November 2021 the Bergamo Check Point adhered to the Cobatest network that connects CBVCT centers promoting STI testing in Europe and shares an instrument to collect data on sexual health care and transmittable diseases so to promote testing, early diagnosis and access to care for all.

Methods: At the Check Point the possibility to compile, together with a trained operator, the Cobatest questionnaire is offered to all clients. We analyzed results on data obtained in the first 4 months of use of this instrument (Nov 2021 to Mar 2022)

Results: The questionnaires concern 43.58% females and 56.42% males. More than half (50.37%) of males ages between 18 and 30 years, 44.78% ages between 31 and 55 and 4.85% has more than 55 years. For females the same figures are 74.88%, 24.15% and 0.97%, respectively (figure A). Overall, 87.37% of clients refers to be Italian and 12.63% of foreign origin. Limited to people reporting a sexual intercourse in the last 12 months, 63.79% of subjects refer a heterosexual relationship, 19.79% with a person defined of the same gender and 6.53% both with men or women. A remaining 9.89% do not respond or did not have a relationship in the last 12 months (figure B). For 47.27% of persons that was the first HIV test ever done (62.25% females and 38.58% males). Knowledge of the Check Point existence was in 4% of cases due to information given by relatives or friends, in 21.3% through paper-based propaganda, 19.26% through web-based research and 24.8% because directly reached by a direct e-mail sent during the European testing week thanks to a collaboration with the “Consulta” of students and the rectorate of the Bergamo University. Finally, 2% of persons reaches the service because involved in a program of awareness raising and information held at a high school level in the year 2021/2022 (figure C & D).

Conclusions: We believe that the high proportion of people that performs the HIV test for the first time is an index of a growing attention to personal sexual health and well-being and of a rising awareness of the potential risks especially among young people. The high prevalence of young subjects highlights the efficacy of strategies based on awareness rising programs in high schools and of a constant collaboration with the University management. Young women seem more sensitive to these factors compared to male peers. The interaction among different services, institutions and third sector organizations already operating on the territory allows the construction of a positive network as confirmed, among the key populations, by the good prevalence of MSM accessing the test. Some of them seems to be already sensitized about this topic (previous test already performed) but still prefer and find more friendly this type of service.

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Access to test and educational aspects

OP 28 VENETO REGION "RECALL" PROJECT TO DISCOVER HCV+PEOPLE: THE EXPERIENCE OF THE "OSSERVATORIO INFETTIVOLOGICO" IN VERONA

V. Del Punta, M. Fiscon, G. Giammarresi, S. Nardi, M. Malena

UOS Osservatorio Infettivologico Aziendale Azienda ULSS 9 Scaligera

Background: The RECALL PROJECT (Research of Hepatitis C through the reading of laboratory data) is part of the Veneto Region plans for the HCV elimination. The goal was to identify the subjects HCV positive who have not started yet the antiviral therapy with DAA. The identification has been possible by the integration of administrative with microbiological data.

Methods: The main activity was carried out from April to June 2021. ULSS 9 Scaligera provided two lists of people classified as "to be recalled" (people HCV RNA+) and "to be investigated"(HCV Ab+). We had a comprehensive screening list of 609 patients to be evaluated. We searched the telephone number of the patients using the regional registry. When the number was lacking, or not updated we decided to refer to the general practitioner. When even this data was not available, a last attempt was made by sending a paper letter. Some of the letters went back because the person was not found. We dedicated a psychiatrist to better manage the telephone counseling.

Results: Of the 609 patients, to our knowledge 46(5%) had already been treated or recovered spontaneously, so they were excluded from the initial list. We also excluded: 4(0.6%)minors, 3(0.4%) prisoners and 11(1.2%) living out of our district. The unreachable people were 29(4.8%). We also found that 18(3%) listed patients were already followed by another center. We found that: 135(22%), had already spontaneously recovered or treated, 12(1.9%) were not interested in undergoing the treatment, and 76(12%) were not aware of the positivity for HCV and expressed their intention to refer first to their general practitioner. Six patients(0.9%) were not eligible for treatment because of serious concomitant pathologies. Only 43(7%) patients accepted an appointment, but 22 did not show up. Among 21 patients who came to be visited, 3 were already cured, 5 refused the treatment and only 13 people were lastly put on treatment, only 1,2% from the original list.

Discussion: Our Psychiatrist spent 6 hours a day for 20 working days only for the first approach to the patients. The impression is that the communication regarding the existence of new therapies for HCV infection has been well received, although some people expressed feelings of discomfort due to the revival of such a delicate topic in a completely unexpected way and moment. The main difficulties we encountered were the management of information based on privacy rules, particularly when a family members of the older people answered the call. About 15% of calls needed an appropriate emotional containment and resulted in a prolonged time of the dialogue (20-30 mins) out of the estimated time (10 mins).

Conclusions: In our opinion this method to discover HCV+ people requires an unproportioned amount of efforts and time, compared to the small number of people who actually underwent a treatment. The presence of the psychiatrist was certainly an added value in the management of the communication.

Access to test and educational aspects

OP 29 PREJUDICE AND PERCEIVED HIV RISK AMONG HIGH SCHOOL STUDENTS

C. Pellegris[1], I. Mercurio[1], P. Meli[1], E. Zanetti[1], F. Maggiolo[2], I. Fontana[3]

[1]Società Cooperativa Sociale Don Giuseppe Monticelli, [2]ASST Papa Giovanni XXIII, [3]Ufficio Scolastico Territoriale Bergamo

Background: #cHIVuoleconoscere is a project to promote sensitization, information and formation about HIV/AIDS in high schools aiming to improve the knowledge about the prevention, increment the acceptability of screening tests and fight the stigma.
Methods: The project engages high school students through interactive programs. The courses (on average 3 meetings of 2 hours each) for single classes are conducted by trained experts and afterwards evaluated by means of a pre- and post-intervention questionnaire, derived from those of the AIDS Project of Caritas Italiana. The questionnaire includes 2 questions about the perception of infection risk and 5 about stigma. All answers may be graded on a scale from 1 to 10. A comprehensive score combining the 5 questions on stigma was calculated with a range from 5 to 50 (being 5 the minimum stigma). This report focuses on these 2 aspects.
Results: Between October 2019 and March 2022, 4386 students participated into the project and compiled the questionnaires. Overall, only 3.5% of students did not show any prejudice (score = 5) toward PLWH at baseline. Before the intervention several variables were significantly associated to the individual prejudice. Type of scholastic institution being professional Schools at higher risk of stigma than technical institutes and both of them than Prep Schools (figure panel A); gender with males showing greater stigma than females, as well as students of foreign origin compared to Italians, and students born in the latter years compared to those of previous years. However, in the Probit multivariate analysis only the type of Institute and the gender retained significance. Interestingly, both these variables were significantly associated ($P = 0.008$) to the perception of risk, too. After the intervention all scores improved significantly ($P < 0.0001$) (figure panel B). As an example, at the question “Do you think that it is appropriate for a person living with HIV to work with children?” being the possible choices in the range from 1 (not at all) to 10 (yes, absolutely the mean score raised from 6.1 to 9.5 ($P < 0.001$). The comprehensive score improved, too, lowering from a mean of 17.6 to 12.3 ($P < 0.0001$). However, the proportion of students showing no prejudice raised only to 11.2% and a 8% of students did not change their opinion or radicalized their stigma (score increment ≥ 3). The perception of a potential risk of acquiring HIV infection raised from a mean score of 2.8 to 3.14 ($P < 0.0001$).
Conclusions: Through the project #cHIVuoleconoscere a scientifically sound, correct and updated information is conveyed to students. Despite the fact that even younger people show a significant grade of prejudice toward PLWH, the educational project induces a clear reduction of the perceived stigma. We believe that betting on younger generations is a winning strategy to obtain 2030 WHO endpoints to end the HIV epidemics and defeat stigma.

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Access to test and educational aspects

OP 30 PILOT EXPERIENCE OF COMPREHENSIVE SEXUALITY EDUCATION AMONG ITALIAN ADOLESCENTS: PRELIMINARY RESULTS FROM THE EDUFORIST PROJECT, APRIL 2022

A. Chinelli[1], D. Martinelli[2], L. Ceccarelli[1], E. Torri[1], R. Galipò[3], P. Meli[4], A. Camposeragna[5], L.Rancilio[6], M. Farinella[7], L. Colaprico[8], M. Oldrini[9], M.C. Salfa[10], A. Cellini[11], M. Ubbiali[12], A. Caraglia[13], L. Mortari[12], A.T. Palamara[11], B. Suligoi[10], L. Tavoschi[1]

[1]University of Pisa, Department of Translational Research on New Technologies in Medicine and Surgery, [2]University of Foggia, Department of Medical and Surgical Sciences, [3]ANLAIDS - National Association for the Fight against AIDS, Rome, [4]CICA - Italian Coordination of HIV/AIDS Housing Homes, Bergamo, [5]CNCA - National Coordination of the Hospitality Community, Rome, [6]Caritas Ambrosiana, Milan, [7]Circolo di cultura omosessuale Mario Mieli, Rome, [8]Italian Red Cross, Rome, [9]LILA - Italian league for the fight against AIDS, Rome, [10]Italian National Institute of Health, Rome, [11]Sapienza University of Rome, [12]University of Verona, Department of Human Sciences, [13]Ministry of Health, Department of Prevention, Rome

Background: Comprehensive sexuality education (CSE) is an integrated approach to sexual health and wellbeing promotion, empowering young people by providing them with accurate, age-appropriate, evidence-based information and teaching. CSE is internationally recognised to be highly effective in preventing HIV and sexually transmitted infections (STIs), especially when experienced in school contexts, but it is not yet included in Italian school curricula. This study describes the preliminary results of a pilot CSE experience ongoing among Italian adolescents attending 20 lower secondary schools (LSS) of 4 Regions within the EduForIST project, funded by the Italian Ministry of Health.

Methods: The pilot experience consists of 5 modules of 2 hours conducted per classroom. Modules have been developed by a research team coordinated by pedagogists, constantly interfacing with academics, HIV/AIDS civil-society organisations (CSOs), sexuality education (SE) experts and educators from CSOs that are leading the activities in the schools. Four theoretical and practical modules address the domains: A) acknowledging changes in adolescence, B) handling emotions and relationships, C) sexual identities and diversity, D) sexual consent, STIs/pregnancy prevention, sexual health services. The last module is dedicated to the student evaluation of activities, by using standardised pre/post tests (table1) and satisfaction questionnaires.

Results: The pre-test results referred to 14 classrooms of 5 schools within 2 Italian Regions, for a total of 228 students. Among these, 37,7% reported to be unsure that personal identity is built through social comparison (domain A, item 4); 21,5% wrongly answered that emotions don't get more intense during adolescence, while 18,9% were unsure about the response (domain B, item 1); 43,4% reported a higher level of uncertainty concerning the definitions of gender identity, sexual orientation and stereotype (in domain C, item 3). Students reported the highest uncertain answers about domain D related to STIs symptoms (item 2: 58,8%), impact of treatment on HIV+ people (item 3: 62,7%) and efficacy of contraceptive pills in preventing STIs (item 4: 42,1%). The preliminary results of the pre/post analysis showed an increase of correct answers ($p<0.05$) for 7 of 15 items investigated. A smaller number of students responded to the satisfaction questionnaire, with preliminary positive results.

Conclusions: Since activities are ongoing, further data will be soon available for more exhaustive analyses. Initial pre-test results revealed lacks of knowledge and uncertainty among LSS students, especially regarding sexual identity and STIs symptoms. Early pre/post evaluations suggest that the pilot experience seems effective in enhancing knowledge and decreasing uncertainty in the different domains addressed in the pilot. Evidence collected through this study will inform policy makers on the urgency of introducing CSE in Italian school curricula.

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Predictors of COVID-19 severity

OP 31 HOSPITALIZATION FOR COVID-19 OR WITH SARS-COV-2 INFECTION DURING TWO DIFFERENT EPIDEMIC PERIODS IN MILAN, ITALY: DATA FROM LUIGI SACCO HOSPITAL REGISTRY

A. Giacomelli[1], A.L. Ridolfo[1], L. Pezzati[1,2], M. Piscaglia[1,2], S. Caronni[1,2], F. Sabaini[1,2], L. Oreni[1], F. Borgonovo[1,2], M. Matone[1,2], M. Galimberti[1,2], M. Zacheo[1,2], A. Civati[1,2], A. Behring[1,2], M. Schiavini[1], G. Rizzardini[1], S. Antinori[1,2]

[1]Department of Infectious Diseases, ASST Fatebenefratelli-Sacco, Luigi Sacco University Hospital, Milan, Italy, [2]Luigi Sacco Department of Biomedical and Clinical Sciences DIBIC, Università degli Studi di Milano, Milan, Italy

Background: The aim of our study was to compare the clinical characteristics of hospitalized patients with SARS-CoV-2 infection at the peak of hospitalization of the 3rd and the 4th Italian epidemic wave of the COVID19 pandemic.

Material and methods: We searched the Luigi Sacco COVID-19 Hospital registry and extracted a list of patients, who were being hospitalized with a positive nasopharingeal swab (NPS) on March 21st, 2021 (T1: peak of COVID19 hospitalizations during the 3rd epidemic wave) and on January 21st, 2022 (T2: peak of COVID19 hospitalizations during the 4th epidemic wave). The patients' characteristics at hospital admission (e.g. maximum oxygen support and outcome death/discharge) were retrieved. Patients' categorization was based on the reason of hospital admittance: either COVID-19 or another reason with a concomitant positive NPS or a subsequent hospital acquired SARS-CoV-2 infection.

Results: At T1 153 patients and at T2 119 patients were hospitalized for SARS-CoV-2 infection (Table 1-2). At T2 patients were more frequently women (49.6% vs 34 %; p< 0.013), older [75 (IQR 65-84) vs 68 (IQR 57-76) years; p<0.001)], and with more comorbidities (Charlson Comorbidity Index 4 vs 3; p<0.001) when compared to T1. At T2, 22.7% of patients did not require oxygen supply upon hospital admission when compared to 8.5% at T1 (p<0.001). Only one patient at T1 was vaccinated for COVID-19 vs 72 (60.5%) at T2 (1 dose: 6 (5%) patients; 2 doses: 45 (37.8%) patients; 3 doses: 21 (17.6%) patients). At T1, 2 (1.3%) patients were hospitalized for reasons other than COVID-19 [one (0.7%) was a nosocomial infection] when compared to 23 (19.3%) at T2 (p<0.001) [10 (8.4%) were nosocomial infections], of whom 21 (91.3%) were vaccinated. Among those hospitalized for reasons other than COVID-19, 5 patients (20%) required surgical procedures, 2 (8%) had an acute cardiovascular disease, 3 (12%) had a psychiatric disorder, 3 (12%) had a neurological one and the remaining 13 (52%) were hospitalized for other medical conditions. Nineteen out of 119 (16%) patients hospitalized at T2, and 24/153 (15.7%) hospitalized at T1 died. Patients hospitalized at T2 required less C-PAP/high flow or mechanical ventilation support when compared to T1 (21% vs 30.1% and 7.6% vs 26.1%; respectively). Unvaccinated patients were younger [72 (IQR 62-82) vs 76 (IQR 68-85); p=0.083], prevalently females (66% vs 38.9%; p=0.005) and less frequently presented with a severe (29.2% vs 38.3%) or critical disease (8.3% vs 25.5%) when compared to those vaccinated for COVID-19. No difference in death rate was observed between vaccinated and unvaccinated patients (16.7% vs 14.9%, respectively).

Conclusions: When compared to the 3rd epidemic wave of COVID-19, the 4th one was characterized by an elderly population with a less severe clinical presentation and a higher burden of comorbidities, with 1 out of 5 patients presenting with a medical condition usually managed outside the infectious disease ward.

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Predictors of COVID-19 severity

OP 32 PROGNOSTIC VALUE OF TRANSAMINASES AND BILIRUBIN LEVELS AT ADMISSION TO HOSPITAL ON DISEASE PROGRESSION AND MORTALITY IN PATIENTS WITH COVID-19 - AN OBSERVATIONAL RETROSPECTIVE STUDY

R. Palladino, A. Russo, M. Pisaturo, P. Maggi, F.G. Numis, I. Gentile, V. Sangiovanni, V. Esposito, R. Punzi, G. Calabria, C. Rescigno, A. Salomone Megna, A. Masullo, E. Manzillo, G. Russo, R. Parrella, G. Dell'Aquila, M. Gambardella, A. Ponticiello, N. Coppola on behalf of CoviCam group

Infectious Diseases, Department of Mental Health and Public Medicine, University of Campania "L. Vanvitelli", Napoli, Italy, Infectious Diseases Unit, A.O. S Anna e S Sebastiano Caserta, Italy, Emergency unit, PO Santa Maria delle Grazie, Pozzuoli, Italy, Infectious disease unit; University Federico II, Naples, Italy, Third Infectious Diseases Unit, AORN dei Colli, P.O. Cotugno, Naples, Italy, IV Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, Hepatic Infectious Disease Unit, AORN dei Colli, PO Cotugno, Naples, Italy, IX Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, First Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, Infectious Diseease Unit, A.O. San Pio, PO Rummo, Benevento, Italy, Infectious disease unit, A.O. San Giovanni di Dio e Ruggi D'Aragona Salerno, Italy, VIII Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, Infectious Disease Unit, Ospedale Maria S.S. Addolorata di Eboli, ASL Salerno, Italy, Respiratory Infectious Diseases Unit, AORN dei Colli, PO Cotugno, Naples, Italy, Infectious Diseases Unit, AO Avellino, Italy, Infectious Diseease Unit, PO S. Luca, Vallo della Lucania, ASL Salerno, Italy, Pneumology Unit, AORN Caserta, Italy

Introduction: Given the impact of COVID-19 on the world healthcare system, and the efforts of the healthcare community to find prognostic factors for hospitalization, disease progression and mortality, the aim of the present study was to investigate the prognostic impact of transaminases and bilirubin levels at admission on disease progression and mortality in COVID-19 patients.

Methods: Using the CoviCamp database we performed a multicenter, observational, retrospective study involving seventeen COVID-19 Units in southern Italy. We included all adult patients hospitalized for SARS-CoV-2 infection with at least one determination at admission of aminotransaminases and/or total bilirubin. We divided the patients according to the clinical outcome of COVID-19 during hospitalization: mild, moderate, severe outcome and death. The patients with a mild infection did not need oxygen (O2) therapy and/or had a MEWS score below 3 points during hospitalization. The patients with a moderate infection were hospitalized and required non-invasive O2 therapy and/or had a MEWS score equal to or above 3 points (≥3) during hospitalization. The patients with a severe infection needed management in an intensive care unit (ICU) and/or high flow nasal cannula or invasive/non-invasive mechanical ventilation during hospitalization.

Results: Of the 2,054 patients included in the CoviCamp database, 1,641 were included in our study; 789 patients (48%) were considered to have mild, 347 (21%) moderate, 354 (22%) severe COVID-19 and 151 patients (9%) died during hospitalization. Older age [odds ratio (OR): 1.02; 95% confidence interval (CI) 1.01-1.03), higher Charlson comorbidity index (CCI) (OR 1.088; 95%CI 1.005-1.18), presence of dementia (OR: 2.20; 95% CI: 1.30 -3.73) and higher serum AST (OR: 1.002; 95% CI: 1.0001-1.004) and total bilirubin (OR: 1.09; 95% CI: 1.002-1.19) values were associated with a more severe clinical outcome. Instead, the 151 patients who died during hospitalization showed a higher serum bilirubin value at admission (OR 1.1165; 95% CI: 1.017-1.335); the same did not apply for AST.

Including the patients who had both AST and bilirubin determination at admission, we made a comparison between the 1,288 patients discharged alive from hospital and the 115 who died during hospitalization.

Discussion: Bilirubin and AST levels at admission are directly correlated with in-hospital progression of COVID-19 disease and the increase in bilirubin levels at admission is significantly related to hospital mortality.

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Predictors of COVID-19 severity

OP 33 EARLY PREDICTORS OF CLINICAL DETERIORATION IN A COHORT OF OUTPATIENTS WITH COVID-19 IN SOUTHERN ITALY: A MULTICENTER OBSERVATIONAL STUDY

C. Monari[1], M. Pisaturo[1], P. Maggi[2], M. Macera[2], G. Di Caprio[2], R. Pisapia[3], V. Gentile[1], M. Fordellone[4], P. Chiodini[4], N. Coppola[1] on behalf of CoviCam group

[1]Department of Mental Health and Public Medicine - Infectious Diseases Unit. University of Campania Luigi Vanvitelli, Naples, Italy, [2]Infectious Disease Unit, AORN Caserta, [3]Infectious Diseases Unit, AORN dei Colli, Naples, [4]Medical Statistics Unit, University of Campania Luigi Vanvitelli, Naples, Italy

Background: Data regarding early predictors of clinical deterioration in patients with infection of SARS-CoV-2 is still scarce. Aim of the study is to identify early symptoms or signs that may be associated with severe COVID-19.
Methods: We conducted a multicenter observational study on a cohort of patients with COVID-19 in home isolation from March 2020 to April 2021. We assessed clinical data (fever, dyspnea, need for hospitalization) trough video calls at three specific time points: the beginning of symptoms or the day of the first positivity of the nasopharyngeal swab for SARS-CoV-2-RNA (t0), and 3 (t3) and 7 (t7) days after the onset of symptoms. We divided patients in mild, moderate and severe, according to the clinical outcome. Patients with a mild infection did not need O2 therapy and/or had a MEWS<3. Patients with a moderate illness required non-invasive O2 therapy and/or had a MEWS≥3 points. Patients with severe COVID-19 had a severe/critical disease: need for ICU and/or mechanical ventilation, and/or death.
Results: We included 329 patients with COVID-19: 182 (55.3%) males, mean age 53.4±17.4 years, median Charlson Comorbidity Index of 1 (0-3). Of the 329 patients enrolled, 171 (51.98%) had a mild, 81 (24.6%) a moderate and 77 (23.4%) a severe illness; 151 (45.9%) were hospitalized. Compared to patients with mild COVID -19, moderate and severe patients were older (p<0.001) and had more comorbidities, especially hypertension (p<0.001) and cardiovascular diseases (p 0.01). At t3 and t7 we found a significant higher rate of persisting fever (≥ 37°C) among patients with moderate (91.4% and 58.0% at t3 and t7, respectively; p<0.001) and severe outcome (75.3% and 63.6%, respectively; p<0.001) compared to mild COVID-19 outcome (27.5% and 11.7%, respectively; p<0.001). The multivariate analysis performed via the POLR model showed that at t3, persisting fever represented the factor with the strongest association with severe clinical presentation (37-38°C: OR 15.34, 95% CI 7.74-32.44, p<0.001; ≥38°C: OR 39.98, 95% CI 16.78-101.25, p<0.001). As well, at t7 persisting fever was the main factor associated with a more severe clinical presentation: (37-38°C: OR 16.76, 95% CI 7.98-37.19, p<0.001; ≥38°C: OR 61.83, 95% CI 24.69-167.17, p<0.001). Considering the study period, none of the patients in our cohort was vaccinated against SARS-CoV-2.
Conclusions: Persisting fever at t3 and t7 seems to be related to a more severe COVID-19, therefore
patients with fever at t3 and t7 should be closely followed-up for clinical deterioration and rapidly referred to COVID -19 centers for early treatment and/or hospitalization. Considering the novel therapeutic options, i.e. monoclonal antibodies and early antiviral treatment, this data may be useful for healthcare professionals to personalize treatment according to the risk factors of each subject and to better allocate resources at all levels of care. Further studies, including vaccinated patients, are needed

Predictors of COVID-19 severity

OP 34 RISK FACTORS FOR IN-HOSPITAL MORTALITY IN COVID-19 PATIENTS WITH END STAGE RENAL DISEASES REQUIRING MANTEINANCE HEMODIALYSIS

A. Cingolani[1], M. Ambrogio[2], G. Micheli[1], G. De Luca[2], M. Chiuchiarelli[1], A. Spasiano[2], P. L. Salvo[1], E. Rosati[2], S.L. Cutuli[3], E. Rando[1], G. De Pascale[3] and Nicola Panocchia[2] for COVIDialysis-FPG Working Group: M. Ambrogio, G. De Luca, A. Spasiano, E. Rosati, N. Panocchia, R. Baccaro, M. Liberatori, A. Naticchia, F. D'Ascenzo, G. Grandaliano, G. Scoppettuolo, F. Damiano, P. Del Giacomo, F. Raffaelli, R. Losito, G. Maiuro, I. Izzi, A.Dusina, R. Passerotto, F. Iamannna, S. Guerriero, B. Liguoro, F. Salvati, V. Iannone, R. Cauda

[1]Infectious Diseases, [2]Nefrology, [3]Intensive Care Unit, Fondazione Policlinico A. Gemelli, IRCCS, Roma

Background: Patients on maintenance hemodialysis (HD) have a mortality rate much higher than that in the general population. To effectively predict the progression of the disease and improve management strategies, it is crucial to identify the risk factors for mortality. Objective of this study is to evaluate clinical presentation, disease course, outcomes, and risk factors for mortality among ESRD- HD patients with infection from SARS COV2.
Material and methods: All clinical data of patients with end stage renal disease (ESRD) requiring HD admitted to a single clinical center during 3.2020-2.2022 for SARS COV2 infection were reviewed. Factors associated with risk of in-hospital mortality were analyzed by univariate and multivariate regresisone analysis.
Results: 153 patients with ESRD were observed: 66% were male, median age 64y (SD14.3), median Charlson Comorbidity Index was 6.96 (SD 2.01). 140 performed intermittent HD in clinical ward, 13 performed CVVHDF in ICU. 31% were not vaccinated at time of SARS COV2 infection. 47% of patients had a radiological diagnosis of COVID-19-related interstitial pneumonia. The average time of hospitalization was 19.9 days (SD 19.5). The in-hospital mortality rate was 26%. 54.7% causes of death were related to COVID-19 pneumonia. Non-survivor patients were more frequently older (73 y vs 64y, p=0.005), with higher CCI (6.9 vs 5.9, p<0.001), had higher proportion of cardiovascular comorbidity (60% vs 36%, p=0.009), peripheral artery disease (60% vs 28%, p<0.001), malignancy (32% vs 16%, p=0.02), had more symptomatic disease (55% vs 26%, p=0.01) and more frequenly COVID-19 interstizial pneumonia (82% vs 41%, p<0.001) and performed higher median number of HD (7 vs 3, p=0.01) compared with survivors. At multivariable regression analysis, the presence of a peripheral artery disease (AOR 3.17, 95%CI 1.36-7.61, p=0.008), and of a neoplasm (AOR 2.79. 95%CI 1.09-7.21, p=0.03) were independently associated with higher risk of death, as shown in Table 1.
Conclusions: In this single-center cohort of COVID-19 patients with ESRD requiring HD, in-hospital mortality was in line with what has been observed in other cohorts. It does not seem to be predominantly associated with complications of SARS COV2 infection, rather with the presence of comorbidities. These data strongly suggest the need to treat these patients early and to identify alternative management strategies, in order to avoid hospitalization for those patients who do not require it for reasons related to management of COVID19 complications.

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Predictors of COVID-19 severity

OP 35 CLINICAL CHARACTERISTICS AND OUTCOMES OF COVID-19 HOSPITALIZED PATIENTS IN THE CURRENT PANDEMIC PHASE

E.P. Drago[1], M. Poliseno[1], M.A. Poli[3], M. Altamura[2], S.R. Bruno[2], A. Calamo[2], A. Giannelli[2], G. Infante[2], M. Mazzola[2], S.B. Morella[2], D. Moschetta[2], M. Tarallo[2], S. Lo Caputo[1], T.A. Santantonio[1], S. Carbonara[2]

[1]Infectious Diseases Unit, Department of Clinical and Experimental Medicine, University of Foggia, [2]Infectious Disease Unit, Vittorio Emanuele II Hospital, Bisceglie, Barletta-Andria-Trani, [3]Dermatology Unit, Department Internal Medicine, University of Bari

Introduction: The current pandemic phase characterized by the progressive replacement of the SARS-CoV-2 delta variant with omicron, can affect both unvaccinated and vaccinated individuals. The purpose of this work is to evaluate the characteristics of patients with COVID-19 who need hospitalization today and the progression factors towards ICU hospitalization or death.

Material and Methods: All patients consecutively admitted to the infectious disease unit at Vittorio Emanuele II Hospital (Bisceglie, BT, Italy) because of COVID-19 between December 1st, 2021, and February 28th 2022, were retrospectively enrolled in the study. Demographic, clinical, and SARS-CoV-2 vaccine history and outcomes (discharge with clinical stability, intensive care unit (ICU) admission, or in-hospital death) were recorded and analyzed.

Results: Baseline characteristics at the hospital admission of the enrolled subjects and their outcomes, grouped by vaccination status, were reported in Table 1. Patients who were vaccinated with three doses against SARS-CoV-2 were older and presented a significantly higher Charlson comorbidity index than those who were either not vaccinated or vaccinated with only two doses. In particular, fully vaccinated subjects suffered more frequently from chronic kidney disease, chronic obstructive pulmonary disease, or dementia. No difference was found between the three groups at the presentation regarding sex, COVID-19 severity, and median time elapsed from symptom onset to hospitalization. The occurrence of ICU admission or death, as well as the duration of hospital stay, were similar across the three groups of patients. No difference in the risk of ICU admission/in-hospital death was found according to vaccinal status (Image 1).

The requirement for non-invasive ventilation at hospital admission was the only risk factor for an adverse outcome in the Cox regression model (HR 3.67, CI 1.57-8.58, p 0.003) (Table 2).

Conclusions: These results suggest that in the current pandemic phase of widespread Omicron variant and highly vaccinated population, among patients hospitalized in medical wards because of COVID-19, those fully vaccinated (three doses) are more severely comorbid than subjects who received either no dose or ≤2 doses of vaccine. More severe pneumonia, necessitating non-invasive ventilation, represented the only risk factor for poor outcomes, either transfer to ICU or death.

More extensive studies are warranted to clarify the risk factors for COVID-19 associated with severe pneumonia in the latest pandemic era.

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Predictors of COVID-19 severity

OP 36 LABORATORY AND CLINICAL BIOMARKERS HELPS TO PREDICT SEVERITY OF CT SCORE IN COVID19 PATIENTS: AN OBSERVATIONAL STUDY

I. de Luca[1], A. Russo[1], F. Schettino[2], M.A. Pisaturo[1], P. Maggi[1], F.G. Numis[3], I. Gentile[4], V. Sangiovanni[5], V. Esposito[6], R. Punzi[7], G. Calabria[8], C. Rescigno[9], A. Salomone Megna[10], A. Masullo[11], E. Manzillo[12], G. Russo[13], R. Parrella[14], G. Dell'Aquila[15], M. Gambardella[16], A. Ponticello[17], A. Reginelli[2], N. Coppola[1] on behalf of CoviCam group

[1]Infectious Diseases, Department of Mental Health and Public Medicine, University of Campania "L. Vanvitelli", Napoli, Italy, [2]Radiology Unit, Department of Precision Medicine, University of Campania "L. Vanvitelli", Napoli, Italy, [3]Emergency Unit, PO Santa Maria delle Grazie, Pozzuoli, Italy, [4]Infectious Disease Unit; University Federico II, Naples, Italy, [5]Third Infectious Diseases Unit, AORN dei Colli, P.O. Cotugno, Naples, Italy, [6]IV Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [7]Hepatic Infectious Disease Unit, AORN dei Colli, PO Cotugno, Naples, Italy, [8]IX Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [9]First Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [10]Infectious Diseease Unit, A.O. San Pio, PO Rummo, Benevento, Italy, [11]Infectious disease unit, A.O. San Giovanni di Dio e Ruggi D'Aragona Salerno, Italy, [12]VIII Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [13]Infectious Disease Unit, Ospedale Maria S.S. Addolorata di Eboli, ASL Salerno, Italy, [14]Respiratory Infectious Diseases Unit, AORN dei Colli, PO Cotugno, Naples, Italy, [15]Infectious Diseases Unit, AO Avellino, Italy, [16]Infectious Diseease Unit, PO S. Luca, Vallo della Lucania, ASL Salerno, Italy, [17]Pneumology Unit, AORN Caserta, Italy

Background: Laboratory and clinical data performing during admission play an important role in evalueting the prognosis in COVID-19 patients, as CT score of lung. Considering the impact of COVID-19 in low-income countries and the the difficulty of having a wide access to radiological techniques, we aim to evaluate if the clinical and laboratory data may be predictive of severity of CT score.

Material and Methods: From February 28th 2020 to November 1st 2021 we performed a multicenter, observational, retrospective study involving seventeen COVID-19 Units in eight cities in the Campania region including all adult patients, hospitalized with a diagnosis of SARS-CoV-2 infection confirmed by a positive reverse transcriptase-polymerase chain reaction (RT-PCR) on a naso-oropharyngeal swab (Covi-Camp cohort). All demographic and clinical data and therapy details of patients with SARS-CoV2 infection enrolled in the cohort were collected in an electronic database.

From the CoviCamp cohort, we included for the present study all patients for whom a determination at admission of CT score was available. In different Units in the present study, the radiological involvement of the lungs were collected using two different score, the first described by Chung et al, the second described by Pan et al.

To define a cut-off of CT score for severity of COVID-19, we preliminary performed a systematic review of literature enrolling the 938 studies published as full-paper from January 1st 2021 up to March 20, 2022.

Results: According to the systematic review, we identified as CT-score predicting ICU admission, a score >12.5 using Chung TC score, and >13 using Pan Score.

The patients included in this study were 776, 455 using Total Severity Score(TSS), 321 using Computerized Tomography Severity Score (CTSS). Considering all patients, 500 showed a TC score value considered predicting no ICU admission, 276 had a CT score predicting ICU admission (Table 1). The patients with a CT score predicting ICU admission were more frequently males (69.9% vs 62.4%, p<0.035), and older (64.94 vs 60.88 years, p<0.001) (Table 1). Considering clinical and laboratory data at admission Charlson comorbidity index was statistically higher in patients with severe CT score (2.72 vs 2.37, p< 0.029) as for as white cells count, LDH, AST (Table 1). Furthermore, P/F ratio was also predictive to have a CT score predicting ICU admission (Table 1).

Conclusions: CT score considered predictive of ICU admission may be forecasting by some clinical and laboratory data, including male sex, elder age, higher levels of LDH, AST and white blood cells and a lower P/F which may help to identify patients with major risk of ICU admission and worst outcomes promptly.

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HCV eradication: general and key populations

OP 37 LONG-TERM OUTCOMES IN GT3 HCV/HIV CO-INFECTED SUBJECTS TREATED WITH DAAS: IMPACT ON METABOLIC PROFILE

A. Siribelli[1], D. Ceccarelli[2], E. Messina[2], C. Bertoni[1], R. Lolatto[2], G. Morsica[2], C. Uberti-Foppa[1,2], A. Castagna[1,2], H. Hasson[2]

[1]Vita-Salute University, Milan, Italy, [2]Dept. of Infectious Diseases, San Raffaele Hospital, Milan, Italy

Background: the effect of chronic hepatitis C virus (HCV) infection eradication achieved by direct-acting antivirals (DAAs) on glucose and lipid homeostasis changes thereafter is still contradictory. The pathogenetic link between metabolic alterations and chronic HCV infection is complex and possibly associated with HCV genotype. Genotype 3 (GT-3) hepatitis C infection represents both the most difficult and most urgent to treat since it is associated with increased rates of steatosis, fibrosis, and hepatocellular carcinoma (HCC). The primary objective in this study is to investigate the variation of glucose and lipid parameters after achieving sustained virological response (SVR) post DAAs. The secondary aim is to evaluate the renal function and the risk of developing HCC. Follow-up accrued from the date of SVR to the date of last available visit.

Results: are described as median (IQR) or frequency (%).Changes in laboratory parameters were tested by Wilcoxon signed rank test.Methods: overall, 876 people were treated with DAAs at San Raffaele Hospital from March 2015-April 2022: 135 individuals had GT-3 HCV-HIV co-infection and 129 achieved week 12 SVR and were included in this retrospective observational study. All individuals were assessed for biochemical and virological data at DAA start (baseline, BL), at SVR, at 48, 96, 144, 192 weeks from BL. Results: Patients' characteristics at BL were: age 54.7 [52.1;57.5], male sex 86 (63.7%), 82 (60.7%) were ex-drug users, treated with ART drugs since a median of 19.5 years (IQR=14.7-22.7), 43.0% with an INSTI-based regimen. DAAs regimens were dispensed as follows: sofosbuvir/velpatasvir +/- ribavirin 85(63%), ledipasvir/sofosbuvir +/- ribavirin 1(0.74%), glecaprevir/pibrentasvir +/- ribavirin 6(4.4%), sofosbuvir/daclatasvir +/- ribavirin 41 (30.4%), sofosbuvir +/- ribavirin 2 (1.5%). After 192 weeks from BL, we observed a significant increase in fasting glucose [85.0 (77.0;96.0) mg/dL vs 98.0 (89.0;104) mg/dL], total cholesterol [156 (118;184) mg/dL vs 191 (171;209) mg/dL], LDL [91.5 (63.0;118) mg/dL vs 120 (95.0;139) mg/dL] and HDL [44.0 (35.2;56.8) mg/dL vs 49.0 (41.0;58.5) mg/dL]. We also observed a significant drop of CKD EPI [93.0 (81.0;102) mL/min/1.73m2 vs 80.0 (69.0;93.0) mL/min/1.73m2] associated with a rise of creatinine level [0.87 (0.74;0.96) mg/dL vs 0.93 (0.85;1.11) mg/dL]. As expected, PLT levels significantly increased [167 (132;220) 109/L vs 206 (155;231) 109/L] and FIB4 score steadily decreased [8.20 (5.60;13.3) vs 1.59 (1.21;2.09)]. We found a decrease of AFP levels and only one HCC diagnosis.

Conclusions: In people with genotype 3 (GT-3) hepatitis C infection who achieved SVR after DAA treatment, we observed a significant and progressive increase in blood glucose, total cholesterol, HDL, LDL, while there was a significant and progressive reduction in renal filtration rate and apparent lower risk of de novo HCC diagnosis.

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HCV eradication: general and key populations

OP 38 CHRONIC HEPATITIS C CASCADE OF CARE IN PRISONERS. IS THERE STILL SOME WORK TO BE DONE? ANALYSIS OF TWO PENITENTIARIES IN NORTHERN ITALY

A. Cambianica[1], V. Marchese[1], F. Pennati[1], A. Faustinelli[1], M. Tonni[2], F. Roda[2], A. Spinetti[1], S. Zaltron[1], S. Fiorentini[3], E. Quiros-Roldan[1], F. Castelli[1], E. Focà[1]

[1]Division of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili Hospital, Brescia, Italy, [2]Unit of Prison Health ASST Spedali Civili Hospital, Brescia, Italy, [3]Unit Of Microbiology and Virology, Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy

Background: Penitentiaries are a known setting with a high burden of communicable diseases, including HCV infection. According to international guidelines, screening and test-and-treat programmes should be implemented. However, ensuring the continuum of care in prison is a challenge, especially after release. We present the analysis of the HCV cascade of care in two penitentiaries in Brescia, Northern Italy.

Material and Methods: The city of Brescia has one jail (Casa Circondariale) and one prison (Casa di reclusione), with a cumulative capacity of 260 prisoners, although overcrowding is a chronic issue. At the admission all prisoners are offered a voluntary serological screening for HCV, HBV, syphilis and HIV. Those with positive results are referred to infectious disease (ID) specialists, performing in-prison consultations. Patient file is linked to that of the ID Unit, ensuring record availability after release. We performed an observational retrospective study including all the subjects admitted in the 2 penitentiaries of Brescia (Italy) from 01/01/2015 to 31/10/2021 that accepted the screening. Microbiological results were retrieved from the Microbiology and Virology Unit, while sociodemographic and clinical data were collected from patients files. Tests performed at a six-month interval in the same person were considered as a new screening due to possible re-admission.

Results: During the study period, 5378 accesses were registered. At admission, 2932 (54.4%) screenings for HCV were performed in 2600 people, with a mean of 427.7 tests per year and a slight decrease during 2020 (Table 1). HCV antibodies were positive in 267 (9.1%) tests in 188 people (7.2%). HIV/HCV coinfection was detected in 26 (13.8%) people, of which 17 (65.4%) under antiretroviral treatment at admission. HCVRNA was measured in 208/267 (77.9%) positive cases and was detectable in 134 (64.4%) tests, accounting for 96 patients. Genotype analysis was available in 105/134 (78.4%) samples: genotype 1a (42.9%) and 3a (34.3%) were the most frequently reported, followed by 4 a/c/d; double genotype (3a + 4c/d) was detected in 2 patients. DAA treatment was started for 41 patients (42.7%). Sofosbuvir/Velpatasvir (53.7%) and Glecaprevir/Pibrentasvir (34.1%) were administered in the majority of the cases. Sustained virological response (SVR) at twelve weeks was observed in 23 (56.1%) patients, 2 relapsed; 16 patients' outcome is unknown.

Conclusions: Seroprevalence in prison is higher than the general population, as expected. Genotype detection reflects the high injecting drug use habit recorded in the Italian penitentiary system. Treatment rate is higher than other experiences, but losses to follow up remain a challenge and need to be addressed in order to achieve the ambitious goal of HCV eradication by 2030. Dedicated local networks including ID departments, substance abuse services (SERD) and prisons could mitigate this issue.

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HCV eradication: general and key populations

OP 39 HCV POINT OF CARE SCREENING IN PEOPLE TESTED FOR SARS-COV-2 IN A SOCIAL-HOUSING NEIGHBOURHOOD OF MILAN, ITALY

M. Beltrami[1,2], G. Pagani[3], F. Conti[1,2], L. Pezzati[1,2], G. Casalini[1,2], R. Rondanin[4], A. Prina[4], A. Zagari[5], M. Galli[1,2], A. Giacomelli[1]

[1]Malattie Infettive III Divisione, ASST FBF-Sacco, Milan, Italy, [2]Dipartimento di Scienze Biomediche e Cliniche "L. Sacco", Università degli Studi di Milano, Milan, Italy, [3]Malattie Infettive, Ospedale Nuovo di Legnano, ASST Ovest Milanese, Legnano, Italy, [4]Medispa S.r.l., Milan, Italy, [5]Direzione Socio-Sanitaria, ASST FBF-Sacco, Milan, Italy

Background: SARS-CoV-2 pandemic has caused a challenge to the WHO roadmap to achieve HCV elimination by 2030 with a detrimental effect in terms of excess of death especially in the lower middle-income groups . Italy is one of the countries with the highest HCV seroprevalence in Western Europe . We aimed to assess the HCV Ab positivity through point-of-care-testing (POCT) in subjects undergoing COVID-19 screening in the San Siro social-housing neighborhood of Milan, with multi-ethnical population and low social economic status.

Material and Methods: We conducted a cross-sectional prevalence study for the detection of HCV Ab IgG on capillary blood via a rapid immunochromatographic test (RICT) contextually with detection of anti-SARS-CoV-2 IgG performed on capillary blood and a rapid nasopharingeal swab between December 2020 and February 2021. For supply reasons HCV Ab RICTs were not always present during the all the screening period. The primary aim of the study was to estimate prevalence of HCV Ab positivity. The secondary aim was to assess the proportion of acceptance of linkage to care. People currently living in San Siro neighborhood, aged >39 years were eligible. Treatment and follow-up were offered when positivity for HCV-RNA on peripheral blood was confirmed.

Results: Out of 2,394 subjects who participated, 1,637 subjects were eligible, of whom 691 (42.2%) were screened for HCV Ab by RICTs. During the first 14 days of the screening when the HCV Ab RICTs were always available 310 out of 322 subjects eligible for HCV screening were tested accounting for an acceptance rate of 96%. Characteristics of the study population are presented in Table 1. The median age was 64 years [Inter Quartile Range (IQR) 54-74] and 435 subjects were female (62.9%). Five hundred-fifty-three subjects (80%) had at least one Italian parent and 138 (20%) had no Italian parents. Seventeen subjects (2.5%) tested positive for HCV Ab of whom Five subjects (29.4%) were unaware of their serological status; of them: 3 patients declared they were already followed; 1 patient was confirmed to be HCV-RNA positive and underwent DAA treatment and 1 patient opposed to follow-up. Nineteen subjects who tested HCV Ab negative at RICTs reported a previous HCV infection. Of them: 2 refused any kind of follow-up, 2 were confirmed to be HCV Ab positive but HCV RNA negative and 15 subjects reported previous treatment.

Conclusions: We found a prevalence of HCV Ab positivity of 2.5%, with one subject who was confirmed to be HCV-RNA positive (0.16%). In conclusion, although COVID-19 pandemic had negatively impacted the diagnosis and treatment of liver disease in non-COVID-19 patients, we underline the need to put efforts to turn the challenge of the pandemic into opportunity to screen, engage and link to care people for HCV. Effort should be focus on those who face barriers related to the socioeconomic situation, ethnicity, or stigma.

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HCV eradication: general and key populations

OP 40 HEPATITIS C VIRUS (HCV) MICRO-ELIMINATION IN THE HOSPITAL SETTING: THE RESULTS OF THE HCV CASERTA HOSPITAL PROJECT

V. Messina[1], M. Pisaturo[2], L. Alessio[2], A. Russo[2], E. Tripaldelli[3], A. Petruzziello[3], A. Annechiaro[4], M.R. Romano[5], P. Maggi[1,2], N. Coppola[2]

[1]Infectious Disease Unit, AORN Sant'Anna e San Sebastiano, Caserta, Italy, [2]Department of Mental and Physical Health and Preventive Medicine, Infectious Diseases section, University of Campania Luigi Vanvitelli, Naples, [3]Clinical Pathology, AORN Sant'Anna e San Sebastiano, Caserta, Italy, [4]Direzione Sanitaria, AORN Sant'Anna e San Sebastiano, Caserta, Italy, [5]Regione Campania, Naples, Italy

Background: In the present study we evaluated the efficacy of an innovative model of HCV micro-elimination in a hospital setting in an area of high HCV prevalence.

Patients and Methods: Between January and December 2019, a prospective, interventional study for a program of HCV case-finding and linkage-to-care was performed in S. Anna and S. Sebastiano hospital of Caserta, in Campania, a region in southern Italy. All adult patients who were admitted to the Caserta hospital in the study period and resulted positive for anti-HCV were included in the study. The outcomes evaluated were the number of subjects resulting HCV-RNA-positive, those linked-to-care and treated with a DAA and the subjects whose anti-HCV-status was unknown.

Results: In the study period, 14,396 subjects, admitted to the hospital for different reasons, were tested for anti-HCV: 529 (3.7%) subjects resulted positive for anti-HCV.

Figure 1 shows the flow chart of the subjects enrolled in the present study. Of the 529 anti-HCV-positive subjects, 10 died during hospitalization and 243 were already treated with DAA, as demonstrated by the Saniarp database. The remaining 276 subjects were contacted by Infectious Disease Physicians: 145 were unaware of their anti-HCV-positivity and the remaining 131 were not linked to care. All 276 subjects contacted agreed to be evaluated. Of these 276 subjects, 68 patients were HCV-RNA-negative and 194 HCV-RNA-positive. Of the 194 HCV-RNA-positive subjects, 14 refused treatment and 180 were treated with DAAs (sofosbuvir plus velpatasvir for 12 weeks or glecaprevir plus pibrentasvir for 8-12 weeks). SVR was identified in all but 2 subjects, who were lost to the follow-up. (Figure 2)

Conclusions: A simple, rapid, inexpensive model of HCV micro-elimination in the hospital setting allowed us to find anti-HCV-positive subjects with unknown anti-HCV status or not linked to a clinical center.

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HCV eradication: general and key populations

OP 41 PATIENTS' REPORTED EXPERIENCES WITH DIRECT ACTING ANTIVIRAL THERAPY IN AN INTEGRATED MODEL OF HEPATITIS C CARE AND TREATMENT

L. Ceccarelli[1,2], G. Moretti[2], I. Corazza[2], L. Tavoschi[1], M. Vainieri[2]

[1]Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy, [2]Management and Healthcare Laboratory, Sant'Anna School of Advanced Studies, Pisa, Italy

Background and Aims: Patients' Reported Experience Measures (PREMs) are critical for engagement in hepatitis C (HCV) therapy. However, there are no integrated data on patient reported experience among people who live with HCV and undertook direct acting antiviral (DAA) therapy in Italy. We assessed PREs among people who live with HCV on DAA treatment within the frame of an ongoing project on HCV identification and treatment in Tuscany Region, Italy.

Materials and Methods: Within an ongoing cohort prospective study on HCV linkage to care, 72 patients from 3 tertiary care centers received DAA therapy from 05/2021 to 01/2022. PREMs were assessed before the beginning of the therapy, addressing several domains (socio-demographic features, HCV history and diagnosis, relationship with the healthcare professionals, timeliness of diagnosis and treatment, health status perceived). Descriptive statistical analysis was conducted to investigate the characteristics of included patients. Patients' enrollment is still in progress and results will be periodically updated.

Results: A total of 70 patients completed the survey (response rate 97.2%), 52.8% males and 47.2% females. The most represented age group was >53 (median age 57.5 years). Middle school diploma was the most common level of education (43.6%) and 38.9% were retired and 30.6% currently employed. The most frequently reported transmission route was unprotected sexual intercourses (66.7%) for both males and females; patients reporting injecting drug use (PWID) represented the 27.8%, and were mostly males (85%), while hazardous tattooing activity was reported by 23.6% of the patients, mostly females (70.6%). Most of the patients (69.4%) reported having been diagnosed for the first time more than 12 months before the completion of the questionnaire. Linkage to care experience was positive for most patients as 68.1% reported to having felt accompanied in the linkage to care to the tertiary care center, 62.5% obtained a specialistic visit within two weeks from the diagnostic test. Reported overall health status was good for 64.3% of patients while 32.9% reported functional limitations due to the HCV infection. Concerning hard-to-reach populations (people who live in prisons - PiP, PWID), no significative differences were reported in terms of waiting times for the specialist visit or linkage to care effectiveness, but 26.3% of PWID reported a poor health status against the 7.8% of general population.

Conclusion: PREMs showed an overall weaker health status reported by PWID but HCV healthcare services appeared to be responsive for hard-to-reach populations as for general population. No significant differences emerged from PREMs by different cohort of patients (e.g., PWID, PiP). As PREMs are key for engagement in HCV therapy, tailored testing and treatment interventions could represent a model of HCV linkage to care to enhance treatment uptake in hard-to-reach populations.

HCV eradication: general and key populations

OP 42 CHARACTERISATION OF VIRAL INFECTIONS IN A COHORT OF MIGRANTS LIVING IN SOUTHERN ITALY

S. Capuano[1,9], M. Pisaturo[1,7], A. Loredana[1,7], L. Occhiello[1], M. Macera[1,4], M. Starace[1], E. Cordua[1], L. Onorato[1], G. Scotto[8], G. Di Caprio[3,7], F. Calò[1,6], C. Sagnelli[1,5], N. Coppola[1]

[1]Department of Mental and Physical Health and Preventive Medicine, Infectious Diseases section, University of Campania Luigi Vanvitelli, Naples, [2]L. Vanvitelli University Hospital, Naples, [3]UOC of Infectious Diseases, AORN Sant&Anna and San Sebastiano, Caserta, [4]Abraham Tent; Reception Center, Caserta, [5]Missionary Sisters of Charity Center, Naples, [6]Center for the Protection of Immigrant Health, Naples, [7]Social center "ex-canapificio", Caserta, [8]UOC of Infectious Diseases, Foggia, [9]Social center "ex-opg Je so Pazz", Napoli

Background and Aims: To evaluate the prevalence and the characteristics of HBV, HDV, HCV and HIV infection in migrants.

Methods: A prospective multicenter study was carried out involving 5 first-level clinical centers and 3 infectious disease clinics in southern Italy between January 2012 and February 2020 All migrants attending one of the 5 first-level centers in Southern Italy was screened for HBsAg, HBcab, antiHCV, antiHIV. Migrants with HBsAg, anti-HCV or anti-HIV positivity were followed by an Infectious Disease Unit operating in the same city.

Results: The median age of the 2923 enrolled patients was 27 years (IQR: 12), 83,5% were male and the average months of stay in italy was 7 years (DS 34). The geographical area of origin was Eastern Europe (8.9%), Asia (19.2 %) North Africa (4,3%), Sub-Saharan Africa (66%), America (0,4%) and unknown for 0,5%. Of the 2923 patients, 257 were HBsAg positive (8%), 85 were Anti-HCV positive (2.9%), 16 were HBsAg/HCV positive (0,5%), and 8 were HBsAg/HDV (0.2%). Table 1 showed the epidemiological characteristic of the enrolled subjects.

We confronted 4 groups: HBV mono infection (Control B), HCV mono infection (Control C), HBV /HCV coinfection (case BC), HBV /HDV coinfection (Case BD). The median age in the three groups was similar, without difference in the gender prevalence [Group B males 248 (88%), Group C males 87 (86%), Case BC Males 13 (81.2%), Case BD Males 8 (100%); p B vc BC =0,4, p B vs BD =0.3, p C vs BC=0.6]. There was a higher prevalence of subjects from sub-Saharan Africa for every group (Control B 84,6% vs. Case BC 68% p=0.09, Control B vs Case BD 100% p=0,2 C vs BC=0.5) and an higher prevalence of subject from Indo Pakistan Area in Case BC vs Control B (25% vs 6,4% p=0.005).

The most frequent risk factors were unprotected sexual intercourse, dental procedures and intramuscular therapy, with statistical difference for drug addiction in B vs BC (p=0.00), and C vc BC p=0.001, for sexual intercourse without a condom in B vs BC p=0,03 and for intramuscular therapy in B vs BC p=0,04 and in C vs BC p=0,005. HBV DNA positivity was found in 194 (69%) of the 281 subjects in the Control B group, in 7 (43%) of the 16 subjects of the Case BC group and in 1 (12,5%) of the 8 subjcets from case BD group (p B vs BC = 0.03, p B vs BD = 0,0008); HBV viral load was similar in the 3 groups. HCV RNA positivity was higher in patients with HBV/HCV coinfections compared to those with HCV monoinfection (75% vs 49,5% p=0,057). Case BC had a prevalence of chronic hepatitis of 62%, while control B had 33,4% and control C 39,6% (p B vs BC = 0,017,p C vs BC = 0,08). Liver chirrosis was more prevalent in case BC (25%) and case BD (12,5%) compared to monoinfections (B vs BC,p= 0.006, C vs BC,p= 0.013).

Conclusions: data on viral hapatitis coinfections in migrants and on clinical presentation are scanty so we believe that studies towards this direction should be implemented.

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Viro-immunological correlates of COVID-19 severity

OP 43 PTX3 IS A STRONG PREDICTOR OF DEATH AMONG PATIENTS WITH COVID-19

G. Lapadula[1,2], R. Leone[3], D.P. Bernasconi[4], A. Biondi[1,5], E. Rossi[4], M. D'Angiò[5], B. Bottazzi[3], L.R. Bettini[5], I. Beretta[2], C. Garlanda[3,6], M.G. Valsecchi[4], A. Mantovani[3,6,7], P. Bonfanti[1,2] for the COVID-19 STORM Study Group

[1]University of Milano-Bicocca, Milan, Italy, [2]Department of Infectious Diseases, San Gerardo Hospital, Monza, Italy, [3]Humanitas Clinical and Research Institute – IRCCS, Rozzano (MI), Italy, [4]Bicocca Bioinformatics Biostatistics and Bioimaging Center - B4, University of Milano–Bicocca, Milan, Italy, [5]Department of Pediatrics, European Reference Network (ERN) PaedCan, EuroBloodNet, MetabERN, Fondazione MBBM/Ospedale San Gerardo, Monza, Italy, [5]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milan, Italy, [6]William Harvey Research Institute, Queen Mary University, London, UK

Background: Long pentraxin 3 (PTX3) is an important mediator of inflammation and innate immunity, which has been associated with mortality in many systemic inflammatory conditions. We aimed at assessing its prognostic value in a large cohort of patients hospitalized with COVID-19.

Methods: The STORM Study enrolled consecutive patients (Pt) hospitalized with COVID-19 in San Gerardo Hospital (Monza, Italy) since March 2020. Levels of PTX-3 were measured using in-house sandwich ELISA on frozen plasma samples collected at admission. Cox regressions were modeled to identify predictors of death and death/mechanical ventilation (MV) among those listed in Table 1. The additional discriminatory ability of PTX3 was estimated comparing the cross-validated c-statistics of multivariable models with and without it. Crude mortalities were compared among patients with PTX3 levels higher or lower than the best cut-off estimated with the Maximally Selected Rank Statistics Methods.

Results: Among 152 Pt, 62% were male and 94% Caucasian; median age was 67 (IQR: 55-80) years. Upon admission, 22% required no oxygen, 46% low-flow oxygen, 30% high-flow nasal cannula or CPAP-helmet and 3% MV. Median (IQR) level of PTX-3 was 21.7 (13.5-58.23) ng/ml. In-hospital mortality was 25% (38 deaths); 13 Pt (8.6%) underwent MV during the follow-up.

Using univariable Cox regression, PTX3 was associated with risk of death (per 10 ng/ml increase, HR 1.07; 95%CI 1.04-1.09; P<0.001) and of death/MV (HR 1.07; 95%CI 1.05-1.09; P<0.001). As shown in Table 1, other predictors of in-hospital mortality were older age, Charlson Comorbidity Index, D-dimer and C-reactive protein (CRP). Using multivariable analysis, baseline PTX3, but not CRP or D-dimer, remained a predictor of death (per 10 ng/ml, HR 1.08; 95%CI 1.04-1.11; P<0.001) and death/MV (HR 1.04; 95%CI 1.01-1.07; P=0.011). The addition of PTX3 to the multivariable model increased its discriminatory power by 3.7% (from C=74.4 to C=78.1).

Stratification of Pt according to PTX3 maximizing the association with mortality resulted in the optimal cut-off of 39.32 mg/ml. Using such threshold, mortality was significantly higher in the group with higher level of PTX-3 (55% vs 8%, P<0.001).

In addition, higher PTX3 plasma levels were found in 14 patients with subsequent thrombotic complications (median [IQR]: 51.4 [24.6-94.4] versus 21 [13.4-55.2]; P=0.049).

Conclusions: High PTX-3 levels at presentation are associated with a worse outcome, among patients hospitalized with COVID-19. The evaluation of this marker could be useful in prognostic stratification and identification of patients who could benefit from immunomodulant therapy.

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Viro-immunological correlates of COVID-19 severity

OP 44 THE ROLE OF ANTIGEN LOAD ON VIRAL CLEARANCE AND SEVERITY IN SARS-COV-2 INFECTION

T. Clemente[1,2], P.E. Rovatti[3], M. Punta[3,4], C. Muccini[1,2], L. Galli[2], C. Toffalori[3], R. Papaioannu Borjesson[1,2], M. Bottanelli[1,2], C. Tresoldi[5], F. Ciceri[1,5,6], A. Castagna[1,2], L. Vago[3,6], V. Spagnuolo[2], on the behalf of COVID-BioB Study Group

[1]School of Medicine and Surgery, Vita-Salute San Raffaele University, Milan, Italy, [2]Infectious Diseases Unit, San Raffaele Scientific Institute, Milan, Italy, [3]Unit of Immunogenetics, Leukemia Genomics and Immunobiology, San Raffaele Scientific Institute, Milan, Italy, [4]Center for Omics Sciences, San Raffaele Scientific Institute, Milan, Italy, [5]Immuno-hematology and Transfusion Medicine Unit, San Raffaele Scientific Institute, Milan, Italy, [6]Hematology and Bone Marrow Transplantation Unit, San Raffaele Scientific Institute, Milan, Italy

Background: Host immune response during SARS-CoV-2 infection was widely investigated in order to assess the mechanisms of viral clearance (VC) and immune-mediated complications. However, no data about the possible correlations between antigen load (AgLoad) and VC or disease severity are available.

Material and Methods: Retrospective study on patients (pts) hospitalized for coronavirus disease 2019 (COVID -19) in Infectious Diseases Unit, San Raffaele Hospital, Milan, from February to November 2020. Three severity groups were defined: G2 included symptomatic pts with no need of oxygen therapy, G3 symptomatic pts requiring oxygen therapy but not invasive ventilation, G4 symptomatic pts transferred to intensive care unit. Pts with a baseline arterial oxygen partial pressure/fractional inspired oxygen ratio (P/F) were stratified, using 1.5 mmHg/% as cut-off. For each pt, human leukocyte antigen (HLA) -A, -B, -C, and -DRB1 were tested on genomic DNA with next generation sequencing. HLA diversity was estimated by the means of Grantham's distances for each HLA type. From EPI_ISL_487276 viral strain, epitopes of 8-11 aminoacids (aa) for HLA class I and 15-25 aa for HLA-DRB1 were predicted, excluding low-expressed proteins. HLA class I epitopes were filtered by a dissimilarity score >0.65 or a foreignness score >0.35. From these peptides, HLA strong binders were predicted using: i) NetMHCpan v4.1 and MixMHCpred v2.1, with a rank of elution (RankEL) <0.5%, for HLA class I; ii) NetMHCIIpan v4.0, with a RankEL <2%, and MARIA for HLA-DRB1. For both HLA class I and -DRB1, AgLoad of each pt was estimated as the number of strong binders. Time to VC (tVC) was calculated as the time difference between first positive and first negative swab, performed within 30 days from hospital discharge or death. Associations and correlations were assessed by Kruskal-Wallis and Pearson correlation test.

Results: Overall, 258 pts were evaluated: median age was 63 [interquartile range (IQR)=54-75] years, 195 (75.6%) male, 33 (12.8%) belonged to G2, 192 (74.4%) to G3, 33 (12.8%) to G4, 120 (46.5%) had a P/F <1.5 mmHg/%, 100 (38.8%) ≥1.5 mmHg/%, 160 (62%) reached VC within 30 days from hospital discharge or death, with a median time of 26 (IQR=18-32) days, 29 (11.2%) died because of COVID-19 complications. Then, 11,409 possible epitopes were obtained. For HLA class I, AgLoad, estimated using two different predictive systems, was not related to tVC (figure 1), whereas, for HLA-DRB1, there was a marginal association using MARIA (figure 1), not confirmed with NETMHCIIpan (p=0.67). Furthermore, AgLoad was not associated with severity, evaluated through both severity group and P/F (figure 1). HLA diversity was not correlated with tVC (slope=0.018, p=0.85).

Conclusions: In the cohort analyzed, for HLA class I and -DRB1, AgLoad did not seem to be significantly associated with VC or severity in SARS-CoV-2 infection.

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Viro-immunological correlates of COVID-19 severity

OP 45 DYSREGULATION IN IFN-OMEGA LEVELS AND ANTI-IFN-OMEGA NEUTRALIZING ANTIBODIES CORRELATE WITH BIOCHEMICAL AND HEMATOLOGICAL PARAMETERS PREDICTIVE OF DISEASE SEVERITY IN COVID-19 MALE PATIENTS

F. Frasca[1], M. Scordio[1], L. Sorrentino1, M. Fracella[1], L. Santinelli[2], E. N. Cavallari[2], C. Bitossi[1], A. Viscido[1], G. Ceccarelli[2], A. Pierangeli[1], O. Turriziani[1], C. M. Mastroianni[2], G. Antonelli[1], G. d'Ettorre[2], C. Scagnolari[1]

[1]Laboratory of Microbiology and Virology, Department of Molecular Medicine, Sapienza University of Rome, Italy, [2]Department of Public Health and Infectious Diseases, Policlinico Umberto I, Sapienza University of Rome, Italy

Introduction: Type I interferons (IFNs) are a complex family of cytokines that play a key role in antiviral responses. Among IFN-I molecules, the role played by IFNω in viral infections including that caused by SARS-CoV -2 remains poorly characterized. Thus, our aims were to assess the expression of IFNω in the respiratory and peripheral blood of COVID-19 patients, to evaluate anti-IFNω neutralizing antibodies (NAB) and their correlation with demographic, laboratory markers, as well as the clinical outcome of COVID-19.

Methods: Respiratory specimens from COVID-19 patients (n=50) and healthy donors (HD, n=43) were collected at Policlinico Umberto I Hospital in Rome. Furthermore, blood samples from COVID-19 subjects (n=360), SARS-CoV -2/HIV coinfected patients (n=8) and HD (n=19) were included. Evaluation of the mRNA level of IFNω and IFN stimulated genes (ISGs) was carried out by RT/Real Time PCR. Analysis of NAB and their ability to neutralize IFNα and IFNω was performed using antiviral bioassay.

Results: Results showed that IFNω was highly expressed in respiratory cells of COVID-19 patients compared to HD, $p<0.0001$. Levels of IFNω were similar in COVID-19 patients stratified according to their clinical phenotypes: non oxygen support (n=14), non-invasive ventilation (n=18) and invasive mechanical ventilation (n=4), $p=0.3071$. By contrast, blood transcript amount of IFNω was reduced in COVID-19 patients with respect to HD, $p<0.0001$. Anti-IFN-I NAB screening from sera of COVID-19 patients (n=360) revealed that 3.6% (13/360) had anti-IFNα NAB. In particular, we found that 69.2% (9/13) of sera containing anti-IFNα NAB neutralized IFNω. While 42.9% (3/7) of sera with titers of anti-IFNα NAB <10.000 TRU/ml had auto-Abs against IFNω, 100% (6/6) of sera with titers of anti-IFNα NAB ≥10.000 TRU/ml were able to neutralize IFNω. Longitudinal observation of anti-IFNω NAB patients showed persistence of high titer of anti-IFNω auto-Abs. Analysis of ISGs-mRNA indicated that ISG15 and ISG56 were reduced to an undetectable level (cycle threshold/Ct values less than 45) in patients who had persistently high titers of anti-IFNω NAB. Remarkably, anti-IFNω NAB were associated with male sex, admission to the intensive care unit and death, $p<0.01$. Furthermore, anti-IFNω NAB patients exhibited raised levels of C-reactive protein, lactate dehydrogenases, D-Dimer, and higher counts of hematological parameters compared to COVID-19 patients without anti-IFN-I antibodies, $p<0.05$. Moreover, analysis of anti-IFN-I NAB in a group of HIV infected patients hospitalized for severe COVID-19 showed that 71.4%, (5/7) had anti-IFNω NAB.

Conclusion: A dysregulation in the respiratory and blood production of IFNω characterizes severe COVID-19 patients. Anti-IFNω NAB are detected in a significant proportion of critically-ill patients including those with HIV infection and are associated with a defective ISGs response and alteration of laboratory biomarkers of disease severity.

Viro-immunological correlates of COVID-19 severity

OP 46 CHARACTERIZATION OF IFN RESPONSE IN PBMC FROM CHILDREN AND ADOLESCENT AFTER SARS-COV-2 INFECTION

L. Sorrentino[1], M.G. Conti2, G. Oliveto[1], F. Frasca[1], M. Fracella, M. Scordio[1], A. D'Auria, M. Ardone[1], M. Di Lieto[1], L. Petrarca[2], R. Nenna[2], C. Scagnolari[1], G. Antonelli[1], F. Midulla[2], A. Pierangeli[1]

[1]Virology laboratory, molecular medicine department, Sapienza University, Rome, [2]Maternal-Infantile and Urological Science Department, Sapienza University, Rome

Introduction: SARS-CoV-2 infection generally causes mild symptoms or is completely asymptomatic in children and what prevents to develop severe forms is to be defined. In this context, interferon (IFN) response in peripheral blood mononuclear cells (PBMCs) could have an important role; it has been found in severe COVID-19 patients that IFN expression is altered in NK cells. For this reason, we measured type I IFNs (IFN-I) and some Interferon Stimulated Genes (ISGs) expression in PBMCs from children and adolescent with mild or asymptomatic SARS-CoV-2 infection.

Methods: Children and adolescent, attending Umberto I hospital of Rome after a contact with SARS-CoV-2 positive subjects, were enrolled in this study. Nasopharyngeal swab was performed for SARS-CoV-2 diagnosis. Blood samples were collected at 20-30 days (T1) and 40-60 days (T2) from SARS-CoV-2 diagnosis and peripheral blood mononuclear cells (PBMCs) were collected. RNA was purified from PBMC and gene expression of IFN alpha (IFNA), IFN beta (IFNB), IFN omega (IFNO), IFN epsilon (IFNE), IFNAR1, IFNAR2, ISG15, ISG56, IFI27 and MXA was measured through Real Time PCR. Statistical analysis was performed using SPSS software.

Results: 110 subjects (mean age 11,65 years, range 1-19 years) resulted positive to SARS-CoV-2 and we measured IFN-I and ISGs expression in PBMCs at T1 and T2. We found an upregulation of IFN alpha (IFNA), IFN beta (IFNB), IFN epsilon (IFNE) and IFN omega (IFNO) in T1 PBMC with respect to T2 ($p=0.008$ for IFNA and $p<0.001$ for other IFNs); differently, IFNAR2 subunit expression level was higher at T2 ($p<0.001$). Stratifying children based on symptoms reported during SARS-CoV-2 infection, we did not find significative differences between symptomatic and asymptomatic subjects. However, analysing specific symptoms, we observed higher expression of IFI27 and IFNAR1 at T1, in subjects that reported fever ($p=0.027$ and $p=0.011$ respectively) and higher expression of IFI27 in subjects that reported anosmia ($p=0.027$). Moreover, we found higher expression at T1 of IFNE and IFNO in children that reported Long-COVID (LC) ($p=0.011$ and $p=0.014$ respectively).

Discussion: Overall, our findings showed that the expression of IFN-I genes is relevant at one month after SARS-CoV-2 symptomatic and asymptomatic infections. Our data suggest also the association of IFI27 expression with respiratory symptoms, in agreement with previous studies that have shown in adult COVID-19 patients, an upregulation of IFI27 and a positive correlation between IFI27 expression and viral load. Interestingly, we observed an upregulation of IFNO and IFNE in children that reported LC. In adult mild to moderate patients that suffered from LC, higher levels of IFNB were found in blood. These data suggest a role of IFN-I during the response to SARS-CoV-2 but also in LC; these issues are worthy to be investigated further in larger group of subjects.

Viro-immunological correlates of COVID-19 severity

OP 47 IMMUNOLOGICAL PROFILES OF SARS-COV-2 INFECTION: THE LINK BETWEEN CYTOKINE STORM, CLINICAL SEVERITY AND POST-COVID SYNDROME

A. Parente[2], M. Iuliano[1], R. Mongiovì[1], B. Kertusha[2], A. Carraro[2], R. Marocco[2], G. Mancarella[2], C. Del Borgo[2], T. Tieghi[2], L. Fondaco[2], G. Mangino[1], G. Romeo[1], M. Lichtner[2]

[1]Dept. of Medico-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Italy, [2]Dept. of Public Health and Infectious Disease, S. Maria Goretti Hospital, Sapienza University of Rome, Latina, Italy

Background: SARS-CoV-2 is responsible of COVID19 pandemic and can cause acute respiratory disease, associated with cytokine storm. In some patients a post-COVID syndrome is identified and is poorly understood if there is a link with immunological profiles Our aim is to describe by integrating the laboratory data and clinical evaluation during hospitalization and post-COVID outpatient clinic.

Material and Methods: We evaluated the clinical status at the time of hospitalization, during hospital stay, after~3 months and after 20 months.The cyto-chemokine profile was assessed by SuperX Plex Cytokine Assay) that allowed to detect 11 cytokines at the same time in a sample (i.e., IL-1α, -1β, -6, -8, -10, -12(p70), -27, IFN-γ, IP-10, MCP-1, TNF-α), from serum of: 29 COVID19 donors at T0 hospitalization's moment, T1 after~70 days and 13 vaccinated healthy donors-HD.Samples were sub-stratified by severity in non-ARDS pneumonia and ARDS, and by symptoms in follow-up.

Results: We recruited 29 patients hospitalized at Goretti Hospital, (72.4% F, 27.5% M) average age 55.2 years.70% of patients had ARDS and they needed CPAP helmet placement,30% had mild pneumonia. Upon admission, the most frequent symptom was fever, followed by cough, sore throat and dyspnoea. At follow-up, patients complained of asthenia(70%), dyspnoea(35%).More severe acute infection was not associated with an increased risk of developing post-COVID19 symptoms,57% of ARDS and 63% of mild pneumonia patients had post-COVID symptoms. At 20 months, 62% of ARDS patients still complained of symptoms vs 29% of pneumonia. IL-10, IP-10, TNF-a, IL-1b, IL-27 and IL-8 were deregulated depending on sample and time when compared all patients at T0 and T1.

IL-1b decreased in T0 vs HD (HD13,5±12,9 vs T0 3,9±6,7 pg/mL); higher levels of TNF-a in T0 vs T1(HD36,5±44,7 vs. T0 14,7±38,2; T0 14,7±38 vsT1 448±1439 pg/mL).IL-8 down-modulated at T0 and its expression is lower in T1 vs HD (HD522±199.8 vs T0 207,9±374,4; HD 522±199,8 vs. T1 363±603 pg/mL).

IL-10 (HD 7,5 ±9,5 vsT0 30,7 ±39,5; HD 7,5±9,5 vs T1 82 ±301,6 pg/mL) & IL-27 (HD 2,6 ±8,9 vsT0 3,8±10,3; T0 3,8±10,3 vs T1 18±26,9 pg/mL)increased in T1 vs HD their expression were higher in T1 than T0.IP-10 expression improved from HD to T0, restored levels in T1(HD22,6±30,8 vsT0 154,5±119; T0 154,5±119 vs T1 45,4±49,3 pg/mL).

The sub-layered populations confirmed higher levels of IL-8 in HD vs pneumoniaT0, the upregulation of IL-10 in ARDST0 and pneumoniaT0 vs HD, its expression decreased in ARDST1;higher levels of IP-10 in ARDST0 vs HD and ARDST1. In retrospective analysis,persistently symptomatic patients at 20 months had lower baseline IL-8 levels.

Conclusions: Acute infection phase is characterized by cytokine dysregulation. IP-10 increase in ARDS patients at baseline, as in other studies, would represent an early marker of clinical worsening. We observed the cytokine level normalization trend at follow-up. However, IL-10 maintains higher levels at follow-up in patients with pneumonia, associated in our cohort, with the persistence of symptoms.In these cases IL-10, could be used as a marker of post-COVID19 syndrome, where in our experience, no other inflammation index was alterated.

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Viro-immunological correlates of COVID-19 severity

OP 48 RESPIRATORY AND PERIPHERAL IFN RESPONSE AND FREQUENCY OF T CELL ACTIVATION IN COVID -19 PATIENTS

L. Santinelli[1], L. Maddaloni[1], F. Frasca[2], M. Scordio[2], C.M. Lofaro[1], L.Sorrentino[2], M. Fracella[2], E.N. Cavallari[1], G. Ceccarelli[1], A. Pierangeli[2], C. M. Mastroianni[1], G.Antonelli[2,3], C. Scagnolari[2], G. d'Ettorre[1]

[1]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Italy, [2]Virology Laboratory, Department of Molecular Medicine, Sapienza University of Rome, Italy, [3]Microbiology and Virology Unit, Sapienza University Hospital "Policlinico Umberto I", Rome, Italy

Background: A severe SARS-CoV-2 related immunopathology might be the driver cause underlying the deleterious clinical manifestations observed in COVID-19 patients. One of the major determinants of the fatal outcome of COVID-19 patients might be an impaired type I interferon (IFN-I) response combined with alteration in T cells activation. Focusing on peripheral and lung compartments, this study aimed to provide insights into the immunological pathways triggered by SARS-CoV-2 infection, evaluating IFN-I molecular signature and T cell immune activation levels in patients stratified according to the severity of COVID-19.

Methods: Blood transcript levels of IFN-alfa, IFN-beta and IFN stimulated gene-15 (ISG-15) were analyzed by RT/Real Time PCR on 48 SARS-CoV-2 infected patients and 38 age-matched healthy volunteers. The peripheral frequencies of naïve, central memory (TCM) and effector memory (TEM) CD4+, CD8+ T cells subsets expressing immune activation markers (CD38, HLADR) were evaluated by multi-parametric flow cytometry. Bronchoalveolar lavage (BAL) and peripheral blood mononuclear cells (PBMC) were collected from a subgroup of COVID-19 patients (n=13) admitted to ICU and requiring invasive mechanical ventilation.

Results: A general decrease in the blood transcript levels of IFN-alpha, IFN-beta and ISG15 was observed in SARS-CoV-2 infected patients compared to healthy donors ($p < 0.05$ for all genes). Levels of CD4+ and CD8+ T cell subsets (naïve, TCM and TEM) expressing CD38 and HLADR markers (single and both) were higher in SARS−CoV−2 infected patients compared to healthy donors ($p<0.05$). Also, IFN related genes levels were not different between BAL samples and PBMC collected from SARS−CoV−2 infected patients admitted to ICU ($p>0.05$), but those with fatal COVID-19 outcome had increased levels of IFN-alpha and IFN-beta mRNAs at lung and peripheral district compared to COVID-19 survivors ($p<0.05$).

Conclusions: These findings suggest that dysregulation in the transcript expression of IFN-I genes and alteration in T activation levels in the respiratory tract and blood might help to identify patients with critical or life-threatening COVID-19.

Issues on mental health, sexual health and STIs

OP 49 PREDICTORS OF MENTAL AND SEXUAL HEALTH AFTER COVID-19 PANDEMIC IN A GROUP OF MSM LIVING WITH HIV

F.M. Nimbi[1], G.M. Corbelli[2], G. Giovanardi[1], A. Tanzilli[1], V. Lingiardi[1]

[1]Dept. Dynamic, Clinical and Health Psychology, Sapienza University of Rome, [2]Plus Roma – APS, Rome

Background: The Covid-19 pandemic had pervasive effects on health, changing priorities in care, limiting access to health services as well as changing social behaviors. The long-term effects of social restrictions (lockdown, social distancing, etc.) are still poorly predictable and understood, although some studies have shown a worsening of mental and sexual health in the general population, especially in the most vulnerable groups, such as sexual minorities. The present study aims to identify which are the main predictors of mental and sexual health in a group of Italian MSM living with HIV.

Material and Methods: A total of 115 MSM living with HIV (mean age 45.42 ± 10.15 years, range 24-68) completed an anonymous web survey on mental and sexual health composed by ad hoc questions and validated measures of psychopathology (BSI-18), mentalized affectivity (B-MAS), internalized sexual stigma (MISS-SF), HIV-related stigma (HSS-SV) and minority stress (DHEQ). The survey was sponsored on social networks and dating apps and data were collected from January to March 2022.

Results: Most of the participants defined themselves as cisgender men (99.1%) and gay (95.7%), was single (51.3%) and reported a medium-high education level and a medium to high socio-economic status. 95.7% were in HAART treatment and 94.8% reported an undetectable viral load. BSI-18 scores were used as measure of mental health related to somatization, depression, and anxiety symptoms. Mean scores for all the areas and the Global Severity Index (GSI) were higher than normative scores, indicating a relevant presence of symptoms in the assessed group. The 46.1% of the group negatively evaluated their level of sexual health (ranging from very bad to average). Poorer HAART adherence, HIV personalized stigma, internalized sexual stigma, and difficulties in processing emotions emerged as significant predictors of worse mental health (based on BSI-18 GSI score). The model was significant ($F(6,100)=11.902$; $p<.001$) and accounted for 41.7% of variance explained. An increase of porn use was showed in association to higher GSI levels. Lower socioeconomic status, depression, isolation, HIV personalized stigma, internalized sexual stigma, and difficulties in processing emotions were significant predictors of poorer sexual health outcomes. The model was significant ($F(6,108)=6.943$; $p<.001$) and accounted for 27.8% of variance explained.

Conclusions: Two years after the COVID-19 pandemic, mental and sexual health of MSM living with HIV showed to be poor when compared with normative scores of the general population. Factors emerged from the present study suggest areas for prevention and empowerment projects, such as intersectionality between HIV stigma, sexual stigma (homophobia) and isolation from the LGBT+ community, but also taking care of mental health such as depression symptoms and difficulties in processing emotions, which may, in turn, exacerbate the perceived stress level.

Issues on mental health, sexual health and STIs

OP 50 SINGLE NUCLEOTIDE POLYMORPHISMS AFFECTING NEUROINFLAMMATION BIOMARKERS IN DIFFERENT CLINICAL GROUPS OF HIV-AFFECTED PATIENTS

J. Cusato[1], M. Antonucci[1], A. Palermiti[1], A. Manca[1], J. Mula[1], V. Avataneo[1], M. Trunfio[2], G. Di Perri[2], A. D'Avolio[1], A. Calcagno[2]

[1]Laboratory of Clinical Pharmacology and Pharmacogenetics, Department of Medical Sciences, University of Turin, Amedeo di Savoia Hospital, Turin, Italy, [2]Unit of Infectious Diseases, Department of Medical Sciences, University of Turin, Amedeo di Savoia Hospital, Turin, Italy

Background: human immunodeficiency virus (HIV) is able to penetrate the central nervous system (CNS), leading to neuroinflammation, even though antiretroviral therapy efficiently suppresses virus replication. Several inflammatory biomarkers are correlated to neurocognitive decline, such as total tau protein (t-tau), its phosphorylated form (p-tau), β-amyloid-1,42 (Aβ-1,42), S100 calcium-binding proteinβ (S100β) and neopterin (neo).

ABC transporters are present in the blood brain barrier (BBB), regulating the movement of endogenous and exogenous compounds. Genetic-based alterations in the activity of these transporters could probably impact on neuroinflammation and neurocognitive impairment.

No data are available in the literature concerning variants of genes encoding transporters on neurocognitive impairment features in people living with HIV (PLWH).

For this reason, the aim of this study is to evaluate the role of genetic variants in affecting neuroinflammation biomarkers.

Materials and Methods: adult PLWH who underwent a lumbar puncture for clinical or research reasons were enrolled. T-tau, p-tau, β-1,42, S100β and neo were quantified in cerebrospinal fluid (CSF) with immunoenzimatic tests, whereas genetic polymorphisms were analyzed through real-time PCR.CSF/serum albumin ratio (CSAR) was considered as an indirect marker of the BBB integrity.

Linear regression analyses were performed according to Bonferroni correction ($p<0.005$) in order to evaluate which demographic, clinical, viral and genetic factors correlated with the different neuroinflammation biomarkers (t-tau, p-tau, Aβ-1,42, S100β and neo). Only statistical significant values in univariate model were considered in the multivariate one.

Results: 161 patients (73% males) with median age of 48.5 years were enrolled. Patients were stratified in 5 groups as follows: asymptomatic (34.8%), neurological symptoms with unknown etiology (12.4%), HIV-associated neurocognitive disorders (HAND, 18%), HIV-related CNS disorders (17.4%) and other disorders (e.g. cancer, 17.4%).

By linear regression analyses, CSAR ($p<0.001$, OR 0.720, IC95% 0.486; 0.953) and ABCG21194+928CC ($p=0.001$, OR 6.700, IC95% 2.752; 10.647) resulted associated with neo in the univariate model, whereas CSAR ($p<0.001$, OR 0.679, IC95% 0.451; 0.908) and ABCG21194+928CC ($p=0.003$, OR 5.454, IC95% 1.853; 9.056) were the only retained in the multivariate one. Viral load for t-tau ($p<0.001$, OR 7.84*10-5, IC95% 4.2*10-5; 11.5*10-5) and S100β ($p<0.001$, OR 11.1*10-5, IC95% 6.1*10-5; 16.1*10-5) and HAND clinical group for β-1,42 ($p=0.003$, OR 157.164, IC95% 52.720; 261.607) remained in the different univariate models, respectively. No factors were retained for p-tau levels.

Conclusions: to the best of our knowledge, we have for the first time documented transporter genetic variants association with inflammation markers: genetics chronically affects drug penetration, but the role in affecting neuroinflammation has to be clarified in further studies.

Issues on mental health, sexual health and STIs

OP 51 TREATMENT RESPONSE IN SYPHILIS REINFECTION AMONG PEOPLE LIVING WITH HIV: HIGH BASELINE TITER AND DELAYED ASSESSMENT AFFECTS THE RISK OF SEROLOGICAL-NON-RESPONSE

G. Tiecco, V. Marchese, S. Storti, M. Degli Antoni, M. Gulletta, F. Viola, E. Focà, F. Castelli, E. Quiros-Roldan

Division of Infectious and Tropical Diseases, ASST Spedali Civili di Brescia, Brescia, Italy; Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy

Background: Syphilis infection does not lead to definitive immunity against reinfection and crucial aspects of repeated episodes of syphilis are far from being cleared. Our Infectious Disease Unit assists 3,841 HIV patients, with a dedicated clinic for sexually transmitted diseases (STIs). We offer syphilis test to all newly diagnosed with HIV or STIs, in presence of symptoms or as periodical annual screening. We aimed to analyse risk factors associated to anomalous serological response in syphilis reinfections among HIV+ patients.

Material and Methods: We retrospectively evaluated syphilis notifications from January 2013 to December 2021, both in HIV+ and in HIV- patients (or control group). Demographical, clinical characteristics and risky habits were considered. The number of syphilis reinfections was recorded, and serological response was assessed at 6 and 12 months after treatment. A patient was considered as a serological responder in case of seroreversion or a ≥ 4-fold decline in non-treponemal titers. Serofast status was defined as a ≥ 4-fold decline without seroreversion, or a lower (2-fold) or no decline for 1:2 or 1:4 non-treponemal baseline titers. Multivariate analyses were performed to assess factors associated with syphilis reinfections and anomalous serological response in HIV+ group.

Results: In the study period, 670 patients with syphilis infection were recorded and 264 (39.4%) of them had at least 1 subsequent episode of syphilis. In particular, 382 episodes of syphilis reinfection were recorded, of whom 328 (86%) were diagnosed in HIV+ patients. Up to 6 episodes of reinfection were recorded in the same HIV+ patient. No significant statistical difference was seen in serological response between HIV+ and HIV- reinfection. The generalized linear model showed no statistical significance in gender, origin, sexual orientation or CD4 nadir and syphilis reinfections, whereas homo/bisexual orientation was linked to an increased number of subsequent episodes of syphilis infection in the HIV group (IRR 1.52, 95% CI 1.09, 2.18, p=0.017). According to multivariate analysis, serofast status was not statistically associated with gender, age, CD4 at diagnosis, HIV-RNA and RPR titer in HIV+, both at 6 and at 12 months after treatment. Whereas a RPR titer > 1:16 (OR 2.26, 95%CI 1.14-4.51, p=0.02) and evaluation at 6 months rather than at 12 months after treatment (OR 0.38, 95%CI 0.22-0.65, p<0.001) were statistically associated to serological non-response in the HIV+ group.

Conclusions: Although especially in HIV+ each additional episode of syphilis may result in an altered immune response, seroreversion rate is not statistically different among HIV+ and HIV-. In HIV+ patients, a RPR titer > 1:16 and the assessment at 12 months after treatment increase the possibility to detect an effective serological response, but do not affect the risk of serofast status.

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Issues on mental health, sexual health and STIs

OP 52 INCREASING INCIDENCE OF MYCOPLASMA GENITALIUM INFECTION IN PLWHIV AND PREP USERS

R. Rossotti[1], A. Nava[2], C. Baiguera[1], F. D'Amico[1], E. Inglese[2], C. Rogati[1], D. Fanti[1], N.B. Bana[1], C. Vismara[2], M. Puoti[1]

[1]Department of Infectious Diseases, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy, [2]Chemical-Clinical and Microbiological Analyses, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy

Background: Mycoplasma genitalium (Mg) is an emerging pathogen responsible of urethritis, cervicitis, endometritis, and pelvic inflammatory disease. Although Mg is detected in less than 3% of cases in the general population, this infection is a major concern because of its widespread antibiotic resistance. Aims of the present study are to describe Mg prevalence over time and factors associated with its presence in urine samples.
Methods: This monocentric, retrospective analysis evaluated all urine samples tested for Mg from January 2018 to September 2021. All samples were analyzed with Anyplex II STI7 (Seegene). Demographic characteristics were retrieved from hospital electronical patients' records. Samples were grouped in people living with HIV (PLWHIV), PrEP users, and subjects attending Obstetrics, Medically Assisted Procreation, or other hospital departments. Descriptive statistics (median and interquartile range for continuous variables, absolute and relative values for categorical variables) were used. Pearson's Chi-square test to compare groups was applied. Unadjusted and adjusted regression analyses were performed to test factors associated to Mg infection.
Results: The analysis included 9,153 samples: they belonged mainly to females (51.3%), Italians (76.6%), with a median age of 37 (IQR 31-45) years. HIV-positive subjects were tested in 1,836 (20.1%) and PrEP users in 1,367 (14.9%) cases. The overall prevalence of Mg infection was 2.1% but with a significant increase from 1.2% in 2018 to 3.4% in 2021 ($p<0.001$). The rise was significant for PLWHIV (from 3.0% to 5.7%, $p=0.003$) and PrEP users (from 1.8% to 8.2%, $p=0.002$), while it did not reach the statistical significance in the other groups (Figure 1). Unadjusted and adjusted analyses found that factors associated to Mg infection were calendar year (OR 1.32, 95% CI 1.13-1.54, $p=0.001$), age (OR 0.98, 95% CI 0.96-0.99, $p=0.002$), HIV-positive status (OR 4.71, 95% CI 1.31-16.87, $p=0.017$), and PrEP use (OR 8.19, 95% CI 2.31-29.09, $p=0.001$).
Conclusions: Mg prevalence on urine samples is increasing especially in key populations such as PLWHIV and PrEP users. Given the alarming reports about antibiotic resistance and treatment failures and the high number of unprotected sexual intercourses observed in these patients, additional efforts for Mg testing and treatment are necessary to contain this ongoing epidemic.

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Issues on mental health, sexual health and STIs

OP 53 ALTERATION OF IFN PATHWAYS IN ANAL CELLS FROM HIV-1/HPV CO-INFECTED MEN

M. Fracella[1], M. Scordio[1], L. Sorrentino[1], F. Frasca[1], G. Oliveto[1], A. Viscido[1], L. Santinelli[2], E.N. Cavallari[2], G. D'Ettorre[2], P. Gozzo[2], G. Antonelli[1], C. Scagnolari[1], A. Pierangeli[1]

[1]Department of Molecular Medicine, Virology Laboratory, Sapienza University of Rome, Rome, [2]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome

Background: Viral persistence is a pivotal prerequisite for high-risk (HR) HPV-associated tumor growth, such as anal cancer. HIV(+) men, whose mucosal immune response is deregulated, are more likely to be co-infected with HPV. HIV is able to manipulate the antiviral Interferon (IFN) activity; in particular, the higher expression of several IFN-stimulated genes (ISGs) may help HIV to increase its reservoir in macrophages and dendritic cells. To clarify this process in the anal mucosa in relation to HPV infection, we analyzed the expression of type I/III IFNs related genes in anal cells from HIV(+) and HIV(-) men.

Material and Methods: One hundred eighty-three anal canal brushing samples were collected from male patients attending a proctology clinic. Detection of HPV DNA was performed by PCR and genotyping by sequencing. From purified cellular RNA, transcripts of genes coding for type I IFNs (α2A, β and ε) and their receptor subunits (IFNAR1 and 2), for type III IFNs (λ1 to 3) and their receptor subunit (IL28R1), for Toll-like receptors (TLR2, 3, 8 and 9) and for ISGs (MxA, UBP43, ISG15, ISG56, IRF1, IRF3 and IRF7) were quantified by Real time PCR assays and normalized to the housekeeping GUS gene (the 2^−ΔCt method).

Results: One hundred and fifty-nine Caucasian HIV(+) men, on long-term ART, and 24 HIV(-) men were enrolled in this study. Type III IFNs and their receptor specific subunit IL28R1 coding genes were downregulated in HPV/HIV co-infections [IFNλ1(p= 0.008), IFNλ2 (p= 0.026), IFNλ3 (p= 0.004) and IL28R1 (p= 0.006)] with respect to HPV-negative group. Moreover, IFNλ3 (p= 0.042) and IFNα2A (p= 0.018) were less expressed in HIV(+) men persistently infected with the same HR-HPV genotype, in contrast to HPV-negative men. Comparing HIV(+) and HIV(-) men during HR-HPV infections, TLR3, ISG56 and PKR were activated in HIV(+) men (p= 0.046, p= 0.024, p= 0.048, respectively), as opposed to HIV(-) men. Furthermore, UBP43 (p= 0.025), IRF1 (p= 0.003) and MXA (p= 0.007) were up-regulated in HIV(+) men infected with the same HPV genotype for more than a year, compared to HPV-negative group.

Conclusions: Overall, our investigations on HPV/HIV co-infected men reported a significant downregulation of IFN genes that may facilitate both HIV spread to adjacent cells and HPV persistence (LR and HR). IFN inhibition could be supported by the higher expression of the IFN negative regulator UBP43. We also observed, in HR-HPV/HIV positive men, an overactivation of TLR3, which selectively enhances the expression of IRF1 in macrophages. IRF1, which was overexpressed too, can directly stimulate antiviral ISGs, such as ISG56, MXA and PKR. ISGs restrict HIV replication, contributing to a noncytopathic, but persistent, infection. Hence, clarifying IFN pathway dysregulation in HPV/HIV coinfected patients may help in devising immunotherapeutic strategies to limit the risk of anal cancer.

Issues on mental health, sexual health and STIs

OP 54 EFFICACY OF LATE HPV VACCINATION IN YOUNG HIV+ MSM

E. Cavallari[1], L. Santinelli[1], L. Maddaloni[1], M. Ridolfi[1], M. Scordio[2], A. Pierangeli[2], G. Ceccarelli[1], C.M. Mastroianni[1], G. d'Ettorre[1]

[1]Department of Public Health and Infectious Diseases "Sapienza" University of Rome, Rome, [2]Department of Molecular Medicine "Sapienza" University of Rome, Rome

Background: HPV infection of the anal canal represents a major risk factor for the development of anal cancer. Men who have sex with men (MSM), and in particular HIV+ MSM, show the greatest risk of anal HPV infection and the highest incidence of anal cancer. Immunization against HPV is effective to protect against anal infection and can help to prevent anal cancer. To get the most protective efficacy, HPV vaccine should be ideally administered at an early age, before the first sexual intercourse. Since routine administration of HPV vaccine to boys aged 9 to 12 years has begun only in recent years, currently the majority of immunized adult MSM individuals underwent vaccination after sexual debut. In the present study we aimed to evaluate vaccination rate and prevalence of anal HPV infection and anal dysplasia (squamous intraepithelial lesion, SIL) in HIV+ and HIV- MSM aged <45 years that received HPV vaccination after the first sexual intercourse.

Materials and Methods: 142 MSM, 110 HIV+ and 32 HIV-, younger than 45 years were included in the present study. All enrolled subjects underwent anal HPV DNA test for HPV identification and genotyping. The presence of anal dysplasia was assessed trough anal cytology or anal histology from anal biopsies collected during high resolution anoscopy.

Results: Vaccination rate was 20% among HIV+ and 31.3% among HIV- participants (p=0.169). 76.3% of HIV+ participants and 57.1% of HIV- participants tested positive at anal HPV DNA test (p=0.042). Anal SIL of any grade was observed in 76.3% of HIV+ individuals and 53.6% of HIV- subjects (p=0.017).

The prevalence of anal HPV infection was similar between vaccinated and unvaccinated HIV+ subjects (72.7% vs. 77.3%; p=0.864).

Among vaccinated participants, HPV DNA tested positive in 72.7% of HIV+ and 33.3% of HIV- subjects (p=0.041). On the other hand, 77.3% of HIV+ unvaccinated and 68.4% of HIV- unvaccinated individuals showed a positive HPV DNA test (p=0.415).

Among HIV+ participants, anal SIL was observed in 54.4% of vaccinated and 81.8% of unvaccinated individuals (p=0.01).

Among vaccinated participants, the presence of anal SIL was detected in 54.5% of HIV+ and 33.3% of HIV- vaccinated participants (p=0.283). In unvaccinated participants SIL was detected in 81.8% of HIV+ and 63.1% of HIV- subjects (p=0.073).

Conclusions: Even if administered after sexual debut, vaccination against HPV is useful in reducing the risk of anal dysplasia in HIV+ MSM aged <45 years. Immunization against HPV should be encouraged, particularly in this population.

Neuropsychological complications in COVID-19

OP 55 DEMENTIA AND COVID-19 OUTCOMES: FINDINGS FROM A MULTICENTRIC STUDY IN CAMPANIA REGION

R. Astorri[1], M. Pisaturo[1], A. Russo[1], P. Maggi[2], F.G. Numis[3], I. Gentile[4], V. Sangiovanni[5], V. Esposito[6], R. Punzi[7], G. Calabria[8], C. Rescigno[9], A. Salomone Megna[10], A. Masullo[11], E. Manzillo[12], G. Russo[13], R. Parrella[14], G. Dell'Aquila[15], M. Gambardella[16], A. Ponticiello[17], N. Coppola[1] on behalf of CoviCam group

[1]Infectious Diseases, Department of Mental Health and Public Medicine, University of Campania "L. Vanvitelli", Napoli, Italy, [2]Infectious Diseases Unit, A.O. S Anna e S Sebastiano Caserta, Italy, [3]Emergency unit, PO Santa Maria delle Grazie, Pozzuoli, Italy, [4]Infectious disease unit; University Federico II, Naples, Italy, [5]Third Infectious Diseases Unit, AORN dei Colli, P.O. Cotugno, Naples, Italy, [6]IV Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [7]Hepatic Infectious Disease Unit, AORN dei Colli, PO Cotugno, Naples, Italy, [8]IX Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [9]First Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [10]Infectious Diseease Unit, A.O. San Pio, PO Rummo, Benevento, Italy, [11]Infectious disease unit, A.O. San Giovanni di Dio e Ruggi D'Aragona Salerno, Italy, [12]VIII Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [13]Infectious Disease Unit, Ospedale Maria S.S. Addolorata di Eboli, ASL Salerno, Italy, [14]Respiratory Infectious Diseases Unit, AORN dei Colli, PO Cotugno, Naples, Italy, [15]Infectious Diseases Unit, AO Avellino, Italy, [16]Infectious Diseease Unit, PO S. Luca, Vallo della Lucania, ASL Salerno, Italy, [17]Pneumology Unit, AORN Caserta, Italy

Background: Dementia emerged as a risk factor for poorer COVID-19 outcomes. The aim of our study was to investigate the impact of dementia in patients hospitalized in Campania region.

Materials and Methods: We engaged in a multicentre observational retrospective cohort study involving 9 COVID -19 Units in 7 cities of Campania region, in Southern Italy; SIMIT Campania coordinated the study of the "CoviCam" network.

We included COVID-19 patients hospitalized from March 2020 to July 2021 (waves I, II, III). At the admission (T0), demographic, clinical, biochemical, virological, and therapeutic data were collected in an electronic database. Charlson comorbidity index was used to evaluate the burden of underlying medical conditions. Dementia was defined by patients' history. COVID-19 severity was defined accordingly to the Centers for Disease Control and Prevention (CDC) criteria.

Results: A total of 1625 patients were included. Table 1 shows epidemiological, biochemical, clinical data, and relative outcomes, comparing patients with dementia (N=80) versus patients without dementia (N=1445). Male subjects were significantly less represented in the dementia subgroup (N= 30, 37.50%), compared to patients without dementia (N=957, 61.94%) (p <0.001). Patients with dementia were also older than patients without dementia (mean age: 77.47±SD12.73 vs 61.53± SD15.86; p=0,002). Hospitalization was more prolonged in patients with dementia (mean length, days: 17.26±SD12.73). The Charlson comorbidity index was significantly higher in patients with dementia (mean: 5.62±SD2.16) compared to patients without dementia (mean:2.85 ±SD2.34) (p= 0.026). Cardiovascular disease (CVD) and chronic obstructive pulmonary disease (COPD) were significantly more frequent in dementia patients (p<0.001 and p=0.001, respectively) in univariate analysis, while the prevalence of other comorbidities didn't statistically differ between the two groups. At the time of admission (T0), subjects with dementia had significantly higher values of creatinine, creatin phosphokinase (CPK) and PaO2/FiO2 ratio than patients without dementia (p=0.036; p<0.001; p= 0.012, respectively). Fever, cough and skin lesions also appeared to be more frequent in the dementia subgroup, as shown in Table 1. Additionally, dementia patients were largely more affected by SARS-CoV-2 pneumonia than patients without dementia (92.5% vs 28.93%; p<0.001), with significantly higher development of severe COVID-19 (57.50% vs 29.97%; p<0.001) and death rates (40% vs 7.51%; p<0.001). Multivariate analyses are reported in Table 1.

Conclusions: Our multicentric study supports the evidence of dementia as a risk factor for poorer outcomes in COVID-19 patients.

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Neuropsychological complications in COVID-19

OP 56 COVID-19 NEUROCOGNITIVE IMPAIRMENT (COVID-19-NCI): AN ATTEMPT FOR DEFINITION AND CLINICAL ASSESSMENT

G. Del Duca, A.C. Brita, I. Mastrorosa, A. Vergori, S. Lanini, M. Camici, M. Annalisa, C. Caligiuri, C. Pinnetti, A. Antinori

Lazzaro Spallanzani National Institute for Infectious Diseases, Rome, Italy

Background: Patients with post-acute COVID-19 syndrome experience a wide range of cognitive changes, but is still debate how to identify and define such condition. Aim of our study was to propose a unique definition of COVID-19-NCI, using the analysis of neuropsychological assessments (NPA), performed during the post-acute COVID-19 period.

Material and Methods: We include all the patients attending the post-COVID outpatient service of the Lazzaro Spallanzani National Institute for Infectious Disease, regardless of neurocognitive symptoms. They underwent NPA via a standardized battery of 20 tests, at 3, 6 and 12 months after infection. Two different types of analysis were performed, in order to evaluate the neurocognitive performance: 1) calculation of Z scores for each cognitive domain, 2) comparison of tests with the reference cut-off and classification of the scores into equivalent points (PE). The presence of NCI was assessed, cognitive areas and tests deficit-related were classified and diagnostic criteria for a clinical definition were established for NCI in DSM-5.

Results: We included 408 participants (median age: 55 years, IQR 47-61), 53% female, median education 13y and we noticed that: 199 (53%) complaining patients (PC) reported alterations in at least one cognitive area, 96 (26%) complaining patients (NC) did not report any alteration in any cognitive area, 57 (15%) not-complaining patients (PNC) reported alterations in at least one cognitive area, 22 (6%) not-complaining patients (NNC) did not report any alteration in any cognitive area (Fig.1).

We found COVID-19-NCI at the presence of alterations (<cutoff-PE = 0) in at least one test of the five cognitive areas (memory, attention, language, executive functions, speed of mental processing) in patients with the onset of cognitive deficits (reported or evaluated) within 3-6 months after acute COVID-19 and in the absence of clinical history of cognitive deficits prior to the COVID-19 event. Interestingly, COVID-19-NCI were also characterized by reversibility, and functional and instrumental activities were not systematically affected.

The above-mentioned definition should be distinguished from the COVID-19 SUBJECTIVE-NCI, defined as the presence of cognitive deficits, reported by the patient and characterized by a perceived alteration of neurocognitive performance in daily study and work activities, with no documented/calculated alterations in the five cognitive areas (>cutoff-PE = 1,2,3,4).

Conclusions: On the basis of clinical criteria and of the second type of analysis (<cutoff-PE=0), most complete and widely used in clinical settings than first type of analysis, we elaborate COVID-19-NCI and COVID-19 SUBJECTIVE-NCI definitions. Although this definition needs to be standardized in longitudinal studies on large cohorts, it may help clinicians in the evaluation of neurocognitive disorders in the post-acute COVID-19 phase.

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Neuropsychological complications in COVID-19

OP 57 NEUROPSYCHOLOGICAL PERFORMANCE (NP) FOLLOWING COVID-19: PREVALENCE AND PREDICTORS

A. Vergori[1], G. Del Duca[1], S. Lanini[1], A.C. Brita[2], C. Pinnetti[1], I. Mastrorosa[1], M. Camici[1], A. Mondi[1], V. Mazzotta[1], P. Chinello[1], P. Mencarini[1], M.L. Giancola[1], A. Abdeddaim[1], E. Girardi[3], F. Vaia[4], A. Antinori[1,5]

[1]Clinical Department, National Institute for Infectious Diseases L.Spallanzani, IRCCS, Rome, Italy, [2]Psychology Unit, National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy, [3]Scientific Direction, National Institute for Infectious Diseases L.Spallanzani, IRCCS, Rome, Italy, [4]General Direction, National Institute for Infectious Diseases L.Spallanzani, IRCCS, Rome, Italy, [5]Health Direction, National Institute for Infectious Diseases L.Spallanzani, IRCCS, Rome, Italy

Background: Aims of this analysis were to describe prevalence and predictors of impaired NP after acute COVID19.

Methods: We included patients (pts) referred to the post-COVID19 service assessed within and beyond 6 months (w6M, b6M) after COVID19. NP was evaluated using a standardized battery of 20 tests across 5 areas (memory, attention, language, executive functions, processing speed psychomotor). Neurocognitive impairment (NCI) was classified on the basis of the scores into equivalent points (PE) in each test and defined by the presence of alterations (<cutoff-PE = 0) in at least one test; in addition, the Beck Anxiety Inventory (BAI), the Beck Depression Inventory (BDI II) and the Pittsburgh Sleep Quality Index (PSQI) were administered. We used Chi-square test for comparisons and a multivariable logistic regression model to identify factors associated with test results after adjusting for main confounders.

Results: N=408 pts: median age 55 years (IQR 47-61), 53% female, 13 y of education (13-18), 54% with >1 comorbidity, 52% previously hospitalized. Overall, we found NCI in 69% of pts evaluated w6M, of whom 15% didn't complain any symptoms, and in 60% of pts evaluated B6M, of whom 46% complained symptoms (Figure 1). 38% of pts reported deficitary performances in the Digit Symbol test w6M and 29% in the Categorical Verbal Fluency test, expression of the involvement of the language and executive areas. Similar results were found for evaluations b6M. Only two test frequencies significantly worsen b6M: Rey Words Test-Delayed Recall (+5%, p=0.092) and Multiple Features Target Cancellation-Errors test (+3%, p=0.028) (Table 1), expression of the impairment of memory and attention areas. By fitting a multivariable regression model, being previously hospitalized and evaluated for the first time b6M were associated with an increased risk of having an impairment in Rey Words Test-Delayed Recall [aOR 1.67 (0.89-4.19); p=0.06 and 1.85 (0.95-4.19; p=0.095), respectively]. BAI>85% was found in 36% of pts w6M vs 44.4 b6M (difference +8.8%, p=0.075), BDI>85 44% vs 40.7% (difference -3.3, p=0.506) and PSQI 12.9% vs 35.6% (+22.6%, p>0.0001) w6M and b6M, respectively. The risk of an altered BAI>85 and PSQI seemed to be significantly associated with female gender [M vs F -3.55 (0.30-0.71), p<0.001 and -2.69 (0.30-0.83), p=0.007]. PSQI>5 was also associated with the condition of a previous hospitalization [5.03 (2.30-6.69), p<0.001).

Conclusions: Our preliminary data show a consistent prevalence of NCI in long COVID19 haulers, which remains stable over 6 months of observation pertaining to the linguistic-executive area. Pts previously hospitalized are likely to have a worse NP than non-hospitalized pts w6M, manifesting a long-term verbal memory deficit. Women seem to be at higher risk of anxiety-depressive and poor sleep quality than men, persistently over 6 months from COVID19.

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Neuropsychological complications in COVID-19

OP 58 IS PLASMA NEUROFILAMENT LIGHT CHAIN MEASUREMENT RELEVANT IN LONG-COVID?

M.A. Zingaropoli[1], P. Pasculli[1], T. Latronico[2], F. Dominelli[1], M. Guardiani[1], E. Tortellini[1], G. Saracino[2], G.M. Liuzzi[2], M. Lichtner[1,3], C.M. Mastroianni[1], M.R. Ciardi[1]

[1]Department of Public Health and Infectious Diseases, Sapienza, University of Rome, [2]Department of Biosciences, Biotechnology and Biopharmaceutics, Aldo Moro, University of Bari, [3]Infectious Diseases Unit, SM Goretti Hospital, Latina, Sapienza, University of Rome

Background: As the SARS-CoV-2 pandemic continues, several authors have reported neurologic sequelae following COVID-19 recovery. Neurofilament light chain (NfL), a specific biomarker of quantitate neuro-axonal damage, is normally measured in cerebrospinal fluid (CSF). Novel methods have given the possibility to measure NfL in plasma instead. The aim of the study was to evaluate plasma NfL levels after three months from discharge in hospitalized COVID-19 patients.

Material and Methods: Plasma NfL levels were evaluated in hospitalized COVID-19 patients and age and sex matched healthy donors (HD). For COVID-19 patients, longitudinal assessment of plasma NfL levels on hospital admission (baseline) and after three months from discharge (Tpost) was performed. COVID-19 patients were stratified according to disease severity into ARDS and non-ARDS groups, and the differences in plasma NfL levels were evaluated.

Results: Seventy-nine hospitalized COVID-19 patients and 31 HD were enrolled. All COVID-19 patients had interstitial pneumonia, 43% had ARDS and 6.3% died. At baseline, COVID-19 patients showed significantly higher plasma NfL levels compared to HD (21.8 [11.9-36.4] and 9.1 [5.7-12.4] pg/ml, p<0.0001). Higher plasma NfL levels were observed in ARDS compared to non-ARDS group (28.4 [15.2-59.3] and 15.5 [10.2-29.8] pg/ml, respectively, p=0.0032). Both ARDS and non-ARDS groups showed higher plasma NfL levels compared to HD (p<0.0001 and p=0.0016, respectively).

The longitudinal evaluation of plasma NfL levels performed in 74 COVID-19 patients showed a significantly decrease at Tpost compared to baseline (15.1 [9.8-21.3] and 20.4 [11.6-34.1], respectively, p<0.0001). At Tpost, higher plasma NfL levels compared to HD (p=0.0041) were observed. At Tpost, both ARDS and non-ARDS groups showed a reduction of plasma NfL levels compared to baseline (for ARDS group: 17.2 [11.9-21.9] and 27.1 [14.7 -50.8], respectively, p=0.0009; for non-ARDS group: 12.6 [8.4-21.6] and 15.5 [10.2-29.8], respectively, p=0.0002). However, at Tpost, plasma NfL levels were still significantly higher in ARDS group compared to HD (p=0.0002) whereas no statistically significant differences were observed between non-ARDS group and HD.

Conclusion: Long-term health problems, including neurological symptoms, are associated with long-COVID. Our data suggests a CNS damage in COVID-19 patients during the acute phase of the disease, especially in those who developed ARDS in which higher levels of NfL compared to HD, even after 3 months post-discharge were observed. Conversely, in patients who did not develop ARDS during hospitalization we observed a complete normalization of plasma NfL levels after three months from hospital discharge. Measurement of NfL levels in plasma samples is convenient and provides a simple and easy to perform method to assess neuronal damage in the context of long-COVID.

Neuropsychological complications in COVID-19

OP 59 SARS-COV-2 HAMPERS DOPAMINE PRODUCTION IN IPS-DERIVED DOPAMINERGIC NEURONS

G. Cappelletti[1], E.M. Carsana[2], G. Lunghi[2], S. Breviario[2], C. Vanetti[1], A. Barnaba Di Fonzo[3], M. Clerici[3], M. Aureli[2], C. Fenizia[3]

[1]Department of Biomedical and Clinical Sciences, University of Milan, Milan, Italy, [2]Department of Medical Biotechnologies and Translational Medicine, University of Milan, Milan, Italy, [3]Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy

Background: Recent studies show that an increasing number of patients, even with an initial favorable COVID-19 outcomes, will experience prolonged symptoms, the profile and timeline of which remains uncertain, currently named Long COVID. It was reported that the majority of hospitalized patients present at least one persistent symptom sixty days after symptoms onset, which commonly are fatigue, dyspnea and a number of neurological conditions. It has been hypothesized that SARS-CoV-2 might affect dopaminergic neurons due to distinctive traits typically displayed during acute COVID-19 and Long COVID-19. However, to date, no scientific evidence has been produced yet.

Material and Methods: We exploited an in vitro model of SARS-CoV-2 infection of iPS reprogrammed to dopaminergic neurons. We employed 3 doses (106, 105 and 104 TCID50) of the EU (B.1), the Delta or the Omicron variants. After five days, mRNA, protein and supernatant were collected and analyzed by real-time PCR, Western Blot and ELISA, respectively. L-DOPA (1, 10 and 50 μM) was administered to the cells during rescue experiments.

Results: First, we infected the neuronal cells with three different doses of SARS-CoV-2. Together with an intense activation of antiviral intracellular innate response and neuronal stress markers, we found alterations in the dopamine synthetic pathway. In particular, in a virus dose-dependent manner, the tyrosine hydroxylase (TH) was significantly increased at the mRNA level, while almost completely abrogated at the protein level. Other proteins involved in the dopamine synthetic pathway, such as the DOPA decarboxylase (ADCC) and the dopamine transporter (DAT), were significantly decreased both at the mRNA and the protein level. Overall, SARS-CoV-2 infection resulted in a significant decrease of dopamine production and release, as shown by the ELISA quantification performed on both cells and supernatant. Strikingly, out of the three different SARS-CoV-2 variants employed (EU, Delta and Omicron), the Omicron variant produced no reduction in dopamine production and release. As controls, heat-inactivated EU SARS-CoV-2 (iSARS) and the recombinant Spike protein were tested. While the iSARS did not produced any significant change, the Spike protein induced a strong cellular response. Finally, the administration of L-DOPA in vitro (1, 10 and 50 μM) was able to rescue such lack of dopamine released in the supernatant.

Conclusion: These preliminary observations led us to speculate that the dopamine synthesis might be affected in SARS-CoV-2 patients. Based on these very reasons, we believe that such issue needs to be urgently addressed and confirmed by multiple studies in vivo. Indeed, this might even partially explain some of the neurological symptoms, together with the so-called Long COVID symptomatology. Further, the evaluation of Dopamine production in vivo might even be an early predictive index of neurological implications and/or Long COVID, which might be putatively attenuated by L-DOPA administration.

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Neuropsychological complications in COVID-19

OP 60 EARLY PHASE APPROACH IN SARS COV-2 INFECTION: A SINGLE CENTER ONE-YEAR REAL LIFE EXPERIENCE

D. Di Trento[1], S. Garattini[1], M. De Masi[2], A. Gasperin[1], A. Grimaldi[1], S.G. De Maria[1], S. Corazza[1], S. Gismondi[2], B. Bartolozzi[2], D. Caianiello[3], S. De Filippis[1], B. Kertusha[2], A.Carraro[2], O. D'Onofrio[2], G. Bagaglini[4], G. Bonanni[4], D. Alunni Fegatelli[5], A. Spagnoli[5], S. Di Somma[6], C. Del Borgo[2], M. Lichtner[1]

[1]Department of Public Healt and Infectious Disease, "Sapienza University of Rome", [2]Infectious Disease Unit, SM Goretti Hospital Latina, [3]General pratictioner, AUSL Latina, [4]Pharmacy Service Unit, SM Goretti Hospital Latina, [5]Statistic Department, "Sapienza University of Rome", [6]Department of Medical-Surgical Sciences and Translational Medicine, "Sapienza University of Rome"

Background: In subjects with underlying comorbidities at an early stage of SARS-CoV2 infection, in order to avoid clinical worsening, hospitalization and lethality we have two main classes of early treatment. Besides neutralizing monoclonal antibodies (nMAbs), which provide immediate passive immunity and are now well-established in COVID-19 therapy, there's a more recent option, antiviral drugs both intravenous and oral which prevent viral replication.

Materials and Methods: Since March 2021, a dedicated service for prevention of severe COVID-19 disease was set up. Patients were enrolled after confirmation of a positive nasopharyngeal swab and best drug was chosen following the AIFA criteria and actual availability. Data about clinical progression, hospitalization for pneumonia/ARDS and death (COVID or non-COVID related) were collected at 7, 14 and 30 days by telephone monitoring. The endpoint was defined as a composite outcome (hospitalization, death for any cause and pneumonia/ARDS). Comparison between groups was performed by chi square test or Mann Whitney test as appropriate. A multivariable logistic regression model was used to estimate the effect of demographic and clinical variables on the prediction of the composite outcome. All tests were two-tailed, and a value of $P < .05$ was considered as statistically significant. Analyses were performed using R version 4.0.1.

Results: Until March 2022 a total of 2564 subjects were treated with nMAbs or antiviral drugs, 1543 (60,2%) of whom were female; median age was 67 years old (11-106); 2023 (79%) were vaccinated, 460 (18%) had no vaccination. At clinical evaluation 162 subjects already presented COVID-19 pneumonia, so they were hospitalized and excluded from this analysis. Among patients with completed 30 days follow up, 534 (53,1%) were female, median age was 64,6 (51,5 -75,6) and rate of vaccination was 70,8% (693/1005) as listed in table 1. At 30 days, 974 patients (96,9%) were not hospitalized and did not have any clinical evolution; 3 patients (0,3%) died of non-COVID-19 related causes. 31 patients (3,1%) required hospitalization: 12 of them (38,7%) developed COVID related pneumonia, 2 (6,4%) ARDS, 1 (3,2%) died for COVID-19. Factors significantly related to clinical worsening were age and vaccination and VOC period (p-value respectively 0,01, 0,041 and 0,015). Multivariable analysis confirmed both parameters as related to increased risk of hospitalization and pneumonia (Fig.1). No significant differences between treatments (nMabs and antivirals) were observed in terms of outcome.

Conclusions: Our analysis has evidenced the benefits of an early treatment for SARS-CoV-2 infection in patients with risk for progression. It also showed that age and vaccination status represent the most important factor in early treated subjects in terms of outcome. The follow up data, even if still ongoing, suggest a promising role of antivirals in comparison to nMAbs.

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New issues on dual therapy

OP 61 EFFICACY AND DURABILITY OF DUAL ANTIRETROVIRAL REGIMENS AS SWITCH THERAPY IN TREATMENT-EXPERIENCED PEOPLE LIVING WITH HIV (PLWH): DATA FROM THE ARCA COHORT

M. Poliseno[1], A. Borghetti[2], F. Conti[3], G. Di Teodoro[4,5], F. Lombardi[6], L. Montemurro[1], L. Pezzati[3], A. Shallvari[5,7], A. Bezenchek[5,7], V. Borghi[8], S. Rusconi[3,9]

[1]U.O. Malattie Infettive Universitaria, University of Foggia, Foggia, Italy, [2]Policlinico Gemelli, Roma, Italy, [3]Department of Biomedical and Clinical Sciences "L. Sacco", University of Milan, Milano, Italy, [4]Dipartimento di Ingegneria informatica automatica e gestionale A. Ruberti, Sapienza Università di Roma, Roma, Italy, [5]EuResist Network GEIE, Roma, Italy, [6]Fondazione Policlinico Universitario A. Gemelli IRCCS, UOC Malattie Infettive, Roma, Italy, [7]InformaPRO SRL, Roma, Italy, [8]Clinica Malattie Infettive, Azienda Ospedaliero Universitaria di Modena, Modena, Italy, [9]OC Malattie Infettive, ASST Ovest Milanese, Ospedale di Legnano, Milano, Italy

Introduction: Antiretroviral treatment simplification to two-drug regimens (2DR) could be a drug-toxicity- and cost-saving strategy for the lifelong treatment of virologically stable PLWH. However, the long-term efficacy of 2DR and the presence of possible patient-related factors that could undermine 2DR durability deserves deeper investigation in real-life cohorts.

Materials and Methods: Data of all >18-yo, ART-experienced PLWH enrolled in ARCA cohort, switched to any 2DR from any ART regimen while having viral load <50 cp/mL for at least 6 months, were retrospectively collected. Descriptive statistics were performed for each 2DR group. Chi-square/Fisher exact test and non-parametric ANOVA were used, as appropriate, to outline differences between groups. Kaplan Mayer curves were calculated over time to assess i) the overall incidence of 2DR discontinuation due to implementation to 3DR, modification of 2DR to another 2DR, patients' death/loss to follow up; ii) the incidence of discontinuation for virological failure (VF) (two subsequent HIV RNA> 50 cp/mL or one HIV RNA > 200 cp/mL). Cox multivariate regression analysis was performed to identify predictors of discontinuation among patients' features. When available, the description of drug resistance mutations (DRMs) selected at failure was included.

Results: Between January 1, 2015, and January 1, 2021, 1,988 patients were switched to a 2DR: 1284 to DTG +3TC; 409 to DTG + RPV; 272 to DRV/r + RPV; 22 to DRV/r + DTG (not included in the analysis due to their small number). Patients' features are reported in Table 1.

1,145 (58%) subjects were switched from a 3DR, while 727 (37%) from a 2DR. Pill burden reduction was the main reason for the switch (880 pts, 45%). Notably, a history of virological failure was reported in 1,317 patients (67%). After a median of 46 (IQR 82-159) weeks, although 778 subjects (40%) discontinued the 2DR, VF was observed only in 18 (2%). A higher risk of discontinuation for any cause was reported among patients in DTG + RPV (aHR 1.25 (95% CI 1.04-1.50), p=.02) and in DRV/r + RPV (HR 1.21 (95% CI 1.00-1.48), p=.05) (Figure 1a)). No differences in the risk of discontinuation for VF were noticed based on the type of 2DR received and the presence of DRMs in the regimen components (Figure 1b) and 2). Longer history of ART (aHR 0.95 (95% CI 0.91-0.99), p=.01), higher number of ART regimens (aHR 1.06 (95% CI 1.01-1.12), p=.01), higher HIV RNA at zenith (aHR 1.00 (95% CI 1.00-1.00), p=.05) and right before the switch (aHR 1.00 (95% CI 1.00-1.00), p=.03), and switch from a previous 2DR (aHR 0.52 (95% CI 0.29-0.93), p=.03) were predictors of discontinuation at multivariable analysis.

Conclusions: Our results confirm the efficacy profile of 2DR. The reduced durability of RPV-based 2DR could be explained by a longer and more complex history of HIV infection and previous ART regimens. Evidence from longer follow-up is needed to properly lead the choice of 2DR in complex situations.

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New issues on dual therapy

OP 62 CHARACTERIZATION OF VIROLOGICALLY SUPPRESSED HIV INFECTED INDIVIDUALS POTENTIAL ELIGIBLE TO THE LONG-ACTING COMBINATION OF CABOTEGRAVIR PLUS RIPLIVIRINE: RESULTS FROM THE ITALIAN ARCA COHORT

A. Cervo[1], A. Russo[2], D. Di Carlo[3], A. De Vito[4], L. Fabeni[5], S. D'Anna[6], L. Duca[6], A. Colpani[4], M. Fois[4], B. Zauli[4], G. Mancarella[7], A. Carraro[7], A. Bezenchek[8], A. Cozzi-Lepri[9], M.M. Santoro[6]

[1]Infectious Diseases Clinic, University Hospital of Modena, Italy, [2]Infectious Diseases Unit, Department of Mental Health, University of Campania "Luigi Vanvitelli", Naples, Italy, [3]Pediatric Clinical Research Center "Romeo and Enrica Invernizzi", Department of Biomedical and Clinical Sciences "L. Sacco" University of Milan, Italy, [4]Unit of Infectious Diseases, Department of Medical, Surgical, and Experimental Sciences, University of Sassari, Sassari, Italy, [5]National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy, [6]University of Rome "Tor Vergata", Rome, Italy, [7]Infectious Disease Unit, Sapienza University of Rome - Polo Pontino, Latina, Italy, [8]InformaPRO SRL, Rome, Italy; EuResist Network GEIE, Rome, Italy, [9]Centre for Clinical Research, Epidemiology, Modelling and Evaluation, Institute for Global Health, London, UK

Background: The approval of the long-acting (LA) combination of cabotegravir (CAB) plus rilpivirine (RPV) represents one of the last achievements among ART regimens in people living with HIV (PLWH) with undetectable viral load. However, clinical trials have shown that individuals' selection is crucial. The aim of this study is to compare HIV-1 infected virologically suppressed individuals today potentially eligible for LA CAB+RPV with those ineligible.

Methods: This was an observational, retrospective, cross-sectional study from ARCA database including HIV-infected adults in virological suppression (at least two consecutive VL <50 cps/ml after Jan 1st 2019) with at least one genotypic resistance testing (GRT) for RT/PRO/INT from plasma and/or PBMCs. Eligibility criteria for LA CAB +RPV were: absence of HBV co-infection, absence of resistance-associated mutations (RAMs) for NNRTIs and of major RAMs for INSTIs (IAS-USA list 2019), absence of previous virological failures (VFs) to INSTIs and/or NNRTIs. Prevalence of eligible individuals with 95% CI was calculated. Potential differences between eligible and ineligible individuals to CAB+RPV were evaluated by T-test or Mann-Whitney exact test for quantitative variables and Chi-squared for qualitative variables, as appropriate.

Results: 514 patients were included: 377 (73.3%) were male, median age was 51 (43-58), 41 (8%) had HBV-coinfection, in ART from 9 years (IQR 4-17) and in virological suppression from 63 months (IQR 34.7-105.2) (Table 1). The median of previous therapies was 4 (2-7). 119 (23.2%), 134 (26.4%), and 17 (3.3%) individuals experienced VF to INSTIs, NNRTIs and RPV, respectively. 382 (74.3%) individuals were infected with B subtype. Individuals with at least one major RAM for INSTIs, for NNRTIs (excluded RPV) and for RPV were 33 (6.4%), 123 (23.9%) and 104 (20.2%), respectively. The most common major RAMs were N155H (2.9%) and Q148H/K/R (2.0%) for INSTIs (Fig.1a), K103N (9.5%) and E138A (6.8%) for NNRTIs (Fig.1b). Cumulative GSS for CAB+RPV was 2 (IQR 1.5-2). Eligible individuals for LA CAB+RPV were 229 (44.5%, 95% CI: 40.8-48.8%): 179 (78.2%) male, median age 48 (38-55), in ART since 2015, with 3 (IQR 2-4) previous regimens (Table 1). Compared to not eligible individuals, those eligible were younger, more frequently male, and less frequently intravenous drug users, and with a lower zenith VL (4.5 vs 5.1 log10 cps/ml) and higher CD4 count nadir (260 vs 170 cells/mm3) (Table 1). They had a more recent HIV diagnosis (2012 vs 2002) and a more recent year of ART-start (2015 vs 2007); as a consequence, they received a lower number of previous regimens (3 vs 6) and drugs (5 vs 8).

Conclusions: Less than ½ of PLWH under virological control with available GRT in our cohort were potentially eligible for LA CAB+RPV. They showed a lower zenith VL, higher CD4 cell count, a shorter history of HIV infection and of exposure to ART compared to those who are not eligible to this new therapeutic strategy.

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New issues on dual therapy

OP 63 LONG ACTING CABOTEGRAVIR PLUS RILPIVIRINE COMPASSIONATE USE PROGRAM: A NARRATIVE DESCRIPTION OF THE ITALIAN EXPERIENCE

R. Rossotti[1], G. Orofino[2], B. Canovari[3], R. Viglietti[4], F. D'Amico[1], N.B. Bana[1], L. Carani[2], M.C. Moioli[1], F. Barchiesi[3], M. Puoti[1,5]

[1]Department of Infectious Diseases, ASST Grande Ospedale Metropolitano Niguarda, Milan, [2]Unit of Infectious Diseases, "Divisione A," Amedeo di Savoia Hospital, Turin, [3]Unit of Infectious Diseases, Azienda Ospedaliera Ospedali Riuniti Marche Nord, Pesaro, [4]UOC Infezioni Sistemiche e dell'Immunodepresso, AORN Ospedali dei Colli, PO D. Cotugno, Naples, [5]School of Medicine, University of Milano Bicocca, Milan

Background: Long-acting cabotegravir and rilpivirine (CARLA) are a novel dual regimen for the maintenance of HIV-1 virologic suppression. In February 2016 a worldwide Compassionate Use Program (CUP) was launched to provide medications to patients in need of life-sustaining therapies before regulatory approval. The present analysis aims to examine efficacy and safety in Italian adult patients with HIV-1 infection who were provided access to CARLA through CUP.

Material and methods. Physicians could participate to CUP under an expanded access program. Each request was separately reviewed and approved by a committee of senior physicians at both supporting companies. Key criteria for granting requests included need for parenteral therapy, advanced disease, absence of key mutations to cabotegravir or rilpivirine, and established retention in care. All patients received a loading dose of CAB 600 mg + RPV 900 mg followed by either a 4- or 8-week maintenance dose. Data were collected by Italian treating physicians who were also responsible for the monitoring of patients' safety, including timely reporting of adverse events.

Results: Six Italian patients were approved to start CARLA under CUP, data were available from 5 of them: they were 3 females and 2 males, with a median age of 45 (IQR 29-54) years and a normal BMI (median 22, IQR 21 -24). They had HIV infection from 17 (IQR 16-27) years acquired through intravenous drug use (1), and vertical (1) and heterosexual (3) contact; one subject had a previous AIDS event. Four were on treatment with an integrase inhibitor-based therapy (one with a dual regimen) before the switch. At baseline, the median CD4 count was 169 (IQR 89-240) cell/mmc, two individuals were viremic: the majority (4) was previously exposed to more than 3 therapeutic lines. They were considered eligible because of swallowing difficulties due to poor adherence (1), pharyngeal cancer (1 T cell lymphoma, 1 vocal cord carcinoma) and neurologic disease (1 progressive multifocal leukoencephalopathy, 1 motoneuron disease). One patient did not start CARLA because she died of septic shock before the first administration.

The majority (4) chose the 8-week administration. The follow up lasted 41 (IQR 17-60) weeks. Figure 1 shows immuno-virologic trend over the first 48 weeks. No virologic failure was observed (genotypic resistance test was performed on a week 32 viral blip but no mutation was found, subtype CRF_02AG). One patient needed to stop treatment because of rilpivirine-related injection-site reaction but was re-started after 8 weeks.

Conclusions: CARLA proved to be safe in this very fragile population with co-morbidities or other issues preventing enteral administration of antiretroviral drugs. Virologic success was achieved despite a long history of infection, with exposure to several regimens and poor immunologic conditions. Shortly, CARLA would be a valuable option also for the general population with no swallowing difficulties.

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New issues on dual therapy

OP 64 IMMUNOLOGICAL RECOVERY IN PLWHIV STARTING DOLUTEGRAVIR PLUS LAMIVUDINE AS FIRST-LINE REGIMEN: DATA FROM THE ODOACRE COHORT

A. Ciccullo[1], A. Dusina[2], A. Borghetti[2], M.V. Cossu[3], D. Farinacci[4], F. Lamanna[4], R.A. Passerotto[4], F. Lombardi[4], A. Capetti[3], G. Baldin[2,5], S. Di Giambenedetto[2,4]

[1]UOC Malattie Infettive, Ospedale San Salvatore, L'Aquila, Italia, [2]UOC Malattie Infettive, Fondazione Policlinico Universitario A. Gemelli IRCCS, Roma, Italia, [3]Division of Infectious Diseases, Department of Infectious Diseases, Luigi Sacco University Hospital, Milan, Italy, [4]Università Cattolica del Sacro Cuore, Roma, Italia, [5]Ospedale Mater Olbia, Olbia, Italia

Background: Clinical trials have highlighted the efficacy and safety of the two drugs regimen of dolutegravir +lamivudine (DTG+3TC) as a first line regimen for treatment naïve PLWHIV. However, long-term data from clinical practice are still scarce. Aim of our study was to confirm, in a real-life setting, the efficacy of this regimen.
Materials and Methods: We collected data from a multicenter cohort of treatment-naïve PLWHIV starting a first-line regimen with DTG+3TC, evaluating the virological efficacy and the immunological recovery. Changes from baseline were evaluated via linear mixed models for repeated measures. Linear regression analyses were performed to explore variables associated to significant changes in laboratory parameters.
Results: We analyzed a cohort of 28 PLWHIV: 22 (78.6%) were males, with a median age of 38 years (IQR 28 -52). Median nadir CD4+ cell count was 368/mm3 (IQR 251-491), while median HIV-RNA at baseline was 4.78 log10 copies/mL (IQR 4.52-5.07). Median follow-up time was 21 months (IQR 13-26). Full population characteristics are shown in Table 1.
During a cumulative follow-up time of 48 PYFU, all PLWHIV achieved virological suppression and we did not observe any VF or DTG+3TC discontinuation.
Regarding immunological parameters, we observed, after 48 weeks, a significant increase in both absolute CD4+ cell count (median increase +203, p<0.001) and CD4/CD8 ratio (median +0.34, p<0.001). Similarly, after 96 weeks, we registered a trend in improvement for both CD4+ (median +230, p=0.068) and CD4/CD8 ratio (median +0.42, p=0.068), although not significant. CD4+ cell increase was inversely associated with age (per 1 year older, B -3.7, 95%CI -7.5 to -0.1, p=0.048) and CD4+ cell count at baseline (per 10 cell more, B -4.8, 95%CI -8.3 to -1.3, p=0.009) in our multivariate analysis. All PLWHIV performed a genotypic resistance test before starting DTG+3TC: none of them had the M184V/I mutation while 1 of the individuals had the Y188C and D232N resistance mutations.
Conclusions: In our cohort DTG+3TC as a first line regimen showed overall great efficacy and tolerability. We observed an optimal immunological recovery at the 48 weeks and 96 weeks timepoints, more pronounced in younger PLWHIV and those starting ARV with a lower CD4+ cell count.

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New issues on dual therapy

OP 65 COMPARISON OF EFFICACY AND TOLERABILITY OF DOLUTEGRAVIR / RILPIVIRINE AND DOLUTEGRAVIR / LAMIVUDINE IN EXPERIENCED HIV-1 POSITIVE PATIENTS SWITCHED FROM A THREE-DRUG REGIMEN BASED ON NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS: A MULTICENTER COHORT STUDY IN ITALY

F. Lagi[1], A. Giacomelli[2], V. Borghi[3], A. Ciccullo[4], L. Taramasso[5], G. Madeddu[6], G. D'Ettorre[7], A. Giacometti[8], F. Ducci[9], A. De Vito[6], R. Pincino[10], S. Di Giambenedetto[4], C. Mussini[3], S. Antinori[2], G. Sterrantino[9]

[1]Infectious and Tropical Diseases Unit, Careggi University Hospital, Florence, Italy, [2]Luigi Sacco Department of Biomedical and Clinical Sciences, University of Milan, Italy; Department of Infectious Diseases, ASST Fatebenefratelli-Sacco, Milan, Italy, [3]Department of Infectious Diseases, Azienda Ospedaliero-Universitaria Policlinico of Modena, Modena, Italy, [4]UOC Malattie Infettive, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy, [5]Infectious Diseases Unit, Ospedale Policlinico San Martino - IRCCS, Genoa, Italy, [6]Infectious Diseases Operative Unit, University Hospital of Sassari, Sassari, Italy, [7]Department of Public Health and Infectious Diseases, Policlinico Umberto I, Sapienza University of Rome, Rome, Italy, [8]Institute of Infectious Diseases and Public Health, Università Politecnica delle Marche, Ancona, Ancona, Italy, [9]Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy, [10]Infectious Diseases Unit, Department of Health Sciences (DISSAL), University of Genoa, Genoa, Italy

Background: Clinical studies show that switching to RPV/DTG or 3TC/DTG once daily is effective and well-tolerated. However, a head-to-head comparison between DTG plus RPV or 3TC is missed in trials, and real-life data is limited. Notably, specific data about patients who switched from a standard 3-drug regimen based on 1 NNRTI (Non-Nucleoside Reverse Transcriptase Inhibitor) + 2 NRTI (Nucleoside Reverse Transcriptase T-Inhibitor) is lacking.

Materials and Methods: This is a multicenter cohort retrospective study involving eight Infectious Diseases Units in Italy. We enrolled all people living with HIV (PLWH), ART experienced with an HIV-RNA <50 copies/mL, over 18-year-old who switched to RPV/DTG or 3TC/DTG from any three-drug NNRTI-based regimen. The study outcomes were discontinuation due to all causes assessed by means of incidence rate and rate ratios, discontinuation due to virologic failure (VF), and adverse events.

Results: Of the 415 patients included in the study, 278 (66.9%) switched to 3TC/DTG, and 137 (33.0%) to RPV/DTG. The follow-up time was 757.8 py in the 3TC/DTG and 214.3 py in the RPV/DTG group. Cisgender men were 313 (75.4%). Clinical/demographic characteristics were summarized in table 1. No significant differences at baseline were observed except for the median duration of NNRTI therapy, which was longer in the 3TC/DTG group (3.2 years vs. 2.7 years, p-value = 0.049), the number of previous ART regimens which was higher for RPV/DTG group (58.4% vs. 43.1%: p=0.004) and the pre-switch regimen containing TDF which was more common in 3TC/DTG group (50.7% vs. 17.5%: p<0.001). The most frequent pre-switch NNRTI was RPV in both groups [49.6% in the 3TC/DTG and 65.7% in RPV/DTG group (p=0.003)]. The most common reason for switching to dual therapy was simplification (Overall 66.0%), followed by the switches due to any toxicities which was higher in the 3TC/DTG group (27.3% vs. 7.3%, p=0.001; respectively).

Overall, 48 patients (11.6%) discontinued the treatment: 38 in the 3TC/DTG and 10 in the RPV/DTG arm with similar discontinuation rate: 5.01 x 100 py [95%CI 3.64-6.94] and 4.66 x 100py [95%CI 2.51-8.67], respectively. The most common reason for discontinuation was toxicity (26 patients, 22/278 (7.9%) in the 3TC/DTG group and 4/137 (2.9%) in the RPV/DTG group), mainly neurologic toxicity (no adverse event above grade 2). Two patients had a virological failure, all in the 3TC/DTG arm. The adjusted discontinuation ratio for RPV/DTG compared to 3TC/DTG was HR 1.11 [95% CI 0.50-2.48; p= 0.785]. We did not observe any significant difference in renal function and lipid parameters in the two groups at the 48 weeks even in the subgroups of patients coming from a TDF-containing regimen.

Conclusion: This study showed that a two-drug regimen of 3TC/DTG or RPV/DTG in clinical practice is characterized by a low rate of VF and discontinuation in NNRTI-based regimens virological suppressed pre-treated PLWH.

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New issues on dual therapy

OP 66 COMPARING THE EFFICACY AND TOLERABILITY OF DOLUTEGRAVIR PLUS RILPIVIRINE VERSUS DOLUTEGRAVIR PLUS LAMIVUDINE IN A MULTICENTER COHORT

A. Ciccullo[1], G. Baldin[2,3], M.V. Cossu[3], A. Giacomelli[4], F. Lagi[5], F. Lamanna[6], D. Farinacci[6], V. Iannone[6], R.A. Passerotto[6], A. Capetti[3], G. Sterrantino[5], S. Antinori[4], S. Di Giambenedetto[2,6]

[1]UOC Malattie Infettive, Ospedale San Salvatore, L'Aquila, Italy, [2]UOC Malattie Infettive, Fondazione Policlinico Universitario A. Gemelli IRCCS, Roma, Italy, [3]Division of Infectious Diseases, Department of Infectious Diseases, Luigi Sacco University Hospital, Milan, Italy, [4]UOC Malattie Infettive III, DIBIC Luigi Sacco, University of Milan, Milan, Italy, [5]Division of Tropical and Infectious Diseases, "Careggi" Hospital, Florence, Italy, [6]Catholic University of the Sacred Heart, Rome, Italy

Background: In the last decade, INI-based 2-drug regimens (2DR) have become commonly used in clinical practice. We tried to investigate and compare the efficacy and safety of two dolutegravir-based 2DR: dolutegravir plus lamivudine (DTG+3TC) versus DTG+rilpivirine (DTG+RPV).

Methods: We retrospectively analyzed a multicenter cohort of virologically suppressed PLWHIV switching to DTG +3TC or DTG+RPV. We excluded from the analysis PLWHIV with no available pre-switch genotypic test or with known resistance mutation to one of the study drugs. The incidence of virological failures (VF, single viral load, VL>1000cp/ml or 2 consecutive VL>50cp/mL) and treatment discontinuations (TD) were evaluated; predictors were analyzed by Cox-regression. Immunological and metabolic parameters' changes were analyzed via parametric and non-parametric tests, as appropriate.

Results: We analyzed 475 PLWHIV, 406 in the 3TC group and 169 in the RPV group. PLWHIV in the RPV group were less predominantly males, had longer duration of HIV-infection and of ART, more previous VF, were more frequently HCV-positive. Full population's characteristics are shown in Table 1.

In the 3TC group, during 660.3 person-years of follow-up (PYFU), we observed 9 VF (a rate of 1.4 VF per 100 PYFU), while 32 individuals discontinued the regimen during 665.8 PYFU: 4 discontinued for VF, 12 for toxicity (of with 5 for CNS toxicity), 7 for switch to other STR, 1 for pregnancy, 8 other/unknown reasons. In the RPV group, there were 4 VF during 376.9 PYFU (1.1 VF per 100 PYFU) and 15 TD during 379.2 PYFU, due to: 2 VF, 6 toxicity (of which 3 neurological), 1 switch to other STR, 6 other/unknown. No differences regarding causes of discontinuations were observed between groups (p=0.679). The estimated probability of remaining free from VF at 96 weeks was 97.1% for 3TC and 97.3% for RPV (log-rank 0.807). We found a higher risk of VF in patients with Zenith HIV-RNA>500000cp/ml in the 3TC group (aHR 4.7, p=0.034); a non-significant trend was observed instead in the RPV group (aHR 5.8, p=0.078). The estimated probability of remaining in the study regimen at week 96 was 87.8% with DTG+3TC and 94.2% with DTG+RPV (log-rank 0.228). Having at least 1 previous VF was associated with a higher risk of discontinuing DTG+3TC (aHR 2.9, p=0.004), but not DTG+RPV (p=0.112).

A significant decrease in total cholesterol (TC) and triglycerides (TG) levels at week 96 was observed solely in the 3TC group (-10 mg/dl, p<0.001 and –15 mg/dl, p<0.001 respectively). PLWHIV in DTG+3TC also had a significant increase in CD4+ cell count at 96 weeks (+41 cell/mm3, p=0.004).

Conclusions: DTG+RPV and DTG+3TC were used in populations with different characteristics in our real-life scenario: while both regimens showed good effectiveness and tolerability, only PLWHIV starting DTG+3TC had a significant improvement in lipid profile after 96 weeks of follow-up.

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Cardiovascular diseases, osteoporosis but not only

OP 67 WEIGHT GAIN IN PEOPLE LIVING WITH HIV UNDER ANTIRETROVIRAL THERAPY: DO OUR STRATEGIES MAKE A DIFFERENCE?

C. Muccini[1,2], D. Ceccarelli[1], R. Lolatto[1], V. Spagnuolo[1], C. Oltolini[1], A. Danise[1], I. Mainardi[1,2], R. Monardo[1,2], A. Castagna[1,2]

[1]Department of Infectious Diseases, IRCCS San Raffaele Scientific Institute, Milan, Italy, [2]Vita-Salute San Raffaele University, Milan, Italy

Background: Antiretroviral therapy (ART), including more recent regimens, can contribute to weight gain in people living with HIV (PLWH). Aim of our study is to evaluate if switching ART may lead to weight loss in PLWH with a reported weight gain.

Methods: This is a retrospective analysis conducted on adult PLWH on virological suppression who switched ART between 2008 and 2021 with at least two determinations of increasing weight before switching ART and two determinations of weight after the switch.

We considered the last available switch for each PLWH and we assessed weight changes according both to the antiretroviral class of the anchor drug received and the most used ART regimens before switching. Patients' characteristics were reported as median (interquartile range) or frequency (%).

Two weight determinations before switch were averaged and used as baseline-weight; weight change after switch since baseline was then calculated using linear regression. Individual slopes were obtained and used to represent mean change after switch.

Results: At the time of ART switch, we evaluated 1165 PLWH: median age was 50 (43-55) years, 946 (81.2%) were male, median exposure to HIV infection was 15 (8-22) years and to ART 11 (5-18) years. Median CD4 count was 669 (482-876) cells/μL and median Body Mass Index (BMI) 24.6 (22.4-27.3) kg/m².

ART regimens pre-switch were based on protease inhibitor in 513 (44.0%) PLWH, non-nucleoside reverse transcriptase inhibitor in 268 (23.0%), integrase inhibitors in 196 (16.8%) and other regimens in 188 (16.1%).

The overall mean change of weight post switch was 0.47 (-0.61, 1.63) kg/year, the median calendar year of switch was 2015 (2013-2017), the median time spent with the pre switch ART was 2.9 (1.5-5.1) years and the median follow-up from the last pre to the last post observation was 2.6 (1.4-3.8) years.

The mean change of weight post switch was 0.47 (-0.37, 1.52) kg/year in PLWH with BMI<=25 kg/m², 0.48 (-0.87, 1.87) kg/year in 25<BMI<=30 kg/m² and 0.29 (-1.38, 2.17) kg/year in BMI>30 kg/m².

There was no antiretroviral class associated with a reduction in weight after switching ART in PLWH with an increased weight (Figure 1). Among the most used pre switch ART regimens, we observed a rising trend of weight after the switch from rilpivirine (RPV)+emtricitabine (FTC)+tenofovir disoproxil fumarate (TDF) and efavirenz+FTC +TDF to RPV+FTC+tenofovir alafenamide (Figure 2).

Among PLWH included, 409 (35.1%) had a 25<BMI<=30 kg/m² and 110 (9.4%) >=30 kg/m² before switching ART: after the switch, 391 (33.6%) had a 25<BMI<=30 kg/m² and 121 (10.5%) >=30 kg/m².

Conclusions: Switching ART after an increase in weight does not have any effect on weight loss; in fact, PLWH maintained their weight stable or had a physiological weight gain, estimated about 0.3-0.5 kg/year for European adults. Considering the impact on health of being overweight or obese, a multidisciplinary strategy may be required to achieve weight loss goals.

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Cardiovascular diseases, osteoporosis but not only

OP 68 PLWH (PEOPLE LIVING WITH HIV): A SINGLE CENTRE RETROSPECTIVE OBSERVATIONAL STUDY ON CARDIOVASCULAR RISK FACTORS

G. Gasparro[1], B. Rossetti[2], M. Ruggeri[1,3], M. Tumbarello[4,5]

[1]Corso Formazione Specifica in Medicina Generale AOU Meyer/Formas, Regione Toscana, Firenze, Italy, [2]Infectious Disease Department, USL SUDEST, Toscana, Misericordia Hospital, Grosseto, Italy, [3]General Practitioner, Società Italiana di Medicina Generale e delle cure primarie, SIMG, Firenze, Italy, [4]Dipartimento di Biotecnologie Mediche, Università degli Studi di Siena, Siena, Italy, [5]UOC Malattie Infettive e Tropicali, Azienda Ospedaliero Universitaria Senese, Siena, Italy

Background: The life expectancy of PLWH (People Living With HIV) is increased due to the reduction of AIDS incidence thanks to efficacy and widespread availability of antiretroviral therapy. Non-AIDS-defining Illnesses are a rising challenge and HIV is associated with an increased risk of cardiovascular disease (CVD) because of chronic inflammation, traditional risk factors and antiretroviral therapy side effects.

Material and Methods: We conduct a single centre retrospective observational study to investigate factors predictive of Hypertension, Dyslipidemia and Diabetes and risk factors of major and minor cardiovascular events. We included HIV positive patients followed in Infectious Diseases Unit of Azienda Ospedaliera Universitaria Senese with last follow-up in 2020-2021. Clinical and laboratories data were analysed with descriptive statistic and logistic regression, the data statistically significant ($p<0.05$) in univariate statistic regression were analysed in multivariate analysis to define the predictors of Hypertension, Dyslipidemia, Diabetes, major and minor cardiovascular events.

Results: Of the 286 PLWH (70% male, median age 54.36 IQR 46.8-59.54, 33% smokers, median seropositive time 14.67 years IQR 8.08-24.9, median antiretroviral exposure 12.27 years) 56.6% had dyslipidemia, 37.8% hypertension and 7% diabetes. During clinical history 9 PLWH had at least one major CV event (acute myocardial infarction or stroke) and 27 had at least one minor CV event (Peripheral arterial disease, acute pulmonary embolism, transient ischemic attack, heart failure, angina, deep vein thrombosis, revascularization). At multivariate logistic analysis were predictors of dyslipidemia: hypertension (aHR 2.206, IC 95% 1.255-3.876, p 0.006), previous Protease Inhibitors exposure (aHR 2.082, CI 95% 1.212-3.578, p 0.008), residual detectable viraemia (aHR 1.902 CI 95% 1.11-3.259 p 0.019) and age ≥50 years (aHR 1.935, CI 95% 1.105-3.389, p 0.021). Predictors of Hypertension were dyslipidemia (aHR 2.871, CI 95% 1.516-5.436, p 0.001), age ≥50 years (aHR 2.618, CI 95% 1.311-5.227, p 0.006) and BMI >30 kg/m2 (aHR 5.182, CI 95% 2.169- 12.383, $p<0.001$). Hypertension was associated to a diagnosis of Diabetes II (aHR 3.649, IC 95% 1.070-12.445, p 0.039) and for major (aHR 9.231, CI 95% 1.108-76.878, p 0.04) and minor cardiovascular events (aHR 6.538, CI 95% 2.068-20.961, p 0.001).

Conclusion: In post-cART era the importance of non-AIDS-defining illnesses is raising, especially concerning CVD and cardiovascular risk factors. We confirm that traditional risk factor, as hypertension, dyslipidemia, age, BMI, and peculiar risk factors, as Protease inhibitors and residual detectable viraemia, contribute to the burden of cardiovascular health in PLWH.

Cardiovascular diseases, osteoporosis but not only

OP 69 RELATIONSHIP BETWEEN VITAMIN D DEFICIENCY AND CARDIOVASCULAR DISEASE IN VIROLOGICALLY SUPPRESSED HIV-1-INFECTED PATIENTS

L. Calza[1], V. Colangeli[1], M. Borderi[1], R. Riccardi[1], F. Malerba[1], I. Bon[2], P. Viale[1]

[1]Unit of Infectious Diseases, IRCCS S.Orsola Hospital, [2]Unit of Microbiology, IRCCS S.Orsola Hospital, University of Bologna, Bologna, Italy

Background: Vitamin D deficiency is a common condition associated with an increased risk of cardiovascular disease (CVD) and other comorbidities in general population, but data among its clinical consequences on HIV-infected patients are lacking still today.

Patients and methods: A cross-sectional study was performed to investigate correlation between deficiency of 25-hydroxyvitamin D (vitamin D) and presence of CVD in adult virologically suppressed HIV-infected patients affering to our HIV Clinic between 2019 and 2021. Vitamin D deficiency was defined as serum level <20 ng/mL, and CVD was defined by a previous diagnosis of coronary artery disease, myocardial infarction, coronary revascularization, peripheral vascular disease, heart failure, transient ischemic attack, or stroke. Multivariate analysis was performed to evaluate the relationship between vitamin D deficiency and CVD.

Results: On the whole, 1242 patients were enrolled: 83% were men, 92% Caucasian, and the mean age was 51.2 years (range, 38-73). The mean CD4 T lymphocyte count was 562 cells/mm3, 61% were smoker, 28% had hypertension, 9% had diabetes mellitus, 22% had metabolic syndrome, 39% had reduced bone mineral density (BMD). The mean serum concentration of vitamin D was 34.6 ng/mL, and 722 patients (58.1%) had a vitamin D deficiency. Overall, CVD was diagnosed in 217 subjects (17.5%) : 81 patients (6.5%) had coronary artery disease, 61 (4.9%) had myocardial infarction, and 53 (4.2%) had transient ischemic attack or stroke. Compared with subjects without vitamin D deficiency, patients with vitamin D deficiency were more likely to have CVD (adjusted odds ratio 2.77; 95% confidence interval: 1.55 to 3.98), coronary artery disease (adjusted odds ratio 3.88; 95% confidence interval: 2.51 to 5.47), myocardial infarction (adjusted odds ratio 2.49; 95% confidence interval: 1.36 to 4.02), and stroke (adjusted odds ratio 2.75; 95% confidence interval: 1.27 to 4.13). Vitamin D deficiency was also significantly associated with body mass index >25 Kg/m2, waist circumference >90 cm, metabolic syndrome, reduced bone mineral density, hypertension and hypertriglyceridemia. In multivariable models too, the vitamin D deficiency was significantly associated with CVD (adjusted odds ratio 2.36; 95% confidence interval: 1.29 to 3.63), coronary artery disease (adjusted odds ratio 2.97; 95% confidence interval: 1.59 to 4.36), and myocardial infarction (adjusted odds ratio 2.24; 95% confidence interval: 1.31 to 3.09).

Conclusion: In our study, vitamin D deficiency was significantly associated with CVD in virologically suppressed HIV-infected parsons, so it seems crucial to maintain optimal levels of vitamin D in this population in order to prevent cardiovascular complications.

Cardiovascular diseases, osteoporosis but not only

OP 70 EFFECT OF BISPHOSPHONATES ON VERTEBRAL FRACTURES IN HIV INFECTED MALES: A 7-YEARS STUDY

L. Pezzaioli[1], T. Porcelli[1], S. Storti[2], G. Tiecco[2], M. degli Antoni[2], S. Amadasi[2], F. Castelli[2], E. Quiros-Roldan[2]

[1]Unit of Endocrinology and Metabolism, Department of Clinical and Experimental Sciences, University of Brescia and ASST Spedali Civili Brescia, Brescia, Italy, [2]Department of Clinical and Experimental Sciences, Unit of Infectious and Tropical Diseases, University of Brescia and ASST Spedali di Brescia, Brescia, Italy

Introduction: Osteoporosis and vertebral fractures (VFs) are frequently observed in HIV-infected men. Whereas bisphosphonates seem effective on bone mineral density (BMD) in HIV-men, data on fractures are lacking. The study aimed to evaluate the long-term efficacy of bisphosphonates on VFs in HIV-infected men.
Methods: This is a longitudinal retrospective, real-life study. We assessed 118 patients (median age 53). The median time of follow-up was 7 years. We adopted the following inclusion criteria: age >18 years, stable HIV infection, no previous bisphosphonates treatment, blood samples from the same laboratory, and three densitometries and morphometric assays performed with the same densitometer.
Results: At baseline, VFs were detected in 29/118 patients (24.6%). Fractured patients were older (p. 0.042), had a longer duration of HIV infection (p. 0.046), antiretroviral exposure (p. 0.025) and higher luteinizing hormone (LH) (p. 0.044). Of the 29 patients already fractured at inclusion, 11 developed new VFs, of which 8 were under treatment with bisphosphonates (p. 0.018). Among the 89 patients without VFs at inclusion, 11 developed VFs, of which 2 were treated with bisphosphonates. Patients with worsened bone conditions (in terms of BMD and/or new VFs, n. 32) had more frequently high LH levels (> 9.4 mIU/mL, p. 0.046) and a higher rate of HCV coinfection with respect to patients with stable bone condition (p. 0.045). Noteworthy, 38.6% of the patients discontinued bisphosphonates, due to medical indication or personal choice, and 14.0%
never started them.
Conclusions: Conclusively, oral bisphosphonates were not completely effective in preventing VFs. This may be due to the multifactorial pathogenesis of fragility fractures. Also, poor adherence to treatment represents an important issue in this population. Our findings underscore the need for fracture prevention and active screening among PLWH, especially for those at risk of a worsening in bone conditions.

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Cardiovascular diseases, osteoporosis but not only

OP 71 ASSOCIATION BETWEEN HEALTH LITERACY, CARE ENGAGEMENT AND ASSESSMENT OF RISK BEHAVIOURS IN AN ITALIAN COHORT OF PEOPLE LIVING WITH HIV

V. Massaroni[1], V. Delle Donne[1], A. Borghetti[2], S. Pierluigi[2], F. Lamanna[2], D. Farinacci[2], A. Ciccullo[3], G. Baldin[4], S. Di Giambenedetto[1,2]

[1]Infectious Diseases Institute, Department of Safety and Bioethics, Catholic University of Sacred Heart, Rome, Italy, [2]UOC Infectious Diseases, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [3]UOC Infectious Diseases, Ospedale S. Salvatore, L'Aquila; Italy, [4]Mater Olbia Hospital, Olbia, Italy

Background: Health literacy (HL) is the ability to understand and apply health information to have appropriate health behaviors. This study aimed to evaluate HL in person living with HIV (PLWH) and the association between HL, care engagement and the assessment of risk behaviours.

Material and Methods: We conduct a cross-sectional survey enrolling 101 PLWH. Exclusion criteria were age <18 years and difficulties with the Italian language. HL was measured using Brief Health Literacy Scale (BHLS) and Newest Vital Sign (NVS). Higher scores in BHLS indicate better subjective estimation of HL, while in NVS better objective HL. The Patient Health Engagement Scale (PHE-S) was used to measure PLWH active involvement in the treatment. Physical Risk Assessment Inventory (PRAI) was used to evaluate the assessment of risk behaviours in two factors "Sports" and "Health". We explored the correlation between HL and PRAI and the distribution of HL levels across the engagement position. Furthermore, demographic and clinical factors associated to HL scales were explored.

Results: Many of PLWH were male (67.3%, n=68), aged 46 to 60 (39.6%, n=40), with upper secondary school degree (50.5%, n=51). Most of the PLWH (68.3%, n=69) were >10 years ago diagnosed with HIV and 63.4% (n=64) of them received >10 years ago for the first time ART. Overall, 93.1% (n=94) reported HIV-RNA<50 copies/Ml. 59.4% (n=60) reported a good health status, 46.5% (n=47) an excellent adherence. According to NVS scale, 59.4% (n=60) of PLWH had adeguate HL. In the PHE-S, most of PLWH were in the adhesion position (54.5%, n=55). There was a positive correlation between PRAI and HL scales, BHLS (PRAI sport r.217, p=.029; PRAI health r.500, p=<.001) and NVS (PRAI sport r.192, p=.055; PRAI health r=.373, p=<.001). PLWH in blackout phase showed lower mean BHLS, NVS and PRAI scores compared to PLWH in the other phases (HL p=0.006; PRAI p=0.003). Furthermore, PLWH with detectable viremia, poor adherence to ART and poor health status showed lower mean BHLS scores (p=<.001, p=<.001, p=<.001, respectively). Moreover most PLWH with undetectable viremia, excellent health status and excellent adherence showed adeguate HL according to NVS (98.3%, 59/60, p=.025; 80.8%, 21/26, p=0.025; 76.6%, 36/47, p=.005, respectively). Finally, most of PLWH with adeguate HL were without HCV co-infection (93%, 56/60, p=.020).

Conclusions: In conclusion, our findings underscore a relationship between low subjective and objective HL, poor care engagement and high score in the assessment of risk behaviours in PLWH. Specifically, PLWH with poor adherence to ART, health status and with detectable viremia show limited HL. Therefore, it is important the individuation of patients with low HL and the construction of interventions improving these skills. Enhancing HL in PLWH is crucial to put them at the center of the treatment by developing better relationship with healthcare workers and better communication of their needs.

Cardiovascular diseases, osteoporosis but not only

OP 72 MENTAL HEALTH ASSESSMENT IN PEOPLE LIVING WITH HIV/AIDS (PLWHA): PRELIMINARY DATA FROM A REFERRAL HIV CENTER

F. Di Gennaro[1], D. Montalbò[2], R. Schiavoni[1], G.G. Panico[1], D.F. Bavaro[1], L. Diella[1], M. Di Tullio[3], A. Calluso[3], C.R. Santoro[1], G. Brindicci[1], F. Balena[1], N. De Gennaro[1], A. Belati[1], D. Fiordelisi[1], M. Sgambati[2], A. Bertolino[2], A. Saracino[1]

[1]Clinic of Infectious Diseases, Department of Biomedical Sciences and Human Oncology, University of Bari, University of Bari "Aldo Moro", Bari, Italy, [2]Department of Basic Medical Science, Neuroscience and Sense Organs, University of Bari "Aldo Moro", Bari, Italy, [3]C.A.M.A. – L.I.L.A, sezione Bari

Introduction: Mental health (MH) is a significant global health concern, which is extremely relevant when referring to people living with a chronic infection such as HIV/AIDS (PLWHA), even if rarely investigated during routinary follow-up visits. In fact, MH disorders are responsible for more 'years lost' to disability than any other condition. Covid pandemic might also have worsened the MH status of patients. The aim of this study was to determine the prevalence of anxiety, depression, post-traumatic stress disorder, alcohol-drug abuse, and stigma in PLWHA patients followed at the Clinic of Infectious diseases of University of Bari, Italy.

Methods: From January 10th to April 7th, 2022, all PLWHA patients accessing the outpatient service or hospitalized in our Clinic were screened using the following standardized tools: HAM-A for anxiety, BDI for depression, PC-PTSD-5 for post-traumatic stress disorder, CAGE-AID for alcohol-drug abuse. Prevalence of positivity to the MH screening was assessed. Factors associated with the positivity to the 4 MH conditions were evaluated with a multivariable logistic regression model. The study is still ongoing.

Results: Overall, 278 PLWHA (Table 1) were included in the study (25% females, median age: 49 years); in 22.6 % (n.63) of them, at least one screening tool for MH disorders resulted positive. In fact, HAM-A was positive (≥8) in 15.8% (n.44) of the sample, BDI was ≥10 in 18% (n.50), PTSD-5 ≥3 in 5% (n.14), and CAGE was ≥2 in 6.1% (n.17), respectively. Concomitant MH disorders were found in 7% (n.19) of patients. The multivariable logistic regression showed a greater probability to result HAM-A ≥8 for smokers (AOR: 2.02, 95% CI: 1.05-3.94), for men who have sex with men (MSM) (AOR: 3.08, 95%CI: 1.50-6.89), and for those who were under a Dolutegravir-based regimen (AOR: 6.52, 95%CI 3.30-13.2). Furthermore, a BDI ≥10 was also associated with Dolutegravir therapy (AOR: 4.76, 95%CI 2.49-9.19), and previous or concomitant AIDS condition (AOR: 3.94, 95%CI 1.09 -12.9). History of drug dependency (AOR: 1.13, 95%CI 1.06-4.35), family stigma (AOR: 2.45, 95%CI 1.62;3.94), and social stigma (AOR: 2.72, 95%CI 1.55-4.84) seemed to be associated to CAGE ≥2, while PTSD-5 ≥3 was associated with regimens therapy with Dolutegravir (AOR: 3.31, 95%CI 1.07-10.2) and with COVID pandemic (AOR: 3.13, 95%CI 1.26-8.36).

Conclusion: Our preliminary data demonstrate that at least 1:5 PLHWA suffers of disturbances of the mental status, including ansia and depression. This reinforces the urgent need for a multidisciplinary health policy action with focused intervention on mental health in PLWHA, especially in the pandemic era. Integration of mental health screening and care into all HIV testing and treatment settings could probably improve ART adherence and linkage to care, but also increase the access of our patients to mental health services and care.

Vulnerable and key populations: local experiences

OP 73 COMMUNITY-BASED CENTERS (CBCS): SEXUAL HEALTH NEEDS AND PREVENTION KNOWLEDGE AMONG MSM IN LAZIO

G.M. Corbelli[1], V. Lingiardi[2], F.M. Nimbi[2]

[1]Plus Roma – APS, Rome, [2]Dept. of Dynamic, Clinical and Health Psychology, Sapienza University of Rome

Background: The implementation of community-based centers (CBCs) for MSM and other sexual minority individuals is increasing in many western countries, such as in Italy. STIs testing, access to prevention tools and counseling with peers are among the most common services offered in these centers. The present study, supported by an unrestricted grant of ViiV Healthcare, aimed to analyze sexual health needs and prevention knowledge among MSM, considering the services implemented in CBCs such as the newborn "Checkpoint Plus Roma".

Material and Methods: A total of 491 MSM living in Lazio region (mean age 38.94 ± 11.77 years, range 18-69) completed an anonymous web survey on sexual health behaviors and needs. Data were collected from January to March 2022.

Results: The survey collected data from a group of MSM that were defining themselves as cisgender men (97.4%), and gay (88.2%) or bisexual (9.6%), 54.18% had at least an STI diagnosis in their life and 16.5% were living with HIV. 13% declared they have practiced chemsex at least once in their life.

Most participants perceived their sexual health as good/very good (62.1%), although 24.8% were not satisfied with the way they take care of their sexual health. What is most often done to take care of one's sexual health is STIs testing, either in public hospitals (42.6%), in CBCs (32.8%) or in private care centers (25.3%). Less participants reported regular visits with other health care providers (HCPs), such as infectious diseases or mental health professionals. Most responders believe that attending a visit with a urologist or a sexual health professional may significantly improve their sexual health (respectively 36.9% and 35.4%). In fact, only 8.3% of men had a visit with a urologist and 5.1% with a sexual health specialist in the previous year. Main reasons reported to the lack of attention to sexual health care were lack of time (45.6%) and money (37.5%), but also lack of awareness of centers/professionals (32.4%), fearing of being judged for their sexuality (18.1%) and feeling that nobody may help them (10.2%).

Regarding prevention tools, condom is often used by most participants (67.4%). Rates of knowledge and use of PrEP (52.3% and 12.6%), PEP (40.7% and 4.5%) and HPV, HAV, and HBV vaccination (58.7% and 33%) are also reported. The most required services at CBCs were STIs tests (90%), access to prevention tools (71.9%), HCPs consultations (68.2%), psycho-emotional workshops (46.2%), cultural-scientific meetings and events (45.2%), consultation with peers (42.4%); peer support groups (35.4%), and to have access a specific chemsex counseling (32.6%).

Conclusions: The results may be helpful to understand the sexual health needs of a specific population like MSM living in Lazio. The promotion of sexual health contemplates an in-depth discussion and recognition of both pleasurable and distressing aspects of sexual experience, its motivations over time, knowledge, and access to care.

Vulnerable and key populations: local experiences

OP 74 INJECTING DRUG USE, IRRESPECTIVE OF HARM REDUCTION MEASURES, IS STRONGLY ASSOCIATED WITH HCV INFECTION: RESULTS OF A STRUCTURED QUESTIONNAIRE ADMINISTERED DURING HCV SCREENING SESSIONS IN LOW THRESHOLD HARM REDUCTION SERVICES

A. Soria[1], G. Ghilardi[1], M. Comolatti[1], M. Di Gennaro[1], C. Gaboardi[2], A. De Pace[3], P. Di Gloria[2], C. Bregamo[2], R. Gallizzi[2], A. Barni[3], MG. Marconi[4], GM. Migliorino[1], P. Bonfanti[1,5], G. Lapadula[1,5]

[1]Infectious Diseases San Gerardo Hospital ASST Monza, Monza, [2]Cooperativa Lotta Contro L'Emarginazione, Monza, [3]Comunità Nuova, Monza, [4]ATS Brianza, Monza, [5]University of Milano-Bicocca, Monza

Introduction: WHO recommends HCV screening in high risk settings to achieve eradication by 2030. Prisons and addiction centers are privileged locations for screening, but risk to miss active consumers or marginalized people with difficult access to services. HCV screening in harm reduction settings (mobile units, drop-in, shelters) may favor detection of submerged infections. Investigation on drug consumption habits and possible association with HCV infection could inform on most risky behaviors and orient future outreach and screening programs.

Methods: Rapid oral tests for HCV/HIV antibodies (HCV/HIV-1&2Ab OraQuick®) were offered to people seen in different harm reduction contexts: mobile units dislocated near smuggling and open drug consumption points, drop-in (indoor units for essential services as needle and syringes exchange, shower, laundry), homeless shelters. While waiting for the result, a questionnaire was administered to investigate personal behaviors related to drug consumption.

Results: Among 77 people who were tested and accepted to answer to the questionnaire, 9 (12%) women, mean (range) age 41 (19-68) years, 38 (49%) were seen in mobile units and 39 (51%) in indoor settings (13 in drop-in and 26 in shelters). Any drug consumption was reported by 48 (62%) individuals: injecting in 27/48 (56%), snorting in 16/48 (33%), smoking in 26/48 (54%); 33/44 (75%) use drugs in company with other people; 11/27 (41%) share material for injection. Any drug use was more common in people seen in mobile units with respect to indoor settings: 35/38 (92%) vs 13/39 (33%), p<0.001. No major differences in routes of drug use were observed among different screening locations, except for snorting, which was more common in indoor settings: 8/13 (61%) vs 8/35 (23%) in mobile units, p=0.012. We detected 3 (5%) HIV and 19 (25%) HCV infections. No HCV infections were detected in people not using drugs. Among users, HCV was strongly associated with injecting use: 18/27 (67%) vs 1/21 (5%), p<0.001, while no association was found for needle sharing or use in company with other people. A higher percentage of HCV infection was detected in people screened in mobile units with respect to indoor settings: 13/38 (34%) vs 6/39 (15%), p=0.055. In a logistic regression analysis considering only people using drugs, injecting use was the only factor associated with HCV infection: OR 66.66, 95%CI 4.82-920.97 p=0.002, while no association was found with mobile unit, use in company with other people, and needle sharing.

Conclusions: Risky behaviors for HCV acquisition are still common in people using drugs. Injecting use is strongly associated with HCV infection irrespective of other harm reduction measures (such as use of personal equipment for injecting), whose adoption is probably not consistent over time. Continuous offer of HCV screening to people who inject drugs should be fostered to maximize detection of unknown HCV infections and subsequent linkage to care for treatment.

Vulnerable and key populations: local experiences

OP 75 HIGH PREVALENCE OF HCV INFECTION AMONG PEOPLE SCREENED IN UNCONVENTIONAL LOW THRESHOLD SETTINGS: RESULTS OF AN OUTREACH PROGRAM OF SCREENING AND LINKAGE TO CARE FOR PEOPLE USING DRUGS

A. Soria[1], G. Lapadula[1,2], M. Comolatti[1], M. Di Gennaro[1], C. Gaboardi[3], A. De Pace[3], P. Di Gloria[3], C. Bregamo[3], R. Gallizzi[3], A. Barni[4], MG. Marconi[5], G. Scaffidi[6], M. Bramani-Araldi[6], A. Caruso[6], D. Leto[7], A. Cardia[7], P. Fortuna[8], G. Galimberti[8], S. Torlasco[9], C. Fanzaga[10], M. Belloni[10], E. Chiesa[11], GM. Migliorino[1], P. Bonfanti[1,2]

[1]Infectious Diseases San Gerardo Hospital ASST Monza, Monza, [2]University of Milano-Bicocca, Monza, [3]Cooperativa Lotta Contro L'Emarginazione, Monza, [4]Comunità Nuova, Monza, [5]ATS Brianza, Monza, [6]SerD Carate-Brianza ASST Brianza, Carate-Brianza, [7]SerD Limbiate ASST Brianza, Limbiate, [8]SerD Monza ASST Monza, Monza, [9]Corpo Italiano Soccorso Ordine di Malta Monza Brianza, Monza, [10]Servizi Sociali Comune di Monza, Monza, [11]Casa Circondariale di Monza, Monza

Introduction: WHO goals of HCV elimination by 2030 pass through screening and linkage to care in most affected populations, as people using drugs (PUD). Poverty, marginalization, and stigma could limit access to testing and care. Screening programs in unconventional settings might reduce such barriers and favor patient engagement. Data on HCV prevalence and cascade of care in these settings are scarce.

Methods: Through multiple collaborations between Infectious Diseases of San Gerardo Hospital, addiction services, and local associations of street educators with historic experience of harm reduction projects with PUD, rapid oral test for HCV antibodies (HCVAb OraQuick®) has been offered to people seen in different contexts with low threshold access: drop-in (indoor units for essential services like needle and syringes exchange, shower, laundry), mobile units dislocated near smuggling and open drug consumption points, shelters for homeless, addiction centers (SerD).

Results: Between February 2020 and November 2021, 156 HCVAb tests were administered during 30 distinct screening sessions; 28 of them (18%) returned a positive result. Prevalence of HCV-Ab positivity was distributed as follows: 10/61 (16%) of the test administered in SerD, 12/38 (32%) in mobile units, 3/31 (10%) in drop-in, 3/26 (11%) in shelters. Higher HCV prevalence was seen in people screened in mobile units with respect to indoor settings (32% vs 14%, Fisher exact test p=0.0161), probably reflecting a higher proportion of active drug use. Among 28 tested HCVAb positive, 4 (14%) had already cleared HCV (either naturally or by previous treatment), 15 (54%) have been referred but did not show up, 9 (32%) have been linked to care and successfully treated with direct acting antivirals (DAA) (Figure 1).

Conclusions: Targeted HCV screening in PUD in unconventional settings has shown high HCV prevalence, especially in mobile units which probably intercept active consumers. As a comparison, these percentages of HCV prevalence are almost the double of what seen in prisons, and more than one hundred times what found in age-group-based mass screening governmental campaigns.

The role of addiction centers and related services is crucial in tackling HCV by favoring screening, referral, and linkage to care; however, anti HCV treatment with DAA faced many constraints of access to upper level of care (infectious disease ambulatory in the hospital), exacerbated by COVID-19 pandemic which dramatically reduced chances of direct and repeated outreach contacts to reinforce adherence and gain trust and acceptability of the intervention.

Programs of outreach and screening in open drug scene, accompanied by a strong commitment for delivering care with innovative settings (such as mobile units with point-of-care finger stick blood tests and direct delivery of DAA) should be tested, implemented, and publicly funded, if we really want to prevent HCV recirculation and eliminate HCV in most affected populations.

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Vulnerable and key populations: local experiences

OP 76 DESCRIPTIVE ANALYSIS AND RETENTION IN CARE OF A COHORT OF HIV-POSITIVE MIGRANTS (AMIGO: A HIV-POSITIVE MIGRANTS COHORT AT AOU CAREGGI)

F. Lagi[1], S.T. Kiros[1], M. Turco[3], B. Borchi[1], F. Bartalesi[1], P. Corsi[1], E. Gotuzzo[4], G. Sterrantino[2], A. Bartoloni[1,2]

[1]SOD Malattie Infettive e Tropicali, AOU Careggi, [2]Dipartimento di Medicina Sperimentale e Clinica, Università degli Studi Di Firenze, Firenze, [3]Sezione di Dermatologia, Dipartimento di Scienze della Salute, Università degli studi di Firenze, Firenze, [4]Universitad Peruana Cayetano Heredia, Lima, Peru

Background: A better understanding of the dynamics of HIV infection in the migrant population is needed to propose targeted interventions. The objectives of the study were:

1. Describe a cohort of HIV migrant patients taken in care at the SOD of Infectious and Tropical Diseases (MIT) of the Careggi University Hospital (AOUC).
2. 90-90-90 estimation
3. Estimate the post-migration acquisition rate of HIV infection.
4. Evaluate the likelihood of maintaining in care and the predictors of loss at follow-up.

Methods: retro-prospective, single-center cohort study collecting data of HIV-positive migrants taken in care from 01/01/2014 to 01/12/2021 at the AOUC MIT clinic. Parametric and non-parametric tests were used where indicated. Cox's regression model was used to identify factors associated with follow-up loss and virologic failure. The end of the study was the date of loss to follow-up or death or end of follow-up (12/31/2021).

Results: We enrolled 184 patients [Table 1]. In 59.2% (n = 109) of cases, the diagnosis of HIV was performed in Italy. In the Peruvian population, who were the majority (33.6%) of patients, we observed a high proportion of transgender women (71.0%: p <0.001) and sex workers compared to the non-Peruvian migrant population (69.3%: p <0.001). The 14.1% (n = 26) of study subjects had at least one ART resistance mutation at baseline.

At the end of follow up, of the 184 people included, 125 (67.9%) remained in care, of these 100% were on ART and 88% (110 patients) achieved viral suppression (viraemia <50 copies/ml). The incidence of follow-up loss in migrants was 12.2 x 100 py [95% CI 9.4-15. 8].

Being <25 years of age and having detectable viremia increase the risk of loss to follow-up (HR 2.23 [95%1.01 -4.94]; p = 0.045) and (HR 4.64 [95%CI 2.52-8.54]; p <0.001), respectively, whereas taking a single tablet regimen protects against loss to follow up (HR 0.37 [95%CI 0.20-0-70]; p=0.002).

Conclusions: In our setting, UNAIDS goals 90 90 90 have not yet been fully achieved in HIV-positive migrants, and high rates of loss to follow-up have been observed. Individualized treatment paths for the migrant population are necessary and can impact the reduction of new infections.

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Vulnerable and key populations: local experiences

OP 77 A QUALITATIVE SURVEY ON FACILITATING FACTORS AND BARRIERS TO ACCESS AND CONTINUUM OF CARE: POINT OF VIEW OF HIV-POSITIVE TRANSGENDER MIGRANT WOMEN LIVING IN FLORENCE

F. Lagi[1], C. Gatteschi[2], M. Tilli[3], N. Zocco[4], A. Avarello[1], S. Bellini[5], S. Contanessi[4], M.R. Zigliani[5], M. Stagnitta[4], L. Mariano[4], E. Gazzarri[4], L. Belloni[6], A. Bartoloni[1,3], G. Sterrantino[3], F. Ierardi[2]

[1]SOD Malattie Infettive e Tropicali, AOU Careggi, Firenze, [2]Agenzia Regionale di Sanità di Toscana, [3]Dipartimento di medicina Speriementale e Clinica, Università degli studi di Firenze, Firenze, [4]CAT Coperativa sociale Firenza, [5]Lega Italiana Lotta all' AIDS, LILA, [6]Centro di riferimento regionale criticità relazionali, AOU Careggi, Firenze

Background: An increased risk of contracting HIV infection, suboptimal adherence, and a loss to follow-up have been observed in migrants, mainly if those individuals are transgender or sex workers. A clear picture of the HIV epidemic among migrants is complex due to the lack of specific national data. We developed a qualitative study that aims to describe the barriers and facilitators (cultural, social, and personal) in the continuum of care for a group of HIV-positive migrants belonging to a key population.

Material and Methods: A semi-structured interview with HIV-Positive transgender migrant female patients already under ART treatment has been conducted at the outpatient clinic of Malattie Infettive e Tropicali, Azienda Ospedaliero-Universitaria Careggi (AOUC), Florence, Italy. Topics explored have been identified through past literature. A group of physicians and psychologists belonging to the AOUC Center for Critical Relationships and territorial associations of CAT and LILA administered the interviews. The analysis method is based on principles of Grounded Theory. Data analysis and processing methodology have been supported by the Agenzia Regionale di Sanità (ARS).

Results: We interviewed 11 HIV-positive transgender migrant women: 8 Peruvian and 3 Brazilian [range 29-49 years old]. The median of the years of HIV positivity, in 60% of cases, the diagnosis was made in the country of origin. Only 3 out of 11 said they had a residence permit.

The interviewees were aware of engaging in risky behaviors, but they continue to maintain unsafe sex under customer pressure. The risk is accepted because of the higher remuneration. The interviews showed the lack of an alternative to sex work: for those individuals, changing their lifestyle is perceived as difficult or impossible due to social prejudices, also present in Italy, mainly linked to being a transgender person. Respondents reported stigma from society and the health system, particularly in the country of origin, due to the disease itself and gender identity.

However, in Italy, this experience was circumscribed to generalist care's places of access (like the Emergency department), where structural barriers such as language played a key role. Instead, a perception of welcome is reported in the reference clinic, thanks to the staff's relational skills and attempts to break down language barriers through mediators.

[Figure 1] summarizes factors that hinder and facilitate interviewees' health behavior in a conceptual map.

Conclusions: Knowledge of this population's personal experience regarding the barriers and factors that facilitate access to the HIV care system is essential for planning public health interventions capable of responding to the real needs of patients. Specific staff training to improve interpersonal and empathic skills or a structural presence of trusted figures, such as mediators in the health sector, represents a system resource.

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Measuring HIV stigma and disclosure

OP 78 TACKLING THE MISUNDERSTANDING AND STIGMA OF HIV: A SURVEY ON 1007 ITALIAN CITIZENS

D. Calzavara[1], A. Tavelli[1,2,3], A. d'Arminio Monforte[1,2,3]

[1]Associazione Milano Check Point, Milano, [2]ASST Santi Paolo e Carlo, Milano, [3]Fondazione Icona

Background: Breaking down stigma and discrimination is one of the biggest challenges facing HIV today. Although scientific research has achieved extraordinary results since U=U (i.e., an HIV-positive subjects under an effective treatment do not transmit the virus), homophobia and serophobia are still common. The aims of this survey are to investigate the depth of stigma in the Italian context.

Material and methods: This online survey named "Tackle HIV" was conducted from 07-Dec-2021 to 14-Dec -2021, as qualitative research supported by ViiV Healthcare Europe, in the 6-nations participating to 'Six Nations Rugby Championship'. Among all the questions collected, this analysis examined seven issues considered as the most significant: 1) acceptance of homosexuality; 2) willingness of testing for HIV; 3) the possible end of a relationship if a partner communicates that he or she is HIV-positive; 4) the reasons why the relationship would be terminated; 5) personal disposition to communicate his or her own HIV-positivity to friends and relatives; 6) knowledge of U=U; 7) whether the participant knows someone living with HIV [TAB1]. The quantitative research collected data on gender, age, geographical origin, relationship status, and level of education: the responses were stratified according to these variables. ViiV did not participate in data collection, analysis and abstract draft.

Results: The survey included 1,007 Italian general population respondents: TAB2 shows demographic features of study population. The question about complete acceptance and support for homosexuals showed a significant difference between men and women (57.8% vs 79%, p <0.001), while there were no differences in terms of HIV perceptions and stigma according to sex [TAB3].

Age resulted to have a significant impact on homosexuality acceptance, willingness of testing for HIV, the possible end of a relationship after the positivity of one a partner said, and U=U knowledge (p <0.001 for all issues): young people were found to have less prejudice and less stigma [TAB4].

Geographic origin had a role only in terms of a previous HIV test performance: 28.5% in the North, 27.7% in the Center 27.7% and 15.4% in the South/Islands (p<0.001) [TAB5].

A higher level of education had an impact on acceptance of homosexuality (65.6% vs 75.3%, p 0.008), and knowledge of U=U (22.3% vs 16.7%, p 0.027) [TAB6].

Conclusions: We observed a high acceptance of homosexuality, which was somewhat unexpected. With regard to HIV perception and stigma, the global picture that emerges is that serophobia is widespread and that the risk of acquiring HIV is not perceived. On the other hand, the result regarding the substantial difference in all questions according to age is interesting, underlining that young people are more inclusive and free from prejudice and stigma, and have a greater knowledge of HIV as compared with older ones, thus suggesting that education and information might be essential in fighting stigma and prejudice.

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Measuring HIV stigma and disclosure

OP 79 HIV-RELATED STIGMA AMONG ITALIAN ADULTS: RESULTS OF AN ONLINE SURVEY

V. Regine[1], L. Pugliese[1], B. Suligoi[1], G. Briola[2], A. Simonetti[2], F. Marchionni[2], V. Saturni[2]

[1]Istituto Superiore di Sanità, Rome, [2]Associazione Volontari Italiani del Sangue, Milan

Background: Some data show that in Italy people with HIV can be discriminated because of stigmatizing opinions. The aim of this study is to evaluate the frequency of HIV-related stigma and to measure associations with socio-demographic factors among Italian adults.

Material and methods: This study is part of the "Head or Heart" project, which investigated habits, knowledge and behaviors of Italians towards people living with HIV through a survey conducted via web (Notiziario Ist Super Sanita 2018 Vol. 31 n.3). The questionnaire collected information also on HIV-related stigma. The dichotomous (yes/no) questions about stigma concerned: a) troubles in sharing a room with an HIV+ person, b) ban for HIV+ children to attending public schools, c) fear of hugging or kissing an HIV+ friend, d) interruption of sexual contacts with a partner known to have acquired HIV. We defined as a person having stigmatization attitudes a person who answered Yes to at least two of the above mentioned questions. A multivariate analysis was carried out to define factors independently associated with HIV-related stigma.

Results: Italians participating in the study were 11,109, median age was 34 years (IQR 25-46 years), 51.7% were women, 56.3% with high school diploma, 51.8% had a job.

Among participants, 37.6% answered Yes to at least one question. Significantly, higher proportions were found among: males (40.6%), people over 50 years of age (42.1%), residents in the South (40.1 %), those with lower secondary school (42.5%), retired people (46.1%), heterosexuals (38.3%), and those who never get information about HIV (46.0%). In the multivariate analysis, all the factors mentioned above remained significantly associated to HIV-related stigma.

Among respondents stigmatization attitudes were distributed as follows: 21.0% would stop having sex with a partner known to have acquiredHIV, 15.7% would be afraid to kiss or hug a friend with HIV, 11.2% would be troubled in sharing a room with an HIV+ person, 5.9% would ban HIV+ children from attending public schools.

Conclusions: More than one-third of respondents reported stigmatizing behaviors, with significantly higher proportions among people with low education level, poor information on HIV, retired, resident in the South, over 50 years of age, male and heterosexual.

Discrimination and stigma suggest a poor knowledge on HIV transmission and a limited updated scientific information. To contrast stigma, it is extremely important to strengthen information campaigns that convey clear and comprehensible messages, tailoring communication according to target populations.

Measuring HIV stigma and disclosure

OP 80 DETERMINANTS OF NON DISCLOSURE OF HIV STATUS IN PLWHIV TO OTHER THAN HEALTH CARE WORKERS

A. Cingolani[1], A. Tavelli[2], V. Calvino[3], L. Cosmaro[4], F. Bai[5], C. Pinnetti[6], D. Tesoro[5], F. Castelli[7], F. Maggiolo[8], A. Antinori[6], M. Cernuschi[9], A. d'Arminio Monforte[5]

[1]Policlinico Fondazione A. Gemelli, IRCCS, Roma, [2]Fondazione ICONA, Milano, [3]ANLAIDS Onlus, Roma, [4]LILA Milano Onlus, Milano, [5]Università degli studi di Milano, Milano, [6]INMI L.Spallanzani, IRCCS, Roma, [7]Università degli studi di Brescia, Brescia, [8]ASST Giovanni XXIII, Bergamo, [9]ASA onlus, Milano

Background: HIV-related self-stigma represents a major risk factor for a range of poor health outcomes. The lack of HIV disclosure to other than health care personnel in PLWHIV could represent a proxy of self-stigma.
Material and Methods: An online anonymous survey on PLWHIV taking antiretroviral therapy (ART) was conducted, in order to investigate the self-reported correlates of disease burden and several other issues including physical, mental, sexual and overall health status. HIV Treatment & Diseases Burden (TDB) was investigated through a questionnaire containing 31 items -in 7 domains using a scale ranging from 1 to 5 (Cingolani et al, 2022) Further, HIV disclosure has been investigated through the question “Whom do you talk to about your HIV infection?”. The response "I only talk about it with my treating physician/nurse" (yes vs no) has been used to categorize HIV disclosure: ‘yes’=non disclosure (ND), ‘no’=disclosure (D). The association between HIV-disclosure and demographic, clinical and TDB has been investigated.
Results: 531 PLWHIV completed the questionnaire. Characteristics of patients are reported in table 1. A total of 257 (48%) participants reported having disclosed their HIV status only to health care workers (ND-PLWHIV); 324 (52%) reported to talk about their HIV status with other people (D-PLWHIV). The HIV-TDB score was 2.14 (95%CI: 2.13-2.15) among D-PLWHIV and 2.21 (95%CI: 2.20-2.22) among ND-PLWHIV, without any statistical difference (p=0.456). ND-PLWHIV reported a more recent diagnosis of HIV (p=0.02), a lower level of current reported CD4 cell count (p=0.02) and were more frequently on first-line ART (p=0.01). Moreover, ND-PLWHIV reported more frequently the need to talk to health care workers about health issues not strictly related to HIV (33% vs 25%) compared to D-PLWHIV (p=0.04), and more frequently would like to obtain information on new ART drugs (43% vs 33, p=0.01). No differences in terms of physical, mental, sexual and overall health was found between ND-PLWH and D-PLWH.
At multivariable analysis, ND-PLWHIV showed an independent higher risk of current reported CD4 counts lower than 200/mmc (AOR 2.48, 95%CI 1.38-4.46, p=0.02), after adjusting for year of HIV diagnosis v and being on first line ART.
Conclusions: The failure to overcome a clinical frailty related to HIV seems to be the main determinant of non-disclosure of HIV outside the HIV care. The relationship with the treating physician and the possibility of having a comprehensive dialogue with him should be pursued as a further strategy for self-stigma elimination.
Table 1.
General characteristics of 531 survey partecipants according with response to the question ” Whom do you talk to about your HIV infection?”.

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Measuring HIV stigma and disclosure

OP 81 KNOWLEDGE AND IMPACT OF U=U AMONG PLHIV, HEALTHCARE PROFESSIONALS AND THE GENERAL POPULATION IN ITALY: A QUALITATIVE STUDY

M. Oldrini[1], M.L. Cosmaro[1], S. Curridori[1], S. Penon[1], D. Savarino[1], S. Mazzilli[2], D. Paganini[2], L. Tavoschi[2]

[1]Fondazione LILA Milano – Lega Italiana per la Lotta contro l'AIDS, Milano, [2]Dipartimento di Ricerca traslazionale e delle nuove tecnologie in Medicina e Chirurgia, Università di Pisa, Pisa

Background: The study, funded by Gilead in 2019 and launched in early 2020, investigated degree of knowledge of the U=U evidence in PLHIV, healthcare professionals (HCP) and the general population through questionnaires administered in Italian hospital settings.

Methods: Three separate questionnaires were developed based on validated tools, with 2 common sections to collect socio-demographic data and consulted sources of information on U=U. Specific sections were designed for each of the 3 target groups to investigate: (i) PLHIV: Clinical history and perceived impact of U=U on stigma and quality of life; (ii) HCP: Knowledge of and attitude towards U=U scientific evidence and information/education of patients regarding U=U ; (iii) General population: Attitude towards U=U; stigma and attitude towards PLHIV. Responses were collected through multiple-choice and Likert scale questions administered by trained community health workers. PLHIV and general population respondents were recruited during check-up visits at hospitals, alongside HCP in 4 hospitals in Milan, Florence, Cagliari and Bari from May to Sep 2021.

Results: 307 interviews were administered to 101 PLHIV; 105 HCPs; 101 general population (socio-demographic data in attachment).

25% PLHIV were not aware of U=U; only 50% answered correctly to questions on the implications of having an undetectable viral load and 10% were unable to indicate their viremia. 50% of PLHIV indicated that U=U has changed/will change their sexual behavior; they had higher scores related to quality of life. Only 44% of the sample were willing to disclose HIV status to others, but 72% expected that knowledge of U=U will contribute to contrast HIV-related stigma.

About 1 in 5 HCP were unaware of U=U; among them, many were 40 years or older. Of the 80% HCP who knew about U=U, only half always discussed U=U with their PLHIV patients, reaching 70% among infectious disease doctors.

Data on the general population were affected by an inadequate sample enrollment, given that 43 out of 101 people declared they know a PLHIV. Overall they had a fair knowledge of U=U, a finding that may not be generalized to the rest of the population. 88% of the sample believed that U=U impacts PLHIV's lives, particularly their social (73%) and sexual (72%) relations. 65% considered that U=U may impact on PLHIV emotional sphere, and 42% also on working relations.

Conclusions: Overall, findings highlighted knowledge gaps on U=U and pointed to the needs for enhanced dissemination of the underlying evidence and potential impact on PLHIV quality of life. Among HCPs improving knowledge of U=U is crucial, as well as fostering its timely and accurate communication to patients. In order to reduce the stigma against PLHIV, efforts are still required to raise awareness of U=U among the general population.

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Measuring HIV stigma and disclosure

OP 82 DO PEOPLE LIVING WITH HIV HAVE A BETTER KNOWLEDGE OF HIV AND STIS COMPARED TO PEOPLE WITHOUT HIV? A SURVEY STUDY IN SARDINIA, ITALY

A. Colpani[1], A. De Vito[1], B. Zauli[1], V. Fiore[1], M.C. Meloni[1], M. Fois[1], A. Bitti[1], S. Bacciu[1], N. Leoni[2], G. Angioni[2], S. Babudieri[1], G. Madeddu[1]

[1]Unit of Infectious Disease, Department of Medical, Surgery, and Experimental Sciences, University of Sassari, Sassari, Italy, [2]Infectious Diseases Unit, SS Trinità Hospital, Cagliari, Italy

Introduction: Poor knowledge of sexually transmitted infections (STIs) and HIV among people living with HIV (PWH) could contribute to a higher prevalence of STIs and self-stigma. We aimed to investigate the knowledge of STIs prevention and transmission and the degree of awareness regarding living with HIV and the U=U campaign, among PWH compared to people without HIV (PWoH).

Methods: We proposed a questionnaire regarding STIs and HIV to PWH attending the outpatient's clinic for Infectious Diseases in Sassari and Cagliari, Italy. The same questionnaire was administered to PWoH. We matched participants 1:2 by age, gender, and level of education (if it was not possible to match for the same level of education, we chose people with a higher level of education). Furthermore, in PWH we investigate the self-stigma and their knowledge about U=U campaign.

We assigned 1 point to correct, 0.5 point to partially correct, and 0 point to wrong answers. We collected data about age, sex, gender, sexual orientation, region of origin, level of education, and employment status.

Then, data were described as numbers on total (percentages) and mean ± standard deviation.

Continuous variables with parametric distribution were compared with Student's t-test. Categorical variables were evaluated with Pearson chi-squared test. The statistical significance level was established as $p<0.05$.

Results: We collected 53 answers from PWH, matched to 106 PWoH. The mean age of the population was 49.7 ±12.3 years (range 22-69). No differences were present in gender, level of education, or work status. On the contrary, there was a higher percentage of homosexual and bisexual people in PWH group. Overall, PWH scored better than PWoH($p=0.0185$). Furthermore, PWH answered significantly better about the route of transmission of HIV($p=0.036$) and the risk of transmission of HIV living with a PWH($p>0.001$) (Table 1). We evaluated the score in the different subgroups of patients. Retired or unemployed people showed a lower score compared with the others (p-value 0.030 and 0.027, respectively). No difference has been found between gender and level of education.

Regarding self-stigma, 33/53(62.3%) declared their status to the general practitioner; reasons for non-disclosure were fear of judgment, shame, and lack of trust. Forty-four(83.0%) disclosed their status to family, friends, or partners. On the contrary, fear to be avoided, being judged, guilt and shame were reasons for non-disclosure. Of notice, 20/53(37.7%) declared U=U has changed their self-perceptions.

Conclusions: Our study reveals a better knowledge of STIs transmission and prevention among PWH than PWoH. However, we registered several gaps in the knowledge of sexually transmitted diseases. Forty (75.5%) patients knew the correct meaning of U=U, and many patients reported its beneficial impact on their lives and sense of self. Finally, more effort is needed to improve consciousness to mitigate self-stigma.

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Measuring HIV stigma and disclosure

OP 83 IMPACT OF HIV-RELATED STIGMA ON SOCIAL SUPPORT, MENTAL HEALTH AND QUALITY OF LIFE IN AN ITALIAN COHORT OF PEOPLE LIVING WITH HIV

V. Delle Donne[1], V. Massaroni[1], A. Borghetti[2], A. Dusina[2], R.A. Passerotto[2], R.J. Steiner[2], A. Ciccullo[3], G. Baldin[4], S. Di Giambenedetto[1,2]

[1]Infectious Diseases Institute, Department of Safety and Bioethics, Catholic University of Sacred Heart, Rome, Italy, [2]UOC Infectious Diseases, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [3]UOC Infectious Diseases, Ospedale S. Salvatore, L'Aquila, Italy, [4]Olbia Mater Hospital, Olbia, Italy

Background: HIV-related stigma still represent a relevant issue to effective disease management for people living with HIV (PLWH).Indeed, it seems to be a barrier to HIV testing, treatment adherence, good mental health and quality of life.Furthermore, PLWH seem to experience higher levels of loneliness than the general population and this lack of social support may contribute to poor adherence to antiretroviral therapy (cART).This study aimed to evaluate the association between HIV-related stigma and social support, mental health and quality of life in a cohort of PLWH.

Material and Methods: We conducted a cross-sectional survey consecutively enrolling 96 PLWH on cART. Exclusion criteria were age <18 years and difficulties with the Italian language.We assessed HIV-related stigma using the "12-item short version of the HIV Stigma Scale" (HSS-12).The perceived social support was examined through 6 statements investigating emotional and instrumental support.To measure Mental Health Status the "Depression, Anxiety and Stress Scale" (DASS-21) was administered.We used 12-item Short-Form Health Survey (SF-12) to investigate physical and mental health-related quality of life.We examined the correlation between HSS -12 and social support.Furhermore, we explored demographic, clinical, mental health and quality of life variables associated to HSS-12.

Results: Many of PLWH were male (60.4%), aged 51 to 60 years (35.4%), with upper secondary school degree (41.7%).Most of the respondents (62.5%) were>10 years ago diagnosed with HIV and received>10 years ago for the first time cART (57.3%).Overall, 80% reported HIV-RNA<50 copies/mL and the mean adherence to cART was 9.38 (SD0.93) on a 0-10 scale.Higher HSS-12 scores were negatively correlated to social support values (r-0.40, p<0.001).Mean HSS-12 scores were significantly higher in women than in men (29.6[SD7] vs 26.4[SD7.2], p=0.034) and in PLWH with heterosexual orientation than those with homosexual orientation (29.3[SD6.9] vs 25.5 [SD7.2],p=0.012).Furthermore, mean HSS-12 scores were significantly higher in PLWH with mild-to-severe levels of depression, anxiety and stress compared to those with average levels (32.5[SD6.8] vs 26.7[SD6.9],p=0.002; 31.2[SD7.1] vs 26.8[SD7],p=0.015; 31.9[SD7.1] vs 27.1[SD7.1],p=0.033, respectively) and in PLWH with elevated negative perception of mental health-related quality of life compared to those with a positive one (32.6[SD7.6] vs 26.7[SD6.8],p=0.003).

CONCLUSION

In conclusion, our findings highlight that HIV-related stigma might be associate to lower emotional and instrumental social support.Moreover, our results suggest that among PLWH women, those with heterosexual orientation and those with mental health issues might suffer higher levels of HIV-related stigma.This overview underlines the importance of defeat HIV-related stigma to facilitate care engagement and improve the psychological wellbeing and quality of life of PLWH, a basic stage for a population with chronic disease.

Models of COVID-19 pathogenesis and response to vaccination

OP 84 HUMAN IPSC-DERIVED MOTOR NEURONS ARE PRODUCTIVELY INFECTED BY SARS-COV-2

G. Cappelletti[1], C. Colombrita[2], F. Limanaqi[1,5], D. Trabattoni[1], C. Moscheni[1], A. Tosoni[6], M. Nebuloni[1,6], S. Santangelo[2,3], V. Silani[2,4], A. Ratti[2,3], M. Biasin[1]

[1]Department of Biomedical and Clinical Sciences L. Sacco, University of Milan, Italy, [2]Department of Neurology and Laboratory of Neuroscience, IRCCS Istituto Auxologico Italiano, Milan, Italy, [3]Department of Medical Biotechnology and Translational Medicine, University of Milan, Italy, [4]Department of Pathophysiology and Transplantation, "Dino Ferrari" Center, University of Milan, Italy, [5]Department of Pathophysiology and Transplantation, Milan, Italy, [6]Pathology Unit, L. Sacco Hospital, Milan, Italy

Background: COVID−19 typically causes respiratory disorders, but surprisingly a high proportion of patients also reported CNS symptoms as well as myopathies during and after SARS-CoV-2 infection. Notwithstanding, the impact of SARS-CoV-2 exposure on motor neuronal cells has not been investigated so far. Thus, by using human iPSC-derived motor neurons (iPSC_MN) we assessed: i) their infectability by SARS-CoV-2; ii) the expression of SARS-CoV-2 main receptors; and iii) the effect of SARS-CoV-2 exposure on iPSC-MN transcriptome.

Methods: Human iPSC lines from 10 healthy donors were obtained by reprogramming fibroblasts with CytoTune-iPS 2.0 Sendai Reprogramming Kit and MN were obtained by iPSC differentiation for 33 days. iPSC-MN were in vitro infected with 1 MOI of SARS-CoV-2, and viral replication was evaluated by qPCR on two viral targets (N1, N2) in cell culture supernatants at 24, 48 and 72 hours post infection (hpi). Viral infection was monitored also by immunofluorescence and electron microscopy analysis. In parallel, we profiled the gene expression of 46 different genes involved in viral entry as well as antiviral and immune response.

Results: By analyzing N1 and N2 gene expression over time, we observed that human iPSC-MN were productively infected by SARS-CoV-2, although viral replication was not accompanied by cytopathic effect. Image analyses of SARS-CoV-2 Spike and Nucleocapsid proteins by immunofluorescence and electron microscopy are currently underway. Gene expression profiling of the main receptors recognized by SARS-CoV-2 (ACE2, CD147, NRP1, Furin, TMPRSS2) revealed that all of them are expressed with lower level of ACE2 compared to CD147 and NRP1. Furthermore, SARS-CoV-2 infection was accompanied by the activation of the antiviral and inflammatory response (IFITM3, MX1, CXCR4) by iPSC-MN.

Conclusions: Though preliminary, these results suggest for the very first time that SARS-CoV-2 can infect human iPSC-derived MN probably by binding CD147 and NRP1 receptors. New evidence, indeed, indicate that these proteins have higher and broader patterns of expression in the human brain than ACE2 or TMPRSS2.

Further analyses are ongoing to validate the results obtained and to better understand the molecular mechanisms activated in iPSC-MN in response to SARS-CoV-2. Such information will be essential to unveil the neuromuscular disorders characterizing SARS-CoV-2 infection and the so called long-COVID symptoms.

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Models of COVID-19 pathogenesis and response to vaccination

OP 85 SARS-COV-2 INFECTION OF AIRWAY EPITHELIUM TRIGGERS ENDOTHELIAL CELLS ACTIVATION

D. Mariotti, G. Matusali, F. Colavita, C. Agrati, V. Bordoni

INMI L. Spallanzani, Roma

Background: Endothelium and airway epithelium are the key players of COVID-19 pathogenesis. The binding of SARS-CoV-2 to ACE2 receptor on endothelial cells leads to the activation of the complement system, inducing pro-inflammatory cytokines release (e.g. TNFα, IL-1β, IL-6, IL-8) and phagocytic cells recruitment causing endothelium damage. However, the interplay between pulmonary epithelial and endothelial cells upon SARS-CoV -2 infection is still largely unexplored. Thus, the aim of this study was to evaluate the endothelial damage after SARS-CoV-2 infection in an organotypic model of human airway epithelium co-cultured with pulmonary endothelial cells (Figure 1).

Methods: After 2 days of SARS-CoV-2 infection of a co-culture of human airway epithelium (HAE) and human microvascular pulmonary endothelial cells (HPMEC), we analysed SARS-CoV-2 RNA and Spike protein expression in HAE and HPMEC, the expression of markers of endothelial damage (E-selectin, ICAM1, VCAM1), inflammatory cytokines (TNFα, IL-1β, IL-6, IL-8) and IFN-β production. The HPMEC expression of pivotal genes in the antiviral and senescence pathways (NF-κB, IFN-β, p53; p21) were also analysed.

Results: Upon SARS-CoV-2 infection of HPMEC co-cultured with HAE, viral RNA and spike protein of SARS-CoV -2 were detected both in HPMEC and in HAE, although effective viral replication was observed only in HAE, highlighting that HPMEC can be infected but failed to sustain viral replication. SARS-CoV-2 infection of HAE-HPMEC co-culture induced a significant increase of E-selectin and ICAM1 expression in HPMEC ($p<0.01$). In contrast, this effect was not observed in SARS-CoV-2 infected HPMEC monoculture, suggesting a role of infected HAE in triggering endothelial activation. Accordingly, the increase of E-selectin expression was correlated to viral RNA detected on HAE and not in HPMEC ($P=0.03$, $r=0.7$). Unsupervised PCA showed that the samples are well clustered with SARS-CoV-2 infected HAE-HPMEC respect to HPMEC monoculture, suggesting that endothelial damage is strongly shaped by epithelium-derived signals. Specifically, IFN-β and ICAM1 turned out to be the most important variables associated to HPMEC activation in infected co-cultures. Moreover, during HAE-HPMEC co-culture a positive correlation was found between E-selectin expression and IL-6 and IFN-β levels ($r=0.6$, $p=0.01$).

Discussion: Here we show that the effect of SARS-CoV-2 replication in the epithelium triggers endothelial cell activation, involving pro-inflammatory cytokines and IFN-β signaling. These data display the interplay between infected epithelium and endothelial cells, highlighting a bystander endothelium activation triggered by infected epithelium. The organotypic model here described may be useful to dissect the fine cross-talk and the injury to the epithelium-endothelium barrier upon SARS-CoV-2 infection.

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Models of COVID-19 pathogenesis and response to vaccination

OP 86 SPECIFIC CD4+ AND CD8+ T CELL RESPONSE OF SARS-COV-2 S EPITOPES USING TETRAMERS & MONOCYTE DYSREGULATION IN FULLY VACCINATED DONORS AND RECOVERED PATIENTS

A. Parente[2], M. Iuliano[1], R. Mongiovì[1], B. Kertusha[2], A. Carraro[2], R. Marocco[2], G. Mancarella[2], S. Garattini[2], F. Izzo[2], C. Del Borgo[2], T. Tieghi[2], L. Fondaco[2], G. Mangino[1], M. Lichtner[2], G. Romeo[1]

[1]Dept. of Medico-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Italy, [2]Dept. of Public Health and Infectious Disease, S. Maria Goretti Hospital, Sapienza University of Rome, Latina, Italy

Background: SARS-CoV-2 is able to escape immune response. The escape is associated with development failure of T cell memory compartments.SARS-CoV-2 variants do not disrupt the total T cells reactivity. The decrease of humoral immunity response observed, highlights the importance of active monitoring of T cell reactivity. Patients may show alterated dimension of atypically activated monocytes related to severe progression. In flow cytometry a population of bigger monocytes has been related to severe desease but clear polarization into pro-inflammatory M1 or alternatively activated, anti-inflammatory M2 macrophages hasn't been identified. Our aim is to describe these poorly understood immunological profiles

Materials and Methods: We characterized the T memory subsets testing the immune response against class I and II restricted immunodominant epitopes shared by ancestral and variants of SARS-CoV-2 strains. Naïve T cells as well as T memory subsets were analyzed by multiparametric flow cytometry on fully vaccinated healthy donors (HDV) and COVID19 recovered patients (PZ). Memory T subsets were identified using surface markers(CD45RA, CCR7,CD62L): naïve (TnCD45+CCR7+CD62L+), central memory (TcmCD45-CCR7+CD62L+),effector memory (TemCD45-CCR7-CD62L+/-) and recently activated effector memory T cells (TemraCD45+CCR7-CD62L-). Specific cell recognition of SARS-CoV-2 S epitopes was performed by using ProT2 MHC-II tetramers (for CD4+ cells) and ProT5 MHC-I pentamers (for CD8+ cells).Classically activated monocytes were CD14brightCD16-, intermedial monocytes were CD14+CD16+,atypical monocytes expressed CD14dimCD16+. Each subset was clustered by CD86 CD163 expression for M1 or M2 phenotype

Results: Were recruited 9 HDV and 14 PZ, 47.8% F 52.2% M, average age 42 years;average days elapsed since the negativization/vaccination 66.9. Comparing the two cohorts of subjects, there was no statistically significant difference in the percentage of SARS-CoV-2 antigen restricted T clones in both CD4+ and CD8+ subsets even if there is a small increase in the PZ cohort compared to HDV.Looking at CD4+ T memory subsets no difference was recorded between the two cohorts of analyzed patients whereas, in the case of CD8+ T cells a significant decrease of the Tn subset (HDV 49,76±16,49% vs PZ 19,72±14,76%, $p<0,001$) is associated with a parallel significant increase of the Tem(HDV: 24,87±13,72% vs. PZ 46,19±17,51%,$p<0,007$) in the PZ cohort compared to HDV. Classic Monocytes showed a significant decrease on PZ (85 ±4.44%) cohort compared to HDV(89,03±5.67%)

Conclusions: These results suggest that, even if both vaccination and natural infection are equally able to induce the activation of T cell clones restricted for immunodominant peptides, recovered subjects display, in the case of CD8+ T cells, an improved expansion of the effector memory T cell subset compared to vaccinated people. This feature probably reflect the broader T cell repertoire stimulated by the virus during the natural infection compared to the spike-restricted one activated during the vaccination schedule.We also observed, in cohort of patients who recently recovered from SARS-CoV-2 infection, a polarization of monocytes towards an atypical form confirming the inflammatory dysregulation.

Models of COVID-19 pathogenesis and response to vaccination

OP 87 IMMUNE RESPONSES AFTER THREE DOSES OF BNT162B2 MRNA VACCINE IN A COHORT OF HIV-VERTICALLY TRANSMITTED PATIENTS

C. Vanetti[1], M. Stracuzzi[2], F. Cicilano[1], V. Rubinacci[2,4], C. Fenizia[3], G. Meraviglia[2], Clerici[3,5], M. Biasin[1], G.V. Zuccotti[2,4], V. Giacomet[2], D. Trabattoni[1]

[1]University of Milan, Department of Biomedical and Clinical Sciences "L. Sacco", Milan, [2]Ospedale L. Sacco, University of Milan, Department of Pediatric Infectious Diseases, Milan, [3]University of Milan, Department of Pathophysiology and Transplantation, Milan, [4]Ospedale dei Bambini V. Buzzi, Department of Paediatrics, Milan, [5]IRCCS Fondazione Don Carlo Gnocchi

Background: Previous studies have proven that certain vaccines prompt suboptimal responses in people living with HIV. Nevertheless, at present, whether SARS-CoV-2 vaccines can elicit an effective and long-lived immune response in vertically transmitted HIV young individuals has not been fully investigated yet. Moreover, in healthy subjects has been arise the importance of a third dose to elicit an effective immune response against Omicron variant, but data on HIV subjects are still scarce.

Methods: In this study, we assessed SARS-CoV-2-specific neutralizing antibody titer (NTA) against the European (EU, lineage B.1), the Delta (D, B.1.617.2) and the Omicron strains (Omi, B.1.1.529) in 22 BNT162b2 mRNA-vaccinated ART-treated patients reporting vertically-transmitted HIV infection and followed at the Pediatric Infective Disease Clinic of ASST FBF-Sacco, Milan, Italy. Analyses were performed over 10 months from the first vaccine dose (T0: one day before vaccination; T1: 25 days after II dose; T2: 6 months after II dose; T3: 3 months after III dose). Results at T2 and T3 were compared with those obtained in 20 BNT162b2 mRNA-vaccinated HIV-negative age-matched volunteers. Furthermore, SARS-CoV-2-specific cell-mediated immune responses were evaluated at the same time points by flow cytometric analysis.

Results: In people living with HIV the percentage of waning of NTA from T1 to T2 was 67% and 53% in the EU and the D strains, respectively, although the Delta strains displayed a moderate immune escape, as demonstrated by the lower neutralization titer (EU T1= 407; D T1= 146). Omicron variant showed lower waning from T1 and T2, but the percentage of immune escape was relevant (Omi T1= 9, Omi T2= 6). Comparing the NTA at T2 and T3, the third dose showed an efficacy in maintaining higher levels of NTA in EU (NFOLD=5), Delta (NFOLD=5) and specially in the Omicron variant (NFOLD=18). Comparing the results at T2 and T3 months with those obtained in HIV-negative age-matched volunteers, no significant differences emerged between the two groups.

Conclusions: BNT162b2 mRNA vaccine is highly immunogenic, supporting vaccination for ART-responder HIV-infected subjects. NTA is considered a correlate of protection from SARS-CoV-2 and the effects of waning immunity predicts a loss of protection after vaccination. The third dose seems crucial to mount adequate immune response to SARS-CoV-2, even against Omicron variant, also in HIV-vertically transmitted young individuals.

Models of COVID-19 pathogenesis and response to vaccination

OP 88 COMPARISON BETWEEN QUANTIFERON SARS-COV 2 KIT AND ACTIVATION INDUCED CELL MARKERS (AIMS) ASSAY IN 21 NON-VACCINATED PATIENTS WITH LATE COVID19 INFECTION

A. Gatti[1], M. De Paschale[2], P. Clerici[2], M.P. Faggioli[3], A. Tamburello[3], L. Castelnuovo[3], M. Franzetti[4], § S. Rusconi[4], A. Mazzone[3]

[1]Haematology Laboratory - Transfusion Center, [2]Microbiology Unit, [3]Internal Medicine Unit, [4]Infectious Diseases Unit, Legnano Hospital, Milano, Italy, [§]Department of Biomedical and Clinical Sciences DIBIC "Luigi Sacco", University of Milan, Italy

Introduction: CD4+ and CD8+ cells contribute to protection and long-term immunological memory during infections. Recent papers showed that the study of immune response markers in SARS-CoV-2 infection may highlight the role of T cells in COVID19 immunity. Several assays, like QuantiFERON SARS-CoV-2 kit and Activation-Induced Markers (AIMs) by flow cytometry, are used to evaluate antigen-specific T cell response in COVID19 immunity. In this study we have compared these methods in 21 non-vaccinated patients with documented COVID19 infection.

Material and Methods: 21 non-vaccinated patients with previous COVID19 infection (from 90 days to 2 years) were studied. 81% of them were positive for antibodies (CLIA) LIAISON SARS-CoV-2 S1 IgG (DiaSorin, Italy). In 4 cases with infection dating >1 year anti S1 antibodies were not detectable. QuantiFERON SARS-CoV-2 (Qiagen, Germany) tests were performed following the manufacturer's instructions. Reactive status was defined as a 0.20 IU/ml greater level than negative control. For the flow cytometric AIMs assay 200µl of blood incubated in the same QuantiFERON tubes and collected before centrifugation were stained with an antibody cocktail including CD3-FITC, CCR7-PE, 7AAD, CD137-APC, CD69-PE-Cy7, CD45RA-APC-H7, CD134-BV786, CD25-BV605 (Becton Dickinson, USA). CD4+AIM memory T cells were identified by the dual expression of CD25 and CD134, and CD8 +AIM memory T cells by CD69 and CD137 coexpression (Figure 1). The AIM reactive status was defined as a percentage of AIM CD4+ or CD8+ memory T cells greater than 0.05 of all CD4+ cells and of CD8+ memory compartment, respectively.

Results: SARS-CoV-2 reactivity showed concordance between serology and QuantiFERON test in 9/21 cases, whereas QuantiFERON resulted negative in 12/21 cases with positive antibodies. AIMs assay identified 13/21 reactive subjects (2 of them with negative S1 IgG and 1 with just positive total anti S1 antibodies), while in only 6/21 cases the positive serology did not correlate with AIMs expression. In the remaining 2 cases without antibodies AIMs tests were also negative (Table 1). Accuracy for AIM test was 63.6% vs 57.1% for QuantiFERON. In 3 patients we found a strong CD8+AIM reactivity (>2%) and 1 of them reported a recent reinfection. In 6 cases we found a simultaneous CD4+ and CD8+ AIM reactivity, and 5 of them had high antibody titers and positive QuantiFERON. In the other 6 cases only CD8+AIM reactivity was detectable and in 1 case with high antibody titer and positive QuantiFERON we detected only a low percentage of CD4+AIM cells (0.07%).

Conclusions: We have shown that QuantiFERON and AIM are complementary tests to identify SARS-CoV-2 antigen-specific reactivity. Other studies have compared similar assays, but in early infections or in vaccinated subjects within 6 months. We found a significant rate of non-reactivity with both methods in patients with a long time lag (> 1 year) between the viral infection and the immunological assessment.

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Models of COVID-19 pathogenesis and response to vaccination

OP 89 AN IN-DEPTH CHARACTERIZATION OF VOCS CIRCULATION BY USING NGS ANALYSIS OF THE SPIKE PROTEIN

M.C. Bellocchi[1], L. Carioti[1], R. Scutari[1], M. Iannetta[2], L. Piermatteo[1], M. Alkhatib[1], S. Tedde[2], L. Duca[1], L. Coppola[2], V. Malagnino[2], A. Crea[2], L. Ansaldo[2], S. D'Anna[1], M.M. Santoro[1], A. Bertoli[1,2], A. Di Lorenzo[2], R. Salpini[1], V. Svicher[1], E. Teti[2], N. Braccialarghe[2], R.A. Cavasio[2], L. Sarmati[2], M. Andreoni[2], F. Ceccherini-Silberstein[1]

[1]University of Rome Tor Vergata, Rome, Italy, [2]University Hospital of Rome Tor Vergata, Rome, Italy

Background: Different SARS-CoV-2 variants of Concern (VOCs) emerged during the pandemic. This study aims at characterizing these differences by Next-Generation-Sequencing (NGS)
Methods: Nasopharyngeal-swabs (NS) of SARS-CoV-2 infected individuals were collected from Jun-2020 to Jan -2022. NGS of spike (S) gene was obtained by home-made protocol for S or whole genome (WGS), using MiSeq platform. S mutations were defined according to prevalence as: major (>90%), intermediate (>20-89%), minor (2 -20%). Additional mutations were defined as those not present in the VOC consensus sequence.
All individuals had NS RealTime-PCR for envelope(E)-nucleocapsid(N)-RNA-dependent-RNA-polymerase(RdRp) /Spike(S) genes with Cycle-Threshold(Ct) <35.
Results: Sequences were obtained for 433 individuals, 233 by S home-made protocol and 200 by WGS; 57.7% were males, with median(IQR) age of 64(51-73) years, 93.5% were Italian; 166 were hospitalized (80% with pneumonia). Median(IQR) NS Ct of E-N-RdRp/S was 24(20-27)-23(19-27)-25(20-28), respectively.
Overall, 89.4% of individuals carried a VOC, with Alpha/Gamma/Beta/Delta/Omicron detected from Jan/Feb/Apr/Jun/Dec 2021, respectively.
Alpha was observed in 118 individuals, Gamma in 55, Beta in 7, Delta (with 28 sublineages identified) in 158 and Omicron in 49. Notably, >1 additional-major S mutation was frequently observed: 22.9% in Alpha, 41.8% in Gamma, 14.3% in Beta, 34.8% in Delta and 46.9% in Omicron (45.2% in BA.1; 50.0% in BA.1.1).
Stratifying individuals according to type of additional mutations [only major-additional (Ma, N=157), minor+/-major (mMa, N=90), and without-additional mutations (Wa, N=186)], individuals with mMa mutations had higher Ct-values than other groups: [E/N/RdRp/S Ct median(IQR) mMa: 26(22-29)/25(21-28)/26(24-29) vs Ma: 22(20-25)/21 (18-24)/23(21-26) vs Wa: 21(18-24)/20(17-24)/22(19-26), all p<0.001]. Notably, Δ days from first COVID-19 symptoms to NS sampling was significant longer in hospitalized patients with mMa than others [median(IQR) mMa: 8(5-10)days vs Ma: 5(4-7)days vs Wa: 5(4-7)days, p=0.001].
Among 166 hospitalized patients, 75.9% carried a VOC: Alpha/Gamma/Delta/Omicron 36.1%, 15.9%, 42.9% and 3.1%, respectively; no Beta was observed. A different rate of hospitalization within each VOC was found: 40.7% in Alpha, 36.4% in Gamma, 34.2% in Delta, and 8.2% in Omicron, p=0.005.
Of note, 170 subjects were vaccinated: 48.2% males, with a median(IQR) age higher than in unvaccinated [67(54 -77) vs 62(50-71) years, p=0.004].
Different prevalence of hospitalized/vaccinated individuals was observed: 5/15 in Alpha, 3/6 in Gamma, 43/103 in Delta, 4/44 in Omicron, p<0.0001.
Conclusion: The study underlines how SARS-CoV-2 has changed over time and how vaccination strategy has contributed to reduce severity and hospitalization for this infection. Lower hospitalization in Omicron infected individuals than other VOCs was observed, also in line with a higher vaccination rate in Italy during its emergence.

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COVID-19: considerations of special populations

OP 90 IMPACT OF PATIENTS' CHARACTERISTICS AND COMORBIDITIES ON IN-HOSPITAL MORTALITY DURING THE FIRST THREE WAVES OF COVID-19 PANDEMIC. RESULTS FROM THE BRESCIA HUB PROJECT

E. Focà[1], S. Calza[2], S. Piva[3], I. Ettori[1], F. Rasulo[3], C. Agabiti Rosei[4], C. Aggiusti[5], B. Cerudelli[6], F. Quadri[7], M. Metra[8], M. Castellano[9], M. Nardin[10], C. Ricci[11], R. Badolato[12], F. Odicino[13], R. Orabona[13], F. Scolari[14], L.R. Tomasoni[1], F. Marinoni[15], A.M. Roccaro[16], C. Rossi[17], F. Castelli[1]

[1]Unit of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili, Brescia, Italy, [2]Unit of Biostatistics and Bioinformatics, University of Brescia, Brescia, Italy, [3]Unit of Anesthesiology and Critical Care Medicine, ASST Spedali Civili, Italy, [4]Second Unit of Internal Medicine, University of Brescia and ASST Spedali Civili, Italy, [5]Unit of Emergency Internal Medicine, University of Brescia and ASST Spedali Civili, Italy, [6]Unit of Neurology, University of Brescia and ASST Spedali Civili, Brescia, Italy,

[7]Unit of Pneumology, ASST Spedali Civili, Brescia, Italy, [8]Unit of Cardiology, University of Brescia and ASST Spedali Civili, Brescia, Italy, [9]Unit of Internal Medicine and Endocrinology, University of Brescia and ASST Spedali Civili, Brescia, Italy, [10]Third Unit of Internal Medicine, ASST Spedali Civili, Italy, [11]Unit of Gastroenterology University of Brescia and ASST Spedali Civili, Brescia, Italy, [12]Unit of Pediatrics, Children's Hospital University of Brescia and ASST Spedali Civili, Brescia, Italy, [13]Unit of Gynecology and Obstetrics, University of Brescia and ASST Spedali Civili, Brescia, Italy, [14]Unit of Nephrology and Dialysis, University of Brescia and ASST Spedali Civili, Brescia, Italy, [15]Unit of Planning and Management Control Service, ASST Spedali Civili, Brescia, Italy, [16]Unit of Clinical Research and Phase I Studies, ASST Spedali Civili, Brescia, Italy, [17]Chief Medical Officer Institution, ASST Spedali Civili, Brescia, Italy

Background: in the period between February 2020 and April 2021, Italy was hit by three pandemic waves due to the spread of Covid-19. The study aims to analyze demographic characteristics and comorbidities of a subset of patients and assess their impact on in-hospital mortality.

Methods: We retrospectively identified hospitalized patients with COVID-19 infection in the largest Italian hospital receiving COVID-19 patients. The admissions were divided into three periods: the first wave from 21 February to 30 June 2020, the second wave from 1 July to 31 December 2020 and the third wave from 1 January to 30 April 2021. The population was studied considering its demographic characteristics and main comorbidities. We described mortality rate, length of hospitalization, ICU admission rate, ICU mortality, ICU length of stay and factors associated with these outcomes by logistic regression and Cox analysis.

Results: Among a total of 7054 patients, we identified 2550 patients, of whom 1138 in the first, 931 in the second and 481 in the third wave. In the population considered males prevail, 1423 subjects (56%). The prevalence of males remains stable in the first two waves but decreases in the third. The mean age was 61.9 (SD 19.5) and was similar in the first two waves, it decreases in the third one [Mean (SD) 64.4 (17.2), 62.6 (20.2), 54.8 (21.4) in the three waves respectively, p <0.001]. Regarding comorbidities, CV diseases were present in 25% (627/2550) overall, followed by metabolic disorders present in 13% (343/2550) of patients. The mortality rate remains stable in the first two waves decreasing in the third one: 124/1138 (11%) in the first; 94/931 (10%) in the second and 35/481 (7.4%) in the third one. Table 1 describes the characteristics and outcomes of the studied population. By Cox analysis, we evaluated various factors associated with mortality. Increasing age (for 10 years increase) remains a factor associated with a higher risk of death [HR 1.93 95% CI 1.62-2.30 p<0.001; HR 2.84 95%CI 2.21-3.64 p<0.001; HR 1.81 95%CI 1.26-2.59 p<0.001; in the three waves respectively]. Female sex appears to be a protective factor during all the waves [first HR 0.45, 95% CI 0.29-0.70, p<0.001; second HR 0.58, 95% CI 0.37 -0.90, p=0.016; third HR 0.68, 95% CI 0.31-1.51, p=0.3]. CV diseases don't appear to be related to death, while metabolic disorders resulted significantly related to death only in the second wave [HR 1.94, 95% CI 1.02-3.71, p=0.045].

Conclusions: We observed that male patients and the mean age of the population decreased in the third wave compared to the first and second one, confirming an evolution of patients' characteristics during the first 15 months of the pandemic. Mortality, as well as the length of hospitalization, seems to decrease in the third wave probably according to a standardized clinical and therapeutical approach. Increasing age and male gender remain the factors more related to in-hospital mortality.

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COVID-19: considerations of special populations

OP 91 SARS-COV-2 INFECTION AND COVID-19 DISEASE IN PLWH

F. Maggiolo[1], D. Valenti[2], M. Arosio[1], D. Guarneri[1], M. Rizzi[1], A.P. Callegaro[3]

[1]ASST Papa Giovanni XXIII, [2]Associazione FROM, [3]ASST Bergamo Est, Bergamo, Italy

Background: Information about incidence, clinics and outcomes of SARS-CoV-2 infection in PLWH is scarce.
Methods: In a prospective cohort, we included PLWH with confirmed SARS-CoV-2 infection and compared them with PLWH who tested negative for SARS-CoV-2. Severity of COVID-19 was graded according to NIH classification and data were derived from the clinical data-base.
Results: Out of 2834 PLWH currently followed, we identified 155 cases of SARS-CoV-2 infection either by RT-PCR test (41.8%) or serology (58.2%). We compared these cases with 307 asymptomatic PLWH who tested negative for SARS-CoV-2. All of them were on active ARV treatment that continued. Three subject (one positive for SARS-CoV-2 and 2 negative) were diagnosed with HIV during the pandemic and immediately started ARV therapy. Baseline characteristics were not significantly different between SARS-CoV-2 positive and negative patients with the exception of a reduced number of non-Italian subjects among cases (P = 0.016)(figure). Amongst positive cases 20.6% were completely asymptomatic, 50.3% had mild symptoms while 18.1% and 11.0% had a moderate or severe disease, respectively. Only 29 subjects (18.7%) were admitted to hospital. The only variables associated with the severity of clinical picture were increasing age (P=0.001), a concomitant diabetes (P = 0.009), hypertension (P = 0.004), cardio-vascular disease (P = 0.001) and the number of chronic co-pathologies (P= 0.002), however only the first 2 variables retained significance in the multivariate model (figure). Finally 6 patients (3.9%) died because of Covid-19. All of them were males with a mean age higher (67 years; 95% CI 61-74) compared to survivors (54 years; 95% CI 52-55). Along with age several variables were associated with the risk of death, but in a multivariate model only the number of chronic co-pathologies (P=0.002) and a lower CD4 count (P=0.024) retained significance (figure). Ten PLWH acquired SARS-CoV-2 after being vaccinated (1 with 1 dose, 8 with 2 and 1 with 3). Nine of them were males with a mean age of 51 years. In 2 cases the infection was asymptomatic and in 8 mild resembling a flu-like syndrome with fever (6 cases), rhinitis (4 cases) and headache, myalgia or gastro-enteric symptoms (2 cases each). Specific ARV drugs never resulted associated to any of the considered outcomes such as risk of infection, severity of disease and risk of death.
Conclusions: SARS-CoV-2 infection may be asymptomatic in a large proportion of PLWH and that must be counted when epidemiological studies are implemented. Furthermore, as barely a fifth of cases are admitted to hospital studies based on hospital admissions may underestimate the problem. Older age is significantly associated with a more serious disease, while the number of chronic co-morbidities and lower CD4 counts do correlate with mortality.

Partially funded by Gilead Fellowship program 2021 and Ministry of Health finalized research fund n° COVID-2020 -12371675

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COVID-19: considerations of special populations

OP 92 EVOLUTION OF SARS-COV-2 VARIANTS OF CONCERNS (VOC) OVER A PERIOD OF DELTA AND OMICRON VARIANTS CO-CIRCULATION: IMPACT ON CLINICAL OUTCOMES AMONG PATIENTS (PTS) HOSPITALIZED FOR COVID-19 IN AN ITALIAN REFERENCE HOSPITAL IN THE FIRST TRIMESTER OF 2022

A. Mondi, I. Mastrorosa, C. Cimaglia, P. Piselli, G. Matusali, F. Carletti, L. Fabeni, E. Specchiarello, G. Giannico, E. Milozzi, E. Biliotti, S. Di Bari, P. Chinello, A. Beccacece, P.Vittozzi, S. Mosti, N. Tetaj, L. Marchioni, S. Ianniello, E. Nicastri, A.R. Garbuglia, F. Vaia, E. Girardi, A. Antinori

National Institute for Infectious Diseases L.Spallanzani, IRCCS, Rome, Italy

Background: Since December 2021, Europe faced a new raise of SARS-CoV-2 infections, mostly driven by the emergence of the Omicron VOC (sublineages BA.1 and BA.2). Aim of the study was to evaluate, in COVID-19 hospitalized pts, the prevalence of different SARS-CoV-2 VOCs and clinical characteristics and outcomes among Delta and Omicron infections during the period where both VoCs were co-circulating.

Methods: All pts admitted to a COVID-19 reference hospital from Dec-24-2021 to Mar-15-2022 with confirmed COVID-19 diagnosis, underwent the S gene target failure test (SGFT) and subsequently to VoC identification by Sanger sequencing of the Spike coding gene. A positive SGTF was used as a surrogate marker for Omicron BA.1. Only patients with the VoC identified through sequencing were included in the analysis. Evolution of VoCs prevalence throughout the observation period was described. Clinical characteristics and severity at hospital admission were compared according to VoC distribution. Predictive factors of clinical progression within 10 days from hospital admission, defined as a combinate outcome of non-invasive ventilation (NIV), mechanical ventilation (MV) or death, were assessed using multivariable logistic regression.

Results: A total of 423 pts were included in the analysis. Among all, Delta was observed in 127 and Omicron in 296 (of which 274BA.1) pts. Over the study period, Omicron rapidly displaced Delta and constituted >90% of the circulating VoCs by the end of Jan 2022 [Fig1]. Omicron BA.1 was the predominant sublineage (>90%) until mid-Feb, gradually displaced by BA.2 which reach 70% at mid-Mar. Pts with Omicron infections were more likely to be older, with multiple comorbidities, fully vaccinated and to have a shorter time from symptoms onset compared to those with Delta. At hospital admission, respiratory failure (Pa/FiO2 <300 mmHg), fever, cough, dyspnea asthenia or chilling were more likely in Delta infections[Table 1]. Within 10 days from hospital admission, 154 pts (36.4%) experienced the combined outcome of which 55 (43.3%) among Delta and 99 (33.4%) among Omicron (BA.1 34.7%,BA.2 18.2%). At multivariable logistic regression analysis, older age and multiple comorbidities predicted severe clinical outcomes, while complete vaccination (>2 doses) compared to no vaccination was associated with a halved risk of clinical progression. Finally, Omicron showed a significant reduction of the risk for 10-day combined severe clinical outcome (-38% for BA.1 and -72% for BA.2) compared to Delta [Fig2].

Conclusions: In the first trimester of 2022, Omicron rapidly displaced Delta in pts hospitalized for COVID-19 becoming the dominant circulating VoC by the end of January 2022. Clinical profile and presentation of pts hospitalized with COVID-19 seemed to be different between Omicron and Delta infections. After adjusting for the main confounders, Omicron infections showed a substantial lower risk for short-term severe outcomes compared to Delta.

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COVID-19: considerations of special populations

OP 93 NEW ISSUES IN SARS-COV-2 VACCINATION RESPONSE AMONG HEALTH-CARE WORKERS: SLOW RESPONDERS AND PERI-VACCINATION INFECTIONS

S. Arsuffi[1], E. Focà[1], E. Sansone[2], T. Diaferia[2], E. Sala[2], F. Castelli[1], G. De Palma[2], E. Quiros-Roldan[1]

[1]Unit of Infectious and tropical Diseases, University of Brescia and ASST Spedali Civili Hospital, Brescia, Italy, [2]University Department of Occupational Health and Industrial Hygiene, DSMC, University of Brescia and ASST Spedali Civili Hospital, Brescia, Italy

Background: COVID-19 mRNA-based vaccines elicit a strong total anti-RBD IgG binding, in vitro neutralizing activity and efficacy in preventing new infections. More significant and rapid rise in of anti-spike glycoprotein (S) and anti-RBD IgG levels have been described in pre-immune participants who were subsequently vaccinated compared to immunologically naïve participants. However, breakthrough infections have been observed in a small percentage of vaccine recipients, with lower peri-infection S-specific IgG antibody.
In this study we aim to describe antibodies titers in peri-vaccinations infections and in vaccination after natural infection in a HCWs cohort.
Material and Methods: This a retrospective longitudinal single-cohort study, conducted at the ASST Spedali Civili General Hospital. We performed the study relying on data gathered from health, epidemiological and serological surveillance at the workplaces before and after anti-SARS-CoV-2 vaccination program.
Results: The study population included 9436 HCWs. Among HCWs who had a documented infection before vaccination, 87 of them did not show anti-S Ig response and were included in group A. 73 subjects seroconverted for anti-N Ig between T0 and T1 and were included in group B. 4484 HCWs were persistently anti-N Ig negative at T1, T2 and T3 and were included in group C (control group).
A T1, group B has a significant lower anti-S Ig titer (414,50 AU/mL; IQ 159,20-2599,00) compared to group C (1161,00 AU/mL; IQ 677,00-1881,70) (p = 0,001 Mann-Whitney test), while in group A we observed a strong anti-S Ig seroconversion after the first dose of vaccination with highest titers of anti-S (5000,00 AU/mL; IQ 4058,50 -5000,00). These data were confirmed also at T2, when group B maintained a significant lower level of anti-S Ig titers compared to group C (p = 0,023 Mann-Whitney test).
At T3, we observed an important rise in group B anti-S Ig titers (2468,00 AU/mL; IQ 835,20-5000,00) which were significantly higher than group C (610,65 AU/mL; IQ 356,53-1013,00) (p < 0,001 Mann-Whitney test).
In our cohort there was no evidence of distribution of diseases or immunotherapy which could justify or forecast a sub-optimal nor delayed antibody response.
Conclusions: We observed that subjects with SARS-CoV-2 infection after first dose of vaccine had lower anti-S Ig titers compared to control group both 60 and 120 days after first dose of vaccine, reaching control group levels 240 days after. Among subjects with a documented natural infection before vaccination, we evidenced subjects with negative anti-S serology, which have seroconverted only after vaccination.
The possibility of a sub-optimal and delayed response to SARS-CoV-2 vaccination among HCWs, even after a natural infection, could have serious implications for the safety of HCWs themselves and of hospitalized patients, highlighting the need of more personalized recommendations about possible further booster vaccination deses.

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COVID-19: considerations of special populations

OP 94 ANTIBODY RESPONSE IN WOMEN VACCINATED AGAINST SARS-COV-2 DURING PREGNANCY AND RESPECTIVE BABIES AT BIRTH

A. Pani[1], A. Proto[2], S. Agliardi[1], O.M. Gagliardi[1], S. Renica[1], F. di Ruscio[1], C. Vismara[3], D. Campisi[3], F. Scaglione[1], S. Martinelli[2]

[1]Department of Oncology and Hemato-Oncology, Università degli Studi di Milano, Milan, Italy, [2]Neonatology and Neonatal Intensive Care Unit, Niguarda Hospital, Milan, Italy, [3]Microbiology Unit, Niguarda Hospital, Milan, Italy

Background: The risk of severe disease and mortality in pregnant women and newborns is greater if compared to non-pregnant adults' risk in case of SARS-CoV2 infection. Vaccination against SARS-CoV2 has been demonstrated to be safe during gestation. Nevertheless, there are no guidelines regarding the timing of COVID-19 vaccination in pregnancy. Our purpose with this analysis is to understand the occurring relation between the timing of vaccination during pregnancy and mothers' and babies' antibody titer at birth.

Methods: Participants were recruited at Niguarda Hospital of Milan, from May to November 2021. Criteria of inclusion were: pregnant women having received an anti-SARSCoV-2 vaccination with Pfizer/BioNTech or Moderna vaccine) during pregnancy and their respective newborns. Serological IgG antibodies anti-S1 RBD were evaluated through a quantitative chemiluminescent-assay Abbott) and information about vaccination timing was obtained.

Results: 84 women were included in the analysis. 22 mothers out of 84 received just one dose, while 62 received two doses. The geometric mean titer (GMT) of anti-S IgG is 329.2 (7.6) AU/ml for babies (%CV 280) and 571.8 (7.4) AU /ml for mothers (%CV 247) in the group of subjects who received just one dose. In the group of those who received two doses, the GMT was 6271.7 (2.7) AU/ml for babies (%CV 101) and 5480.5 (2.7) AU/ml for mothers (%CV109). The relation between the gestational age and the serological titer of the newborn at birth is significant for the 62 mothers with 2 doses ($p<0.001$): the higher the gestational age when mothers received vaccination the higher the serological titers of the respective newborns at birth (Tobit mixed models regression).

Conclusions: Our data suggest that: 1) The birth titer in children of mothers who received two doses of vaccine during pregnancy results equal to or higher than the mothers' titer. 2) There is a correlation between gestational age at vaccination and serological titer at birth.

COVID-19: considerations of special populations

OP 95 PREDICTORS OF MORTALITY IN A COHORT OF OLDEST OLD SUBJECTS HOSPITALIZED FOR COVID-19

M. Mazzitelli, M. Biasin, M. Trevenzoli, S. Lo Menzo, S. Marinello, A. Ferrari, L. Sasset, M. Brundu, S. Gardin, M. Cola, A.M. Cattelan

Infectious and Tropical Diseases Unit, Azienda Ospedale Università, Padova

Elderly people were those who suffered and died the most for COVID-19. Indeed, the risk of unfavourable evolution of SARS-CoV-2 infection, of being hospitalised and death for COVID-19 progressively increases by age. Previous study found the following features as predictors of in hospital mortality for the oldest old (i.e., age ≥85 years) patients: comorbidities, dyspnoea at admission, high inflammatory biomarkers.

Our study aimed at looking at the predictors of mortality in a cohort of oldest old patients hospitalized for COVID -19 at the Infectious and Tropical Diseases Unit of Padua University Hospital (Northern Italy).

In this retrospective analysis, we included all patients ≥ 85 years of age, admitted for COVID-19 from February 1rst, 2020 to May 31rst, 2021 (the 3 pandemic waves). A logistic regression model was implemented to explore the risk factors related to mortality for COVID-19 were studied.

Over the study period, 200 oldest old were admitted for COVID-19 in our Unit (mostly female, 56.5%,mean age was 89.9 years (SD: 3.6)), 17% during the first pandemic wave, 38% during the second one, and 45% during the third one. 92.5% patients were not vaccinated against SARS-CoV-2. 69% patients were hospitalized from home, 11.5% from a long-term care facility (LTCF), and 19.5% from other hospitals. Mean length of stay was of 14.5 days (±9.5). The overall mortality was 86/200 (43%); 56 (28%) patients died during hospitalization, while 30 (15%) died within the following six months. The most frequent symptoms at admission were fever (65.5%), dyspnoea (55.5%) and cough (34.0%). The factors significantly associated with COVID-19 mortality were: polypharmacy (OR: 2.67), heart disease (OR: 2), lung disease (OR: 2.17) and renal failure (OR: 3.40), pneumonia detected on chest X-rays (OR: 4.45), hypotension (OR: 3.26), use of piperacillin/tazobactam (OR: 3.01) and carbapenems (OR: 4.42), the use of non-invasive ventilation (OR: 2.63) and anticoagulant therapy taken at home (OR: 1.95). Carbapenems use was significantly higher in subjects who died and were hospitalised from other wards or from lLTCF vs. those coming from home (15/56 vs. 11/144, p=0.001). Moreover, mortality was significantly different between those who were totally dependent on others in daily activities by Barthel scale vs. those who were autonomous (32/56 vs. 61/144, p<0.001)

COVID-19 mortality was very high, and it is likely that SARS-CoV-2 infection could have worsen the prognosis in already fragile patients. It is necessary to promptly identify patients with a high risk of fatal outcome, by paying attention to Barthel scale at admission, comorbidities, change of vital signs, anticoagulation, diagnosis of severe pneumonia on chest X-rays, and colonization by multi-drug-resistant bacteria, risk factor for further bacterial infections. The impact of SARS-CoV-2 vaccination on the clinical outcome of this population will be explored in further studies.

Toxicity of antiretroviral therapy

OP 96 EFFICACY AND SAFETY OF SWITCHING TO LAMIVUDINE/DOLUTEGRAVIR IN HIV-1-INFECTED PATIENTS AGED OVER 65 YEARS

L. Calza[1], V. Colangeli[1], M. Borderi[1], R. Riccardi[1], F. Malerba[1], I. Bon[2], P. Viale[1]

[1]Unit of Infectious Diseases, [2]Unit of Microbiology, IRCCS S.Orsola Hospital, University of Bologna, Bologna, Italy

Background: A significant percentage of people living with HIV in the European countries and United States are ≥65 years, and this percentage will increase in next years. Clinical trials of dual regimen lamivudine/dolutegravir (3TC/DOL) demonstrated potent efficacy and favourable safety in both antiretroviral therapy-naïve and -experienced patients, but data about older people are still lacking.

Methods: Retrospective cohort study evaluating records from HIV-infected patients aged ≥65 years at our HIV Clinic who were switched to 3TD/DOL between January 2019 and December 2020. Eligible patients had baseline HIV-1 RNA <50 copies/mL, 48 weeks of follow-up data, and no previous virological failures or known resistance mutations for lamivudine or dolutegravir. The primary endpoint was maintenance of HIV-1 RNA <50 copies/mL at week 48. The impact of switching to 3TC/DOL on drug-drug interactions (DDIs) and safety parameters was also assessed.

Results: Inclusion criteria were met by 58 patients, mean age was 72.1 years (range, 65-88), 84% were men, 93% were Caucasian, mean CD4+ T lymphocyte count was 488 cells/mm3, and 18 (31%) had an AIDS diagnosis. Previous antiretroviral regimen included two nucleoside/nucleotide analogues (NRTIs) plus one boosted protease inhibitor in 24 patients (41%) and two NRTIs plus one integrase inhibitor in 20 patients (35%). The most common reason for switch was simplification (in 46% of cases), followed by toxicity (26%), and DDIs (22%). At week 48, 50 (86%) patients maintained an HIV-1 RNA <50 copies/mL and 7 (12%) had an HIV-1 RNA between 50 and 500 copies/mL. A genotype resistance testing was performed in 4 patients with an HIV RNA between 200 and 500 copies/mL and did not show any resistance mutations for NRTIs or dolutegravir. Forty-five potential DDIs were identified in 27 (47%) patients taking a boosted protease inhibitor or integrase inhibitor at baseline that were resolved after switching to 3TC/DOL. Treatment-related adverse events occurred in 9 (16%) patients (all grade 1 -2) but there was only one case (1.7%) of treatment discontinuation at week 24 because of anxiety and sleeping disturbances. At week 48 the mean change (+ SD) in CD4+ T lymphocyte count was +56 (+38) cells/mm3. Mean variations (+SD) in creatinine, total cholesterol and triglycerides were +0.28 (+0.11) mg/dL, -36 (+19) mg/dL, and -49 (+28) mg/dL, respectively. Mean reduction in total cholesterol in comparison with baseline value was statistically significant (p=0.023). At week 48, mean change (+SD) in body weight was +1.7 (+0.7) Kg (p=0.218).

Conclusions: In this real-world cohort, switching to 3TC/DOL was associated with maintenance of virologic control, good tolerability profile, and avoidance of DDIs among patients aged over 65 years. These data support use of dual regimen 3TC/DOL as a treatment option in older patients with HIV infection.

Toxicity of antiretroviral therapy

OP 97 SPECIFIC NEURODEVELOPMENTAL CONSEQUENCES OF DOLUTEGRAVIR EXPOSURE IN A ZEBRAFISH EMBRYO MODEL AND RESCUE WITH EARLY FOLATE TREATMENT

S. Ferretti[1], E. Quiros-Roldan[1], I. Zanella[2], F. Castelli[1], E. Massardi[3], G. Borsani[3], G. Tiecco[1], S. Storti[1], D. Zizioli[3]

[1]Division of Infectious and Tropical Diseases, ASST Spedali Civili di Brescia, Brescia, Italy; Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy, [2]Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy; Clinical Chemistry Laboratory, Cytogenetics and Molecular Genetics Section, Diagnostic Department, ASST Spedali Civili di Brescia, Brescia, Italy, [3]Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy

Background: Dolutegravir (DTG) has been suggested to have teratogenic effects (neural tube defects). Interference with folic acid (FA) pathway may be a molecular mechanism. DTG is however prescribed for HIV+ pregnant women when the benefits outweigh the risks. Zebrafish has emerged as a useful model organism to study drug toxicity. Transparent embryos allow observing developmental processes, genes and signaling pathways are conserved and the use of transgenic fishes has simplified “in vivo” observations of CNS development. We aimed to explore the effects of DTG±FA during neurogenesis in Zebrafish embryos.

Methods: Embryos were generated from wild-type and tg:nrd1-EGFP transgenic lines. Treatments were conducted at gastrula stage, at least 3 times with 30 embryos/treatment. Mortality after DTG exposure was recorded at 48 hours post fertilization (hpf). Morphology and fluorescence of transgenic lines were evaluated up to 48hpf under microscope. Whole mount in situ hybridization (WISH) was performed with specific antisense RNA probes.

Results: In dose-response curve, we considered a DTG range of 3-10-15-20 μM (Cmin-Cmax = 3-10 μM in humans). We evaluated at 48hpf the % of alive embryos (94%) and choose 10μM as optimal for further experiments. At 24hpf, we analyzed the phenotype “in vivo”, observing two types of embryos: one (67%) with significant morphological alterations (midbrain/hindbrain regions not well formed) and one (33%) with normal/mild phenotype. We also performed experiments with 1μM DTG and did not observe any morphological difference compared to 10μM DTG treated embryos. To deepen the involvement of DTG during neurogenesis, we used a transgenic line expressing EGFP under the promoter of neurod1, a transcription factor involved in migrating and differentiated neural cells. At 24hpf we observed fluorescence decrease in midbrain, hindbrain, and midbrain hindbrain boundary; the phenotype became more severe at 48hpf with morphological defects in anterior-posterior development. We next analyzed by WISH the expression pattern of genes involved in neural development: ntl, expressed in neural tube nascent neurons and ngn1, expressed in freshly migrating neurons located in telencephalon, diencephalon, spinal cord neurons. We observed strong defects in neural tube formation and telencephalon region. FA supplementation rescued DTG-induced neural defects, recovering the formation of neural tube and increasing the number of neuronal progenitor cells in DTG-treated embryos (Fig. 1).

Conclusions: In Zebrafish embryos, DTG exposure at gastrula stage caused defects in neural tube formation, decrease in the midbrain size and midline gap of the hindbrain and perturbed phenotype of neuronal progenitor cells at early developmental stage (24hpf). All effects were rescued by FA supplementation. Our study adds information about the neurotoxic role of DTG in developing Zebrafish embryos and highlights the importance of FA as a molecule with therapeutic effects.

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Toxicity of antiretroviral therapy

OP 98 CAUSES OF HIV TREATMENT INTERRUPTION DURING THE LAST 20 YEARS: A MULTI-COHORT REAL-LIFE STUDY

A. De Vito[1], E. Ricci[2], B. Menzaghi[3], G. Orofino[4], C. Martinelli[5], N. Squillace[6], L. Taramasso[7], G.V. De Socio[8], C. Molteni[9], F. Conti[10], L. Valsecchi[11], C. Costa[12], B.M. Celesia[13], G. Parruti[14], G. Pellicanò[15], E. Sarchi[16], A. Cascio[17], G. Cenderello[18], K. Falasca[19], A. Di Biagio[7], P. Bonfanti[6], G. Madeddu[1]

[1]Unit of Infectious Diseases, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy, [2]Fondazione ASIA Onlus, Buccinasco (MI), Italy, [3]Unit of Infectious Diseases, ASST della Valle Olona, Busto Arsizio Hospital, Busto Arsizio, Italy, [4]Unit of Infectious Diseases, "Divisione A", Amedeo di Savoia Hospital, Torino, Italy, [5]SOD Malattie Infettive e Tropicali, AOU Careggi, Firenze, Italy, [6]Infectious Diseases Clinic, San Gerardo Hospital, University of Milano-Bicocca, Monza, Italy, [7]Infectious Disease Clinic, IRCCS Policlinico San Martino Hospital, Genoa, Italy, [8]Clinic of Infectious Diseases, Department of Medicine, Azienda Ospedaliera di Perugia, Santa Maria Hospital, Perugia, [9]Infectious Disease Unit, Ospedale A. Manzoni, Lecco, Italy, [10]Infectious Diseases Unit, Department of Biomedical and Clinical Sciences 'Luigi Sacco', Università degli Studi di Milano, Milan, Italy, [11]Infectious Disease Unit (I Divisione), ASST Fatebenefratelli Sacco, Milan, Italy, [12]Infectious Diseases Department, SOC 1, USLCENTROFIRENZE, Santa Maria Annunziata Hospital, Florence, Italy, [13]Unit of Infectious Diseases, University of Catania, ARNAS Garibaldi, Catania, Italy, [14]Infectious Diseases Unit, Pescara General Hospital, Pescara, Italy, [15]Department of Human Pathology of the Adult and the Developmental Age "G. Barresi," Unit of Infectious Diseases, University of Messina, Messina, Italy, [16]Infectious Diseases Unit, SS. Antonio e Biagio e Cesare Arrigo Hospital, Alessandria, Italy, [17]Infectious and Tropical Diseases Unit- Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties (PROMISE) - University of Palermo, Palermo, Italy, [18]Infectious Disease Unit, Sanremo Hospital, Sanremo, Italy, [19]Clinic of Infectious Diseases, Department of Medicine and Science of Aging, University "G. d"Annunzio' Chieti-Pescara, Chieti, Italy

Introduction: In the last years, many antiretroviral drugs have been developed, with an increased efficacy allowing to achieve more than 90% of people an undetectable HIV-RNA. Nowadays, the main reasons for treatment switch are adverse events or proactive switch to avoid future adverse events.

Methods: We conducted a retrospective cohort study, merging the data of eight different cohorts of the SCOLTA project: lopinavir/r (LPV), atazanavir/r (ATV), darunavir/r or /c (DRV), rilpivirine (RPV), raltegravir (RAL), elvitegravir/c (EVG), dolutegravir (DTG) and bictegravir (BIC). We collected demographical information, risk factor for HIV infection, viro-immunological data, and cause of treatment interruption.

Our aim was to investigate the reason for treatment interruption in the last 20 years during the first year, and during the entire follow-up, focusing on the adverse events.

Results: We included 4405 people with HIV (PWH), the data of which are reported in Table 1. Overall, 664 (15.07%), 489 (11.10%), and 271 (6.15%) PWH interrupted the treatment in the first, second, and third year. respectively.

Looking at the interruption in the first year, the most frequent causes were adverse events, loss to follow-up, Patients' decision, treatment failure, and simplification (Table 2).

In the multivariate analysis regarding all causes of interruption (Table 3) in the first year of observation in experienced patients, treatment with LPV, ATV, RPV or EVG/c, having less than 250 CD4 cells/ml, having a history of intravenous drugs use (IDU), and HCV positivity were associated with an increased risk of interruption. In naïve people (Table 4), only treatment with LPV was associated with an increased risk, while treatment with RPV was associated with a lower risk. Focusing on interruptions due to adverse events in experienced PWH, treatment with DRV and RAL was associated with a lower risk of interruption.

Looking at three years of follow-up, the proportion of interruptions due to adverse events decreased, from 84/489 (17.2%) in the second to 28/271 (10.3%) in the third year (Figure 1).

At the multivariate analysis for all causes of interruption during all follow-up, female gender, IDU, having less than 250 CD4 cells/mL, having a detectable HIV RNA, being treated with LPV, ATV, RPV or EVG as compared to DTG, were associated with an increased risk of treatment interruption in experienced PWH.

In naïve PWH, HCV antibody positivity and treatment with LPV and RAL were associated with an increased relative risk of treatment interruption; on the contrary, starting treatment with RPV was associated with a lower risk.

Conclusion: Our data on more than 4,400 PWH show that adverse events have represented the most frequent cause of treatment interruptions. Treatment discontinuations were more frequent during the first year of follow up and decreased thereafter. First generation PI and INSTI were associated with higher risk of treatment interruptions.

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Toxicity of antiretroviral therapy

OP 99 FIRST AND SECOND PHASE VIRAL LOAD DECAY IN REAL-LIFE USING NONLINEAR BAYESIAN MIXED EFFECT MODEL

D. Ceccarelli[1], R. Lolatto[1], N. Gianotti[1], C. Muccini[1,2], D. Canetti[1], C. Maci[1,2], C. Oltolini[1], B. Trentacapilli[1,2], A. Castagna[1,2], L. Galli[1]

[1]Infectious Diseases Unit, IRCSS San Raffaele Hospital, Milan, Italy, [2]Vita-Salute San Raffaele University, Milan, Italy

Background: Mathematical modeling has provided many insights into the dynamics of HIV infection in people living with HIV (PLWHIV) undergoing antiretroviral treatment (ART). Viral decay has a 'biphasic' pattern with an initial sharp decrease in viral load, and a subsequent slower decline phase.
The aim of this study was to fit biphasic models to estimate treatment dynamics among patients treated with PI-based, NNRTI-based and INSTI-based regimens.
Material and Methods: Cohort study on adult, naïve PLWHIV, who started ART since 2008, with a PI- or NNRTI- or INSTI-based regimen and with ≥4 viremia determinations during a 1-year follow-up. Follow-up accrued from the date of ART start up to the date of last available visit (up to 1 year since ART start) or discontinuation of the initial regimen or lost to follow-up. We fitted the following biphasic model to study the short-term viral load decay: $V(t) = Ae^{(-\delta t)} + Be^{(-\gamma t)}$, where t=days from ART start, where the two exponentials parametrize the two phases of decay. Posterior distributions of the parameters "A" and "delta" (parameters of the first phase), "B" and "gamma" (parameters of the second phase) were estimated using a Nonlinear Bayesian Mixed Effect model: $V_i(t) = (A+A_i)\exp(-(\delta+\delta_i)t) + (B+B_i)\exp(-(\gamma+\gamma_i)t)$, for i=1,…N_individuals. Markov Chain Monte Carlo (MCMC) simulations using a no-U-turn sampler (NUTS) were calculated for each drug class; viral load posterior predictive distribution during follow-up and posterior distribution of parameters of interest (delta and gamma) were compared among ART classes. Treatment dynamics were estimated overall and into strata of HIV-RNA (> or ≤100000 copies/ml) at ART start.
Results: Overall, posterior distributions of delta (δ) and gamma (γ) (median (IQR)) were: 0.212 (0.198-0.228) [1/days] and 0.012 (0.012-0.013)) [1/days] among PI-based regimens; 0.399 (0.380-0.419) [1/days] and 0.008 (0.007-0.009) [1/days] among INSTI-based regimens and 0.294 (0.261-0.333) [1/days] and 0.020 (0.019-0.022) [1/days] among NNRTI-based regimens. The posterior predictive distributions of viral load during follow-up according to the ART drug class is shown in Figure 1; treatment dynamics were also estimated into viral load strata presented before (Figures 2-3). Figures 4-6 show the bidimensional posterior distribution of delta and gamma of the three ART drug classes overall and into strata.
Conclusions: The viral load decay during the first phase was faster among people treated with INSTI-based regimens and undetectable viral load was reached in almost all cases during this phase. On the contrary, PI-based or NNRTI-based regimens are associated with slower decay during the first phase and undetectable viral load is often (but not all) achieved in the second phase. During the second phase, NNRTI-based regimens achieved a performance even better than INSTI-based in terms of viral load suppression.

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Toxicity of antiretroviral therapy

OP 100 THE EFFECTS OF SWITCHING FROM DOLUTEGRAVIR/ABACAVIR/LAMIVUDINE TO BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE IN VIROLOGICALLY SUPPRESSED PEOPLE LIVING WITH HIV ON NEUROPSYCHIATRIC SYMPTOMS: PRELIMINARY FINDINGS FROM A RANDOMIZED STUDY

B. Rossetti[1,2], M. Ferrara[3], L. Taramasso[4], F. Bai[5], F. Lombardi[6], N. Ciccarelli[7], M. Durante[8], F. Alladio[3], I. Rancan[1,8], F. Montagnani[1,8], A. Di Biagio[9], A. d'Arminio Monforte[5], M. Zazzi[8], M. Fabbiani[1] for DOBINeuro study group

[1]Infectious and Tropical Diseases Unit, University Hospital of Siena, Siena, Italy, [2]Infectious Disease Department, USL SUDEST Toscana, Misericordia Hospital, Grosseto, Italy, [3]Unit of Infectious Diseases, Department of Medical Sciences, University of Torino, Torino, Italy, [4]Infectious Diseases Clinic, Department of Internal Medicine, IRCCS Policlinico San Martino Hospital, Genoa, Italy, [5]Clinic of Infectious Diseases, Department of Health Sciences, ASST Santi Paolo e Carlo, University of Milan, Milan, Italy, [6]Infectious Diseases Unit, UOC Infectious Diseases, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [7]Department of Psychology, Catholic University, Milan, Italy, [8]Department of Medical Biotechnologies, University of Siena, Siena, Italy, [9]Infectious Diseases Clinic, Department of Health Sciences, University of Genoa, San Martino Hospital-IRCCS, Genoa, Italy

Background: Central nervous system (CNS) adverse events (AE) occur with various antiretroviral regimens (ART), and has been a cause of discontinuation of dolutegravir-containing ART, especially when used in combination with abacavir. The main aim of this study was to evaluate whether the switch to bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF arm) is associated with a reduction in severity and incidence of neuropsychiatric symptoms compared to continued dolutegravir/abacavir/lamivudine (DTG/ABC/3TC arm).

Materials and Methods: DOBINeuro is an ongoing, 48-week, randomized trial enrolling PLWH treated with DTG/ABC/3TC for >6 months and with HIV-1 RNA <50 cps/ml for >12 months. Exclusion criteria include previous AIDS events, active alcohol intake or substance abuse, major psychiatric disorders, history of virological failure with InSTI, HBsAg+. At baseline (BL), PLWH are randomized to continue DTG/ABC/3TC (arm A) or switch to B/F/TAF (arm B). The main endpoint is to analyse differences in the evolution of neuropsychiatric symptoms at 3 months; quality of life, suicide risk, other self-reported symptoms (using validated questionnaires) are also evaluated. Here, we describe preliminary findings at 3 months in the first enrolled patients.

Results: We included 22 PLWH (68% males, median age 51 years, median CD4 676 cells/mm3): 12 were randomized to continue DTG/ABC/3TC and 10 to switch to B/F/TAF. At BL, clinical and laboratory characteristics were homogeneous in the two arms; overall, 18.2% of PLWH showed cognitive impairment at BL (def. global Z score ≤-1) with no difference between arms. At 3 months, no significant differences were observed between and within arms regarding self-reported adherence, quality of life assessment and suicide risk. However, the following symptoms were less frequently reported with B/F/TAF than with DTG/ABC/3TC: palpitations (p=0.049), difficulty falling asleep (p=0.020) and restless or disturbed sleep (p=0.048). Only two non-serious adverse events were reported: one grade 3 increase of triglycerides with DTG/ABC/3TC and one self-limited episode of abdominal pain with B/F/TAF, which was not treatment-related and did not lead to drug discontinuation.

Conclusions: Switch to B/F/TAF in virologically suppressed PLWH was associated with improvement in some reported symptoms, including sleep disturbances, compared to continued DTG/ABC/3TC. Further data from the 48-week study follow-up are required to evaluate the potential impact on the incidence and severity of neuropsychiatric symptoms of treatment switch to B/F/TAF compared to continued dolutegravir.

Toxicity of antiretroviral therapy

OP 101 DYNAMIC OF LIPID PROFILE IN HIV NAIVE PATIENTS TREATED BY TAF-BASED REGIMENS: A MULTICENTER OBSERVATIONAL STUDY

S. Martini[1], P. Maggi[1,2], C. Gervasoni[3], L. Onorato[1], S. Ferrara[4], L. Alessio[1,2], C. Bellacosa[5], V. Esposito[6], G. Di Filippo[7], A. Masiello[8], A. Maddaloni[9], S. Madonia[10], G.D'Alessio[11], V. Rizzo[6], N. Coppola[1]

[1]Infectious Disease, University of Campania, Luigi Vanvitelli, [2]AORN Sant'Anna e San Sebastiano of Caserta, [3]ASST FBF SACCO of Milan, [4]University of studies of Foggia, [5]University of studies of Bari, [6]IV Division AORN dei Colli, [7]University Federico II of Naples, [8]AO San Giuseppe Moscati of Avellino, [9]VII Divisione AORN dei Colli, [10]AOU San Giovanni di Dio e Ruggi d'Aragona of Salerno, [11]AORN San Pio of Benevento

Background: The introduction of tenofovir alafenamide (TAF) has deeply modified the choice of the backbone, allowing to prevent bone and renal toxicity related to previous formulation of tenofovir disoproxil fumarate (TDF). To better understand the possible role of TAF in dyslipidemia, antiretroviral naive Persons Living With HIV (PLWH) were evaluated, comparing those treated by TAF/emtricitabine with those by abacavir/lamivudine.

Methods: We enrolled in an observational, retrospective, longitudinal, multicentre study, 270 naive PLWH, who started treatment from 2017 until 2019 and were followed-up for at least 72 weeks. We divided patients in two groups, one treated with a TAF-based backbone in their antiretroviral regimens (Cases) and one without TAF (Controls), to evaluate eventual differences in the dynamic of lipid profile from baseline(T0), to week 24 (T1), 48 (T2) and 72 (T3).

Results: No significant differences were observed at baseline between 2 groups. In Case group we observed a significant development of hypercholesterolemia throughout the follow-up ($p<0.0001$), observed in the Control group only at T3, associated with a significant increase of high-density lipoprotein (HDL). Statin was prescribed in 5 patients in the Case and 6 in the Controls. There were no significant differences between the two groups regarding triglycerides, low-density lipoprotein (LDL) and cardiovascular risk index (CRI). At binary logistic regression analysis, no factor was independently associated to hypercholesterolemia, except for higher age at T0 and female sex at T3.

Conclusions: This real-life study shows that in naive PLWH, TAF is associated with hypercholesterolemia throughout the follow-up. The clinical significance of this hypercholesterolemia should be re-evaluated and confirmed in further larger studies with longer follow-up.

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HIV and SARS-CoV-2: from in vivo to in vitro

OP 102 TRENDS OF HIV-1 DRUG RESISTANCE AND APOBEC EDITING IN PBMC COMPARTMENT OVER THE LAST DECADE

D. Armenia[1], R. Gagliardini[2], C. Alteri[3,4], V. Svicher[5], V. Cento[6], V. Borghi[7], A. Vergori[2], S. Cicalini[2], F. Forbici[2], L. Fabeni[2], A. Bertoli[5,8], W. Gennari[7], V. Malagnino[8], M. Andreoni[8], C. Mussini[7], A. Antinori[2], C.F. Perno[4], M.M. Santoro[5], F. Ceccherini-Silberstein[5]

[1]UniCamillus, Saint Camillus International University of Health Sciences, Rome, Italy, [2]National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy [3]University of Milan, Milan, Italy, [4]Bambino Gesù Children's Hospital, Rome, Italy, [5]University of Rome "Tor Vergata", Rome, Italy, [6]Humanitas Research Hospital, IRCCS, Milan, Italy, [7]University of Modena and Reggio Emilia, Modena, Italy, [8]Polyclinic of Rome "Tor Vergata", Rome Italy

Background: The evaluation of HIV-1 drug-resistance in PBMCs has been increased in clinical practice in the last years, especially in subjects with poor information about previous resistance. Genotypic resistance testing (GRT) in PBMCs is also useful to explore APOBEC editing in HIV-DNA. We aimed at evaluating the temporal trend of drug-resistance and APOBEC editing in a context of suppressed viremia.

Material and methods: We included virologically suppressed individuals for whom protease (PR)/reverse-transcriptase (RT) and integrase (IN, when available) Sanger GRTs in PBMCs were available over the period 2010 -2021. Temporal trends of major resistance mutations (MRM) to PI, NRTI, NNRTI and INI and APOBEC-related mutations (APO-M) were evaluated (Stanford HIVdb algorithm version 9.0).

Results: Overall, 1126 individuals with a PBMC GRT were included (724 for PR/RT/IN; 402 for PR/RT). They were on cART since 11 (5-18) years with a median (IQR) of 4 (2-7) previous regimens. At GRT, individuals were under virological suppression since 44 (4-98) months. Around half of them (45.2%) were previously exposed to INIs (raltegravir: 24.2%; dolutegravir: 22.4%; elvitegravir: 6.7%; bictegravir: 2.4%) and were highly treatment experienced (46.5%). Concerning drug-resistance, 35.2% of individuals harboured at least one MRM (23.4% to NRTIs, 18.8% to NNRTIs, 7.7% to PIs and 1.4% to INIs). APO-M were observed in 11.4% and 15.4% of individuals in PR/RT and IN, respectively, while APO- related stop codons (APO-Stop) were observed in 6.2% and 5.2% in PR/RT and IN, respectively. APO-M associated to drug resistance (APO-DRMs) to PIs, NRTIs, NNRTIs and INIs were observed in 3.7%, 9.7%, 3.7% and 4.4% of individuals, respectively. From 2010 to 2021 no significant changes were found in the proportion of individuals harbouring MRMs to any drug class, PIs, NRTIs, NNRTIs and INIs (Figure, Panel A). Concerning APOBEC editing in PR/RT, no significant changes in trends of APO-M, APO-Stop and APO-DRMs associated to each drug class were observed over time (Figure, Panel B). Concerning APOBEC editing in integrase, a slight increase of APO-M, APO-Stop and APO-DRMs was observed, however without statistical significance. Among specific INI APO-DRMs, only G163R significantly increased from 2012 to 2021, while G140R significantly decreased (Figure, Panel C). Individuals previously exposed to INIs showed a similar prevalence of INI APO-DRMs compared to others (4.4% vs. 4.5%).

Conclusions: In virologically suppressed individuals, resistance in PBMCs and the extent of APOBEC editing were generally stable in the last decade. Interestingly, a slight increase of APOBEC editing in integrase was observed, particular with a G163R significative increase. The low and stable prevalence of APO-Stop underlines that Sanger HIV-DNA GRT provides reliable information to manage treatment switch in individuals under virological control.

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HIV and SARS-CoV-2: from in vivo to in vitro

OP 103 TREND OVER TIME OF HIV-1 DRUG RESISTANCE TO NON-NUCLEOSIDE REVERSE-TRANSCRIPTASE INHIBITORS (NNRTIS) AND THEIR DRIVERS: COHORT STUDY FROM ARCA

I. Rancan[1,2], C. Cassol[1,2], L. Graziani[3], M. Tilli[3], C. Malcontenti[4], C. Russo[5,6], M. Bottanelli[7,8], F. Bracchitta[9], R. Papaioannu[7,8], L. Labate[5,6], S. Mora[12], A. Bezenchek[10,11], A. Shallvari[10,11], A. Di Biagio[5,6], B, Rossetti[13]

[1]Department of Medical Biotechnologies, University of Siena, Siena, Italy, [2]Department of Medical Sciences, Infectious and Tropical Diseases Unit, University Hospital of Siena, Siena, Italy, [3]Department of Experimental & Clinical Medicine, University of Florence, Florence, Italy, [4]SOD Malattie Infettive e Tropicali AOU Careggi, Florence, Italy, [5]Infectious Diseases Unit, San Martino Policlinico Hospital - IRCCS for Oncology and Neuroscience, Genoa, Italy, [6]Department of Health Sciences (DISSAL), University of Genoa, Genoa, Italy, [7]Vita-Salute San Raffaele University, Milan, Italy, [8]Infectious Diseases Unit, San Raffaele Scientific Institute, Milan, Italy, [9]Laboratory of Clinical Microbiology, Virology and Bioemergencies, ASST Fatebenefratelli Sacco, L. Sacco University Hospital, Milan, Italy, [10]INFORMAPRO Srl, Rome, Italy, [11]EURESIST Network GEIE, Rome, Italy, [12]Department of Informatics, Bioengineering, Robotics and System Engineering, University of Genoa, Genoa, Italy, [13]Infectious Disease Department, USL SUDEST, Toscana, Misericordia Hospital, Grosseto, Italy

Background: The rise of HIV-1 drug resistance to non-nucleoside reverse-transcriptase inhibitors (NNRTIs) threatens the long-term success of antiretroviral therapies. Our study aims to describe the circulation of major resistance-associated mutations (RAMs) for NNRTI in both naïve and treatment-experienced PLWH (People Living with HIV) in Italy from 2000 to 2020 and to investigate their predictors.

Material and Methods: We retrieved HIV-1 RNA protease/reverse transcriptase sequences, demographic, and clinical data of adult PLWH from the ARCA database. TDR (Transmitted Drug Resistance) and PDR (Pre-treatment Drug Resistance) were defined as the presence of at least one mutation from the Stanford updated lists.

Results: We included 5982 naïves: 73.9% were males, median age was 39 (IQR 32-47), 67.9% were Caucasian. Median time since HIV diagnosis was 3.14 weeks (0.86-41.93), nadir CD4 cells count 326 cells/µl (159-495), and zenith HIV-1 RNA (viral load, VL) 4.8 log10 copies/mL (4.3-5.4), 72.3% carried subtype B. TDR was found in 12.5% and declined from 17.3% in 2000-2003 to 10.9% in 2016-2020 (p=0.003). All NNRTIs were fully active in >85% according to genotypic susceptibility score (GSS). Predictors of TDR were viral subtype B (vs. non B, aOR 1.94, p <0.001), zenith VL (per 1 log10 higher, aOR 0.86, p=0.013), nadir CD4 cells count (per 100 cells/µl increase, aOR 0.95, p=0.013). We retrieved 28505 genotypes from 9387 treatment-experienced PLWH: 67.6% from males and 64.4% from Caucasians, median age was 43 (IQR 37-49). Median time since HIV diagnosis was 136.7 months (65.1-213.1), nadir CD4 cells count 154 cells/µl (52-282), and CD4 cells count at genotype was 349.5 cells/µl (192-543). Median zenith VL was 5.13 log10 copies/mL (4.50-5.62), and VL at genotype was 3.6 log10 copies/mL (4.5-5.6); 80.8% carried viral subtype B. At least one PDR for NNRTI was detected in 33.2%, and PDR declined from 43.4% in 2000-2003 to 20.9% in 2016-2020 (p<0.001). Cumulative (c)GSS fully active ranged from 58.8% for nevirapine (lowest cGSS), to 68.7% for doravirine (highest cGSS). Predictors of PDR were sexual transmission route (aOR 0.779, p<0.001), time since HIV diagnosis (per 1 month longer, aOR 1.002, p<0.001), viral subtype B (vs. non B, aOR 1.37, p<0.001), VL (per 1 log10 higher, AOR 1.12, p<0.001), CD4 nadir (per 100 cells/µl increase, aOR 0.91, p<0.001), previous exposure to any NNRTI (aOR 2.31, p<0.001) and a more recent calendar year sequence (any span time >2008 vs. 2000-2003, any aOR<1, p<0.001).

Conclusions: RAMs to NNRTIs circulation declined during the last 20 years in Italy. Viral subtype B, higher VL, and lower CD4 cells count were associated with a higher rate of resistance both in naïve and treatment-experienced PLWH. NNRTIs remain pivotal drugs for the management of HIV-1 due to safety concerns and long-acting options.

HIV and SARS-CoV-2: from in vivo to in vitro

OP 104 SOTROVIMAB-EMERGENT RESISTANCE IN IMMUNOCOMPROMISED COVID-19 PATIENTS

F. Novazzi[1,2], D. Focosi[3], F. Drago Ferrante[1], S. Boutahar[1], A. Genoni[1], F. Dentali[2], D. Dalla Gasperina[2], A. Baj[1,2], F. Maggi[1,2]

[1]Laboratory of Microbiology, ASST SetteLaghi, Varese, Italy, [2]Department of Medicine and Surgery, University of Insubria, Varese, Italy, [3]North-Western Tuscany Blood Bank, Pisa University Hospital, Pisa, Italy

Background: The monoclonal antibody (mAb) Sotrovimab is used under the emergency authorization for the treatment of patients at risk for severe COVID-19 progression. Sotrovimab can neutralize all sarbecoviruses, including SARS CoV-2, by binding to a highly conserved epitope within the receptor-binding domain. However, its use, as well as of other SARS CoV-2–specific mAbs, warrants caution being frequent in the development of mutations that confer viral resistance.

Material and Methods: 46 patients were treated with Sotrovimab at the ASST Settelaghi (Varese, Italy) during the B.1.1.529 (Omicron) variant outbreak between January and March 2022. From 15 (32.6%) of these patients, two nasopharyngeal swabs (NPS) were obtained just before the mAb infusion, and on day 10 post-therapy. The presence of SARS CoV-2 RNA was evaluated by the real-time Alinity mSARS-CoV-2 Assay (Abbott). Positive NPS with cycle thresholds (Ct) < 25 were assayed by next-generation sequencing (NGS) of the whole SARS CoV-2 genome on the Miseq platform (Illumina). Genomic analysis was performed by the software platform BaseSpace Sequence Hub (Illumina).

Results: Of the 15 outpatients, 12 (80%) had persistently positive PCR at day 10, while 3 patients resulted in SARS COV-2 RNA negative. Nine of 12 positive samples harbored virus levels at day 10 with Ct < 25, and thus they were furtherly analyzed by whole-genome NGS. Although all the sequenced samples resulted infected by the same Omicron BA.1 VOC, consecutive NPS from 2 subjects revealed Sotrovimab treatment-emergent E340D at genomic analysis (Table 1). Case 1 was a 51-years old HIV-positive female with cerebral toxoplasmosis, and Case 2 was a 43-years old male kidney transplant recipient. The analysis of Omicron sequences deposited in GISAID on March 28, 2022, revealed that E340D mutation was present in only 732 out of 2,390,087 sequences[1]. Notably, mutations at position S:E340K/A/V have been associated with a significant reduction in neutralization by Sotrovimab.

Conclusions: Our data show that SARS CoV-2 RNA persists for at least 10 days in a significant number of Sotrovimab-treated patients and that the appearance of drug-induced mutations is a relatively frequent event. Overall, the findings underscore the importance of mAbs stewardship, particularly because Sotrovimab is one of the few mAbs with retained activity against the B.1.1.529 variant. Genomic surveillance of patients receiving mAbs for the SARS-CoV-2 treatment is essential to minimize the risk of both treatment failure and transmission of potentially resistant SARS-CoV-2 variants in the health care settings and community[2].

References

[1]Outbreak.info Variants | Lineage Mutation Tracker. Accessed at https://outbreak.info/situation-reports on March 28, 2022

[2]Focosi D, Maggi F, et al. Analysis of Immune Escape Variants from Antibody-Based Therapeutics against COVID -19: A Systematic Review. International journal of molecular sciences. 2022;23(1):29.

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HIV and SARS-CoV-2: from in vivo to in vitro

OP 105 TENOFOVIR PLASMA AND INTRACELLULAR PHARMACOKINETICS IN INSTI-BASED REGIMENS

M. Ferrara[1], G. Accardo[1], S. Fantino[1], G. Trevisan[1], F. Alladio[1], E. Drappero[1], M. Tettoni[1], E. De Vivo[2], A. Ianniello[2], J. Mula[2], A. De Nicolò[2], A. D'Avolio[2], G. Di Perri[1], A. Calcagno[1], S. Bonora[1]

[1]Unit of Infectious Diseases, Department of Medical Sciences, University of Torino, Torino, [2]Laboratory of Clinical Pharmacology and Pharmacogenetics, Department of Medical Sciences, University of Torino, Torino

Background: Tenofovir (TFV) as tenofovir alafenamide (TAF), associated with Emtricitabine (FTC), is the backbone of most 3 drugs regimens while Integrase inhibitors (INSTIs) are considered the standard of care as third agents. Scarce data on TFV intracellular (IC, intra-PBMC) accumulation are reported in literature. Therefore, our aim was to evaluated TFV plasma and IC pharmacokinetics (PK) when dosed with bictegravir (BIC) or dolutegravir (DTG) as third drug in the clinical setting.

Methods: Patients (pts) administered with TAF/FTC/BIC as single tablet regimen (STR) and TAF/FTC plus DTG were included, after informed consent given. Plasma and IC TFV-DP concentration as Ctrough were measured by means of UHPLC-MSMS validated method at the end of dosing interval (24+/-4 hours after intake). Non-compartmental PK parameters were expressed as geometric mean (CI95%). Pts characteristics were compared by Mann-Whitney and Spearman's test, as appropriate.

Results: 86 pts were included in the study: 61 on BIC/TAF/FTC and 25 DTG+TAF/FTC. 83% of them were male, age and BMI were 51 years (48-53) and 26.3 Kg/m2 (22.8-29.8). Geometric mean TFV plasma Ctrough plus BIC and DTG resulted to be respectively 14.9 (13.3-16.6) and 10.7 (7.8-13.6) ng/mL (p=0.002). TFV IC Ctrough resulted to be 623.7 (478.7-768.8) and 263.2 (192.7-333.7) ng/mL (p<0.001), and TFV IC/plasma ratio 44.7 (35.0 -54.5) and 27.4 (20.5-34.3) (p=0.040). In total population linear and significative correlation was reported between TFV plasma and IC Ctrough (0.439, p<0.001) and between TFV plasma Ctrough and age (0.432, p<0.001), creatinine (0.380, p=0.001) and inverse with eGFR (-0.453, p<0.001). No difference by gender or correlation with BMI was observed. TFV IC Ctrough (p=0.025) was found to be higher in pts with undetectable viral load.

Conclusions: TFV plasma exposure was found to be higher when dosed with BIC as compared to DTG, with an increase by 46% with BIC and by 5% with DTG as compared to previous data and concomitantly TFV-DP accumulation in PBMCs was different in two groups. These data could suggest impact of adherence (STR vs 2-pill regimens) or saturability of IC metabolism. Further studies are warranted.

HIV and SARS-CoV-2: from in vivo to in vitro

OP 106 POTENT ANTIVIRAL ACTIVITY OF NEW GENERATION HIV-1 MATURATION INHIBITORS ON HUMAN PRIMARY CELLS

L. Duca[1], P. Saccomandi[1], L. Piermatteo[1], R. Salpini[1], C. Stacchiotti[1], S. Aquaro[2], C.F. Perno[3], V. Svicher[1], F. Ceccherini-Silberstein[1]

[1]Università degli Studi di Roma Tor Vergata, Dipartimento di Medicina Sperimentale, Roma, Italia, [2]Università della Calabria, Dipartimento di Farmacia e Scienze della Salute e della Nutrizione, Arcavacata di Rende (CS), Italia, [3]Ospedale Pediatrico Bambino Gesù, Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) Roma, Italia

Background: Drug resistance emergence can seriously affect the effectiveness of anti-HIV therapy, highlighting the need of new drug classes. Among them, maturation inhibitors (MIs), targeting gag-pol cleavage sites, represent a new promising approach. Here, we evaluated the antiviral activity of new generation MIs against HIV-1 wild type (wt) and mutated viral strains in human primary cells.

Material and methods: Monocyte-derived macrophages (MDM) and PBMC-derived lymphocytes were infected with wt CCR5-tropic 81A and CXCR4-tropic NL4-3 laboratory viral strains, respectively. Lymphocytes were also infected with four gag-mutated NL4-3 strains (A364V, V370A, V370Δ and V362I+V370A) known to confer resistance to the first generation MI Bevirimat (BVM).

Four compounds (provided by ViiV Healthcare), defined as MI-1, MI-2, MI-3 and MI-4 were tested at different concentrations (1000nM, 100nM, 10nM, 1nM). BVM was used as a control. Antiviral activity was assessed by quantifying p24 protein in supernatants by ELISA at 7 (for lymphocytes) or 14 (for MDM) days after infection. EC50 was assessed for wt (EC50-wt) and mutated viruses (EC50-mut). Fold change (FC) resistance values were defined as ratio of EC50-mut/EC50-wt.

Transmission electron microscopy (TEM) was used to visualize mature/immature viral particles in presence/absence of tested MIs.

Results: In lymphocytes, all tested MIs showed a good antiviral activity against wt, with MI-1 and MI-2 having an EC50 significantly lower ($p<0.002$) than BVM (EC50 20.38±0.59nM for BVM vs 2.03±0.55nM for MI-1, 3.31 ±0.78nM for MI-2, 37.57±26.78nM for MI-3, 36.51±31.40nM for MI-4). As expected, BVM showed no activity against NL4-3 gag-mutants with high level resistance observed for A364V and V362I+V370A (FC resistance: >500 for both).

Conversely, the antiviral activity of MIs was not significantly affected by V370Δ (FC resistance: <2). Similarly, the antiviral activity of MI-3 and MI-4 was not reduced at all by A364V, V370A and V362I+V370A (FC resistance: ~1). A low level resistance was observed for MI-1 and MI-2 showing 12.2, 3.3 and 3.4 and 4.4, 8.3 and 1.8 FC resistance for A364V, V370A, V362I+V370A, respectively.

Furthermore, all MIs showed a good antiviral activity also in 81A-infected MDM with EC50 lower than BVM (23.89 ±14.26nM for BVM vs 4.61±0.40nM for MI-1, 9.26±9.41nM for MI-2, 19.85±3.46nM for MI-3, 3.57±1.96nM for MI -4).

Finally, by TEM, treatment with different MIs determined an intracellular accumulation of immature viral particles more marked than that observed for untreated 81A-infected MDM, compatible with the inhibited processing of gag polyprotein (Fig. 1).

Conclusions: These results highlight a potent antiviral activity of new MIs against both wt and tested gag-mutated viruses, higher than BVM. The capability of these compounds to suppress HIV replication in both lymphocytes and MDM supports the role of MIs as promising new class of antiretroviral drugs.

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HIV and SARS-CoV-2: from in vivo to in vitro

OP 107 EVALUATION OF THE IN VITRO COMBINATORIAL ACTIVITY OF IBALIZUMAB AND HIV-1 ANTIVIRALS

F. Giammarino, N. Bartolini, L. Fiaschi, F. Dragoni, I. Vicenti, M. Zazzi, F. Saladini

Department of Medical Biotechnologies, University of Siena, Italy

Background: Ibalizumab (IBA) is the first humanized IgG4 monoclonal antibody targeting CD4 receptor recently approved for the treatment of multi-drug resistant HIV-1 infection in adult individuals. Given the importance of the selection of companion drugs in salvage therapy, in this study we aimed to evaluate the in vitro combinatorial activity of IBA together with licensed or investigational antiretrovirals.

Methods: The combinatorial effect of IBA with either tenofovir alafenamide (TAF, NRTI), lamivudine (3TC, NRTI), etravirine (ETR, NNRTI), darunavir (DRV, PI), dolutegravir (DTG, INSTI), temsavir (TMV, AI) or lenacapavir (LEN, CI) was evaluated in a checkerboard assay. MOLT4-CCR5+ cells were infected with the wild-type NL4-3 strain and exposed to a 6x6 drug concentration matrix for 8 days, then the supernatants were used to infect reporter TZM-bl cells. The matrix including the combination of IBA plus IBA was used as control of additive activity. Luminescence values were normalized to calculate the percentage of inhibition of viral replication and elaborated with the SynergyFinder2.0 software. Synergy scores were determined as the mean of at least two replicates and were calculated with ZIP, Bliss, Loewe and HSA models. Values <-10, from -10 to 10 and >10 were likely associated with antagonism, additive effect, and synergy between drugs, respectively.

Results: Globally, all the drugs tested in combination with IBA were predicted to have additive or synergistic activity independently by the synergy model (Table 1). The combinations IBA+ETR, IBA+LEN and IBA+DTG were associated with stronger synergistic effects as determined by all models, while the values calculated with IBA +DRV, IBA+TAF, IBA+TMV and IBA+3TC were mostly predictive of additive activity. The effect of control combination IBA+IBA were correctly identified as additive with all models, resulting in an average synergy score close to zero.

Conclusions: These preliminary data suggest that IBA positively interacts with other antivirals against the replication of the wild-type HIV-1 NL4-3 strain, irrespective of the drug class.

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Acute COVID-19 and post COVID-19 syndrome

OP 108 LONG-COVID SYNDROME DATA FROM 126,752 PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

F. Di Gennaro[1], A. Belati[1], O. Tulone[2], L. Diella[1], D.F. Bavaro[1], R. Bonica[2], V. Genna[2], L. Smith[3], M. Trott[3], M. Barbagallo[2], L.J. Dominguez[1], N. Veronese[2], A. Saracino[1]

[1]Department of Biomedical Sciences and Human Oncology, Section of Infectious Diseases, University of Bari, Bari, Italy, [2]Geriatric Unit, Department of Internal Medicine and Geriatrics, University of Palermo, Palermo, Italy, [3]Faculty of Sport Sciences, University of Murcia, Murcia, Spain

Background: The number of people living with long-COVID is actually unknown. Different types of studies, including national surveys and patient-led studies, have been used to quantify the prevalence of long-COVID worldwide, but a comparison among them is challenging. Based on the WHO definition, considering long-COVID as a condition that persists 3 months from the onset of COVID-19, a systematic review and metanalysis about its incidence and main patient symptoms was performed.

Methods: A systematic search in several databases using the words “COVID-19” or “Novel Coronavirus–Infected Pneumonia” or “2019 novel coronavirus” or “2019-nCoV” or “SARS-CoV-2” and “lingering symptoms” or “persistent symptoms” or “long-term symptoms” or "long-term COVID" or “long-COVID” or “long-term” or “long term” or “long” was performed in several databases until the 12th of January 2022. All observational studies reporting the incidence rate of long-COVID signs and symptoms, divided according to the organ system involved, were enrolled. Reviews, letters, case reports and meta-analysis were excluded.

Results are reported as incidence rate [95% confidence interval (CI)]. Several sensitivity and meta-regression analyses were also performed.

Results: A total of 11,167 articles were initially evaluated. Of these, 4,059 were duplicates and were eliminated. Of the remaining 7,108 initially screened, 6,762 were excluded, based on information in the abstract. Of the 346 remaining articles, 140 were excluded: 91 were not about long-COVID, 18 were letters, 11 were reviews, and 20 were out of scope. At the end, 206 articles were included, for a total of 208 cohorts and 126,752 patients (mean age: 54.4 years; 48.8% females). The median time of follow-up was 6 months. All symptoms and their incidence are showed in Table 1. Overall, 56.9% of patients (95% CI: 52.2-61.6) presented at least one symptom of long-COVID. General symptoms, including fatigue, pain and myalgias, were the most frequently reported (31%), while digestive issues were the less frequent (7.7%).

By performing the meta-regression, female sex was associated with higher incidence of long-COVID (B=0.02, p=0.047) particularly of general, neurological and cardiovascular long-COVID symptoms (B=0.02, p= 0.05; B=0.003, p=0.001; B=0.003, p=0.001 respectively), whilst a higher mean age was associated with higher incidence of psychiatric (B=0.003, p=0.007), respiratory (B=0.004, p=0.009) general (B=0.004, p=0.03), digestive (B=0.002, p=0.04), and skin conditions (B=0.002, p=0.02). Interestingly, being hospitalized and/or having a critical COVID-19, and stay in intensive care unit, were not related with a higher incidence of long-COVID.

Conclusions: The incidence of long-COVID is higher than expected, independently of the severity of the primary infection. Therefore, a multi-disciplinary approach should be adopted, developing appropriate preventive and therapeutical measures in order to better manage patients with long-COVID.

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Acute COVID-19 and post COVID-19 syndrome

OP 109 POST-ACUTE SEQUELAE OF COVID-19 (PASC): AN ITALIAN EXPERIENCE

P. Pasculli[1], M.A. Zingaropoli[1], F. Ciccone[1], F. Paribeni[1], R. Merz[1], F. Dominelli[1], G. Siccardi[1], S. Pellegrini[1], G. Galardo[2], C.M. Mastroianni[1], M. R. Ciardi[1]

[1]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy, [2]Medical Emergency Unit, Sapienza, University of Rome, Policlinico Umberto I, Rome, Italy

Background: The long-term symptomatology of COVID-19 has yet to be comprehensively described. Most patients recover entirely within a few weeks, others referee persistent long-term symptoms, known as post-acute sequelae of SARS-CoV-2 (PASC). The aim of the study was to describe persistent COVID-19 symptoms in a cohort of hospitalized (in-patients) and home-isolated patients (out-patients) in Rome, Italy, in order to assess the most appropriate interdisciplinary approach to the future COVID-19 patients worldwide.

Methods: At Policlinico Umberto I Hospital, Rome, Italy, a retrospective study was conducted on post-COVID-19 patients. Age, gender, ethnicity, and laboratory findings were extracted from electronic medical records. Long-term sequelae were identified as symptoms persisting for a mean of 90-days after discharge. Patients were tested for total anti-spike IgG antibodies to SARS-CoV-2. Patients were divided into hospitalized (in-patient) and home-isolated (out-patient) patients. In-patients were evaluated at two time-points: during hospitalization (T0) and during the post-COVID visit (Tpost).

Results: Three hundred and sixty-four COVID-19 patients (152 females/212males; median age [interquartile range, IQR] of 57.2 [49-86] years) were enrolled. More than half of the patients (238/364) had at least one comorbidity. Over two thirds of the patients (304/364) were admitted to hospital for COVID-19, others managed at home. Patients were assessed at post-COVID follow-up at a mean of 90.7 (SD, 13.6) days after the onset of their first COVID-19- symptom. To date, 73 patients (20.1%) were completely cured, while 291 patients (79.9%) reported persistence of one or more long-term COVID-19-related symptoms or the onset of new one. The more often reported were fatigue (129/291, 44.3%), dyspnea (124/291, 42.6%), non-restorative sleep (73/291, 25.1%), cardiovascular symptoms (66/291, 22.7%), neurological symptoms (49/291, 16.8%). All these patients referred a relative worsening in their quality of life. Among in-patients the most frequent symptoms were fatigue and dyspnea, out-patients reported more non-restorative sleep and fatigue. SARS-CoV-2 IgG resulted negative in 2.9% of patients. At Tpost, the longitudinal evaluation showed a complete recovery of lymphocyte absolute count and a significant decrease of inflammatory markers, such as ferritin, D-dimer, LDH, C-reactive protein (CRP), VES, compared to T0. Only plasma IL-6 values remained elevated at Tpost.

Conclusion: Long-term sequelae are present in a remarkable number of post-COVID-19 patients, both hospitalized and not-hospitalized patients, and pose a new challenge to the healthcare system in order to identify long-lasting effects and improve patients' wellbeing. Multi-disciplinary teams are crucial to develop preventive measures, and clinical management strategies. Finally, SARS-CoV-2 seroprevalence survey is useful for public health management purposes to optimize vaccination campaigns.

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Acute COVID-19 and post COVID-19 syndrome

OP 110 A MULTIDISCIPLINARY MODEL TO SCREEN AND TREAT THE POST-COVID-19 SYNDROME

N. Squillace[1], V. Cogliandro[1], E. Rossi[2], G. Bellelli[3,9], G. Foti[4,9], M. Pozzi[4], F. Luppi[5,9], M. Lettino[6], M.G. Strepparava[7,9], C. Ferrarese[8,9], E. Pollastri[1], A. Rugova[1], E. Ricci[10], P. Bonfanti[1,9] for the STORM Long-COVID Team

[1]Infectious Disease Unit, San Gerardo hospital, ASST-Monza, Italy, [2]Bicocca Center of Bioinformatics, Biostatistics and Bioimaging, University of Milano-Bicocca, Monza, Italy, [3]Acute Geriatric Unit, San Gerardo hospital, ASST-Monza, Italy, [4]Anesthesia and Intensive Care Unit, San Gerardo hospital, ASST-Monza, Italy, [5]Respiratory Disease Unit, San Gerardo hospital, ASST-Monza, Italy, [6]Cardiology Division, San Gerardo Hospital, ASST-Monza, Monza, Italy, [7]Department of Mental Health, Clinical Psychology Unit, San Gerardo Hospital, ASST-Monza, Monza, Italy, [8]Neurology Unit, San Gerardo hospital, ASST-Monza, Italy, [9]School of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy, [10]Fondazione ASIA

Background: Since March 2020, SARS-CoV-2 was responsible for about 5 million infections in Italy (COronaVIrus Disease 2019, COVID-19). The burden of post-acute COVID-19 syndrome (PCS) is still unknown.
To evaluate the frequency and type of PCS, we proposed a multidisciplinary approach. Patients discharged from hospital during the first two pandemic waves were contacted and invited to undergo an evaluation by a team, composed by an infectious disease specialist, a pneumologist, a geriatrician, an intensivist, a psychologist, a cardiologist, and a haematologist. Our aim was to optimize the patients' management, investigating all potentially detrimental sequelae of COVID-19.
Methods : We included patients aged ≥18 years with hospital admission for confirmed SARS-CoV-2 infection. Symptoms were grouped in five macro categories for reasons of clinical homogeneity, hereafter referred to as "disorders": respiratory disorders (dyspnoea or cough), neurological disorders (peripheral neuropathies, headache, impaired mobility, behavioural disorders), psychological disorders (sleep disorders, mood disorders), muscular disorders (arthromyalgia, asthenia), other symptoms (fever, alopecia, diarrhoea, weight loss, smell and taste alterations, sexual dysfunctions). Disorders were evaluated at discharge and at follow-up.
Association between patients' characteristics and presence of disorders at follow up was estimated by a logistic multivariable regression model.
Results: From June 2020 to July 2021, we followed up 361 patients: 128 (35.5%) who were previously admitted to Intensive Care Unit (ICU) and 233 patients to ordinary department. The median length of hospital stay was 20 days (Inter-Quartile-Range 13-32). Complete clinical characteristics are depicted in Table 1.
Most patients (317/361, 87.8%) were still symptomatic at discharge, with one third referring three or more disorders. At follow up, 67.3% (243/361) of patients still complained at least one disorder already present at discharge (See figure 1). Moreover, 159 patients (44%) developed at least one new disorder during follow up: 116 (72.9%) one disorder, 39 (24.5%) two disorders, 4 (2.5%) three or more disorders. At follow up visit 130 of 361 (36%) were still with disorders developed after discharge. At multivariable analysis presence of any disorders at follow-up was associated with male gender (Odds Ratio [OR] 3.23, Confidence Interval [CI] 95% 1.46-7.15), ICU admission (OR 2.78, CI 95% 1.29-5.96) and presence of disorders at discharge (OR 14.39, CI 95% 6.41-32.32).
Conclusions: In our sample, we found that symptoms of PCS are highly variable and fluctuating over time.
PCS was associated with COVID-19 severity and its presence was retrieved in patients both with and without disorders at discharge, underlining the advisability of our multidisciplinary approach.
About 50% of patients developed a new disorder during follow up

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Acute COVID-19 and post COVID-19 syndrome

OP 111 LONG TERM COMPLICATIONS OF COVID-19 IN PATIENTS HOSPITALIZED IN CLINICA MALATTIE INFETTIVE, OSPEDALI RIUNITI, ANCONA

B. Candelaresi, S. Mazzanti, L. Brescini, V. Barocci, M. Di Pietrantonio, P. Mantini, S. Olivieri, F. Pallotta, F. Ginevri, G. Cesaretti

Clinica Malattie Infettive, Ospedali Riuniti, Ancona

Background: “Long COVID” is a term used to describe symptoms and signs that persist or appear after recovery from SARS-CoV-2 acute infection.

Materials and Methods: In this prospective and monocentric study, we monitored 196 patients with severe SARS-CoV-2 interstitial pneumonia that required mechanical ventilation (both invasive or not-invasive). The follow up was scheduled at 1 month, 3 months and 6 months after the discharge from our clinic. At each follow up, we performed a detailed collection of clinical history, physical examination, blood tests and lung ultrasound. Some patients underwent a pulmonary function evaluation (chest-imaging, spirometry) and a cardiological assessment (ECG, echocardiography).

Results: Most symptoms were present after the 1st month, followed by a decrease in the next months. The percentage of patients reporting dyspnea on exertion, cough, asthenia, myalgia and arthralgia, decreased during the complete follow-up period, but they were reported with more frequence than other symptoms; so, they can be considered the long COVID most relevant consequences. Paresthesias were reported constantly; other symptoms like hair loss, psychic and cognitive alterations were reported more frequently at 3 months, while dizziness, hearing and view alterations are characterized by a later onset (more reported at 6 months). At the end of the follow up period we observed in most patients persistant anemia, high level of inflammation index (C-reactive protein, d-dimerus, fibrinogen and IL-6) and lipidic profile alteration (increase of LDL levels, decrease of HDL and increase of triglycerides).

During the 6 months, lung ultrasound showed a decrease in the number of patients who presented interstitiopathy signs (B lines).

In patients evaluated with radiography or tomoscintigraphy, chest imaging showed an almost complete resolution of the lung inflammation in 37% of patients, in 44% a reduction of the inflammation, in 19% was observed initial lung fibrosis.

At 6 months after discharge, in 31% of patients we observed abnormality in lung function (evaluated with spirometry): in 24% it was the decrease of the diffusion capacity of the lungs for carbon monoxide, and in 15% the identification of a restrictive deficit.

Of the 96 patients who underwent a cardiological assessment, in 55 we found cardiological abnormalities: pre existing diseases (like chronic ischemic cardiopathy, valvular stenosis or insufficiency), arrythmias, diastolic disfunction, ipertensive cardiopathy and myopericarditis.

Conclusions: In the COVID era it’s necessary to perform an accurate post-COVID multidisciplinary follow-up, to early identify patients who need monitoring and, if necessary, a treatment, also in patients with SARS-CoV-2 infection who weren’t hospitalized. Our future aim is to extend the follow-up period to 12 months and to investigate possible difference between the features of long covid caused by different SARS-CoV-2 variants.

Acute COVID-19 and post COVID-19 syndrome

OP 112 OUTCOME OF PATIENTS WITH CHRONIC LIVER DISEASE HOSPITALIZED FOR SARS-COV-2: A SINGLE CENTRE MATCHED COHORT

M. Ranzenigo[1], C. Bertoni[1], D. Ceccarelli[2], L. Galli[2], E. Messina[2], H. Hasson[2], A. Siribelli[2], R. Lolatto[2], A. Castagna[1,2], C. Uberti-Foppa[1,2], G. Morsica[2]

[1]Vita-Salute University, Milan, Italy, [2]Dept. of Infectious Diseases, San Raffaele Hospital, Milan, Italy

Background and Aim: Coronavirus-2 (SARS-CoV-2) infection poses a major health threat to healthy individuals and those with comorbidities, but its impact on patients (pts) with preexisting chronic liver diseases (LD) remains elusive. In the present study we aimed to evaluate the impact of SARS-CoV-2 infection on the clinical outcome of patients with LD.

Methods: This retrospective single center study consists of pts with a confirmed acute SARS-CoV-2 infection hospitalized at the San Raffaele Hospital, Milan, Italy between 25, February 2020 and 12, June 2021; patient's data were extracted from the COVID-BioB clinical database of the San Raffaele Hospital. The outcomes were mortality, differences in laboratory characteristics, in pts with LD vs those with no-LD. A 1:3 propensity score matching analysis was performed to match patients with LD to those with no-LD; the variables considered were: age, sex, body mass index (BMI), diabetes mellitus (DM), hypertension. Predictors of mortality were assessed using multivariate logistic regression model. A two-sided P value <0.05 was considered statistically significant. All analyses were performed with software R version 4.1.2.

Results: We identified 1210 pts with a diagnosis of SARS-CoV-2: 41 pts with LD and 1169 with no-LD. Patients' characteristics at hospital admission before and after matching are summarized in Table 1. Briefly, in matched groups LD patients had worse ALP, GGT, PTs, PTINR, lower platelets count and c-reactive protein respect to no-LD group. Duration of hospitalization was of 16 (IQR 9-25) days [LD group: 17 (IQR 8-30) days; no-LD group: 15 (IQR 9-25) days; p=0.455].

At hospital discharge/death, LD pts compared to no-LD pts showed a different chemistry profile: LD group had worse PTINR and PTs: 1.12 [1.06;1.31] vs 1.08 [1.02;1.14] P= 0.012 and 14.6 [13.9;17.1] vs 14.1 [13.4;14.9] respectively, P=0.011; higher AST and GGT levels: 35.0 U/mL (25.0-86.0) vs 28.0 U/mL(21.0-45.0) P=0.007 and 70.0 U/mL (32.8-134) vs 35.0 U/mL (22.0-70.8) respectively, P=0.003; higher bilirubin values: 0.60 mg/dL(0.46 -1.21) vs 0.46 mg/dL (0.36-0.65) P=0.004 and lower platelets count =205 x109/L(103-248) vs 250 x109/L (183 -330) P=0.001. At multivariate analysis, the risk of death was associated with LD [OR= 4.04(95%CI =1.29-12.70) P=0.017] as well as older age [OR=1.15 (95%CI=1.07-1.23) P<0.0001] male sex [OR=6.41 (95% CI=1.64-25.0) P=0.007] and higher creatinine levels [OR (per 0.3 mg/dL increase)=1.56 (95%CI=1.20-2.04) P=0.001].

Conclusions: Patients with LD are at higher risk of mortality. Poor outcome was observed to be also related to older age, male sex and worse creatinine levels. Intensive surveillance and timely diagnosis are essential in high risk patients because early intervention as a complement to vaccination may reduce hospitalization and death associated with SARS-CoV-2 disease.

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Acute COVID-19 and post COVID-19 syndrome

OP 113 CHARACTERIZATION OF THREE WAVES OF COVID 19 OCCURRING IN SOUTHERN ITALY: RESULTS OF A MULTICENTRE COHORT STUDY

V. Pattapola[1], M. Pisaturo[1], P. Maggi[2], A. Russo[1], R. Astorri[1], F.G. Numis[3], I. Gentile[4], V. Sangiovanni[5], V. Esposito[6], R. Punzi[7], G. Calabria[8], C. Rescigno[9], A. Salomone Megna[10], A. Masullo[11], E. Manzillo[12], G. Russo[13], R. Parrella[14], G. Dell'Aquila[15], M. Gambardella[16], A. Ponticiello[17], N. Coppola[1] on behalf of CoviCam group

[1]Infectious Diseases, Department of Mental Health and Public Medicine, University of Campania "L.Vanvitelli", Napoli, Italy, [2]Infectious Diseases Unit, A.O. S Anna e S. Sebastiano Caserta, Italy, [3]Emergency unit, PO Santa Maria delle Grazie, Pozzuoli, Italy, [4]Infectious disease unit; University Federico II, Naples, Italy, [5]Third Infectious Diseases Unit, AORN dei Colli, P.O. Cotugno, Naples, Italy, [6]IV Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [7]Hepatic Infectious Disease Unit, AORN dei Colli, PO Cotugno, Naples, Italy, [8]IX Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [9]First Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [10]Infectious Diseease Unit, A.O. San Pio, PO Rummo, Benevento, Italy, [11]Infectious disease unit, A.O. San Giovanni di Dio e Ruggi D'Aragona Salerno, Italy, [12]VIII Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [13]Infectious Disease Unit, Ospedale Maria S.S. Addolorata di Eboli, ASL Salerno, Italy, [14]Respiratory Infectious Diseases Unit, AORN dei Colli, PO Cotugno, Naples, Italy, [15]Infectious Diseases Unit, AO Avellino, Italy, [16]Infectious Diseease Unit, PO S. Luca, Vallo della Lucania, ASL Salerno, Italy, [17]Pneumology Unit, AORN Caserta, Italy

Objectives: to evaluate the clinical characteristics of patients hospitalized for Covid 19 during the first second and third waves.

Methods: The SIMIT Campania group conducted a multi-centric, observational, retrospective study involving nine COVID-19 units from 7 cities in Campania, Italy. The study population includes hospitalized patients aged ≥ 18 years with SARS-CoV-2 infection confirmed by RT-PCR on nasopharyngeal swab, symptomatic patients and asymptomatic carriers. The enrollment coincided with the beginning of the pandemic, from February 28, 2020 to July 31, 2021.

Preliminary results: 1703 patients were enrolled. The demographic and clinical characteristics of patients are shown in Table 1. Subjects were predominantly male during all three waves (71.48% vs 61.23% vs 61.10%). First wave patients had a higher mean age than second and third wave patients 69.11 vs 62.37 vs 62.52 (P=0.003). During the first-wave the number of healthcare workers hospitalized for SARS COV2 was greater than in the second and third waves: 18.57% vs 0.97% vs 0.14%; p<0.00001 respectively. The mean of the Charlson comorbidity index was 3.11 in the first-wave, in the second wave 3.26 and the third wave 2.73 p<0.00001: Hypertension was present more in the third wave than in the second and first, 49.78% 45.68% and 44.28% respectively(p=0.317); cardio-vascular diseases, showed a higher prevalence in the first wave than in the second and third, 32.85%, 30.88% and 27.01% respectively (p=0.129). Hospitalized patients with previous diagnosis of type II diabetes mellitus were greater in the second than in the first and the second waves,23.11%, 18.57% and 18.52% respectively (p=0.064). Patients did show severe outcomes in the first wave than in the second and the third waves, 78.57%, 34.58% and 28.28% respectively. Similar data is found by analyzing mortality as well showing higher rates in the first wave than in the second and third waves: 74.28%, 11.44% and 28.99% respectively (p=0.000).

Conclusions: In the literature there are few data available on the clinical characteristics of Covid19 patients stratified in the three waves so we think that the preliminary data of this study can help us to have a better knowledge of an infectious disease that continues to surprise us.

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Immunological efficacy of COVID-19 vaccination in vulnerable populations

OP 114 TNF-ALFA EXPRESSION IS NEGATIVELY CORRELATED TO SEROCONVERSION AFTER SARS-COV-2 MRNA BNT162B2 VACCINE IN LUNG TRANSPLANT PATIENTS

M. Guardiani[1], M.A. Zingaropoli[1], F. Cogliatti-Dezza[1], A. Centofanti[2], C. Carillo[2], E. Tortellini[1], F. Dominelli[1], A. Napoli[3], A. Gaeta[1], F. Venuta[2], M. Lichtner[1,4], M.R. Ciardi[1], C.M. Mastroianni[1], G. Russo[1]

[1]Department of Public Health and Infectious Diseases, Sapienza University of Rome, [2]Department of General and Specialistic Surgery "Paride Stefanini", Sapienza University of Rome, [3]Department of Molecular Medicine, Sapienza University of Rome, [4]Infectious Diseases Unit, Santa Maria (SM) Goretti Hospital, Sapienza University of Rome, Latina

Background: Vaccination campaign to contrast the impact of SARS-CoV-2 has raised the issue of vaccine immunogenicity in frail populations. The aim of the study was to explore the humoral and T-cell responses in lung transplant (LuT) patients before (T0) and after the third dose (Tpost) of mRNA BNT162b2 vaccine.

Materials and Methods: LuT patients having completed their vaccine series were included. At T0 and Tpost, by intracellular cytokine flow cytometry assay, upon S peptide libraries stimulation, mono- and polyfunctional specific T-cell responses were evaluated as well as anti-spike (S) antibody titre to SARS-CoV-2. According to humoral response, differences in cell-mediated response were evaluated too. We labelled polyfunctional T cells those cells which simultaneously producing IFNγ, IL2 and TNFα.

Results: Nine LuT patients (2 female/7 male, median age [IQR] of 56[46-62] years) were enrolled. All patients were receiving prednisone and calcineurin inhibitors treatments at vaccination time-points while 67% were treated also with anti-metabolite. Overall, 44% of LuT patients were affected by diabetes, 55% arterial hypertension, 11% dyslipidaemia and 22% cardiopathy. At T0, only 44.4% showed a detected anti-S antibody titre, whereas at Tpost the totality of patients had humoral response (p=0.0294). Also, the longitudinal quantitative evaluation of anti-S antibody titre showed a significant increase compared to T0 (55.3[5.1-31.1] and 4.5[1.9-12.3] binding antibody unit [BAU]/ml, respectively, p=0.0312). According to humoral response at T0, patients were stratified into responders (R, n=4, median [IQR] values: 16.2[8.4-31.7] BAU/ml) and non-responders (NR, n=5, <1.85 BAU/ml). Both R and NR groups showed a specific T cell response upon stimulation. However, significantly higher percentages of polyfunctional CD4+ and CD8+ T-cells in R group compared to NR one was observed (CD4: 0.2[0.1-0.4] versus 0.0[0.0-1.6], respectively, p=0.05; CD8: 0.1[0.7-0.2] versus 0.0[0.0-0.6], respectively, p=0.03).

Finally, at T0, a negative correlation between percentage of CD4 only TNFα+ and anti-S antibody titre was observed (ρ=-0.73 p=0.03) suggesting a detrimental effect of this subpopulation. The longitudinal evaluation of mono- and poly-functional specific T-cell responses showed not significant differences.

Conclusion: This preliminary data showed that after the booster dose, a higher percentage of LuT patients with a humoral response was observed, in which a passive immunization with monoclonal antibody (such as tixagevimab and cilgavimab) seems to be unnecessary. However, in terms of cell-mediated immune response, LuT patients failed to demonstrate responses after 3 months from the second dose of mRNA vaccine as evaluated by their mono- and poly-functional specific CD4+ and CD8+ T-cell responses. Finally, as already shown for other vaccines (such as influenza) the ability to generate a vaccine-specific antibody response is negatively correlated with TNFα.

Immunological efficacy of COVID-19 vaccination in vulnerable populations

OP 115 DIFFERENT SPECIFIC T CELL RESPONSES TO THE THIRD DOSE OF MRNA COVID-19 VACCINE IN MULTIPLE SCLEROSIS PATIENTS UNDER DISEASE-MODIFYING TREATMENTS

F. Dominelli[1], M.A. Zingaropoli[1], M. Tartaglia[2], E. Tortellini[1], M. Guardiani[1], V. Perri[1], P. Pasculli[1], F. Ciccone[1], L. Malimpensa[2], V. Baione[2], A. Napoli[3], A. Gaeta[1], M. Lichtner[1,4], A. Conte[2], C.M. Mastroianni[1], M.R. Ciardi[1]

[1]Dipartimento di Sanità Pubblica e Malattie Infettive, Sapienza, Università di Roma, [2]Dipartimento di Neuroscienze Umane, Centro di Sclerosi Multipla, Sapienza, Università di Roma, [3]Dipartimento di Medicina Molecolare, Sapienza, Università di Roma, [4]Unità di Malattie Infettive, Ospedale S. Maria Goretti/Sapienza Università di Roma, Latina, Italia

Background: Vaccination campaign to contrast the spread of SARS-CoV-2 has raised the issue of vaccine immunogenicity in frail populations, especially multiple sclerosis (MS) patients on disease modifying treatments (DMTs).

Material and Methods: Before (T0) and after 2 months from booster dose of mRNABNT162b2 (Comirnaty®) vaccine (T1), MS patients under DMTs were enrolled. For both T0 and T1, anti-Spike (S) antibody titer as well as IFNγ, IL2 and TNFα T cells production upon S peptide libraries stimulation were assessed. According to DMTs mechanism of action on peripheral blood B and T cells, MS patients were stratified into depleting/sequestering out peripheral blood group (such as fingolimod, which sequestrate T cells into lymphoid tissues, cladribine, ocrelizumab, and alemtuzumab) and sequestering in peripheral blood group (natalizumab, which blocks the extravasation of immune cells in the CNS). “Activated cells” were defined as T cells producing any of IFNγ or IL2 or TNFα while polyfunctional T cells were defined as those simultaneously producing all 3 cytokines. All possible combinations of intracellular expression of IFNγ, IL2, and TNFα in cytokine-producing T cells were evaluated.

Results: 16 MS patients (11 females/5 male, median age [IQR] 38.0[33.5-53.5] years) were enrolled. The longitudinal evaluation of anti-S antibody titers showed an increase at T1 compared to T0 (1930[86-5895] and 199 [80-1140] BAU/ml, respectively, p=0.0017). No differences in the % of “activated” and polyfunctional T-cells were observed (CD4: 0.0[0.0-1.8] and 2.2[1.2-4.5], respectively; CD8: 1.5[0.3-3.5] and 1.9[1.1-2.9], respectively; CD4: 0.0[0.0-0.1] and 0.1[0.0-0.4], respectively; CD8: 0[0.0-0.2] and 0.2[0.0-0.5], respectively). At both T0 and T1, sequestering in peripheral blood group showed higher anti-S antibody titers compared to depleting/sequestering out of peripheral blood group (T0: 871[175-1360] and 100[5-526], respectively, p=0.05; T1: 5410[2655-9893] and 370[50-1975], respectively, p=0.0047). However, evaluating the % of “activated” and polyfunctional T cells no differences were observed. Interestingly, in depleting/sequestering out of peripheral blood group higher % of CD8IFNγ-IL2-TNFα+ (0.7[0.3-1.2] and 0.0[0.0-0.3], respectively, p=0.0201) and lower % of CD8 IFNγ+IL2+TNFα- (0.0[0.0-0.1] and 0.1[0.1-1.0], respectively, p=0.007) compared to sequestering in peripheral blood group were observed.

Conclusion: Our preliminary data showed that humoral response to vaccination in MS patients seems to be significantly influenced by different DMTs mechanism of action while T cell response did not. However, in our cohort sequestering in and depleting/sequestering out of peripheral blood DMTs induced a different CD8 intracellular expression of IFNγ, IL2 and TNFα. As supposed by other authors, IFNγ and IL2 could be implicated in a more robust anti-S T cell response, while the higher expression of TNFα seems to be related to a reduced humoral response.

Immunological efficacy of COVID-19 vaccination in vulnerable populations

OP 116 SARS-COV-2 VACCINATION EFFECTIVENESS IN PEMPHIGUS VULGARIS RITUXIMAB-TREATED PATIENTS

C. Fenizia[1], O. Utyro[2], S. Salanitro[2], C. Moltrasio[1], M. Clerici[1], L. Ottobrini[1], A. Marzano[1], D. Trabattoni[2]

[1]Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy, [2]Department of Biomedical and Clinical Sciences, University of Milan, Milan, Italy

Background: Rituximab (RTX), a monoclonal antibody targeting CD20 on B cells, constitutes the election therapeutic strategy for patients affected by Pemphigus Vulgaris, an autoimmune disorder. Some recent reports have already highlighted the risk of SARS-CoV-2 infection in patients treated with RTX. Besides the risk of a more severe disease course during B cell depleting therapy, a major concern relates to a risk of reduced immunogenicity of vaccination. Therefore, the question arises if patients should withhold or interrupt RTX therapy around COVID -19 vaccination or delay vaccination. However, to date, no scientific evidence has been produced yet.

Material and Methods: To address this question, we enrolled 15 RTX-treated patients with Pemphigus Vulgaris and 20 healthy controls (HC). RTX was administered from 6 to 10 months prior vaccination in the considered cohort. We collected peripheral blood before the vaccinations with BNT162b2 (Pfizer/BioNTech) and a month after each dose of vaccine, including the booster dose. Peripheral blood mononuclear cells (PBMCs) were isolated and in vitro stimulated with a SARS-CoV-2 Spike peptide pool. By flow cytometry, we assessed the B and T cells mediated specific immune response and the memory subsets. In parallel, we assessed the anti-SARS-CoV-2 plasmatic antibody response by the neutralization assay.

Results: Overall, we observed a quite heterogenous scenario in terms of B cells reconstitution upon RTX treatment. While the majority of the patients displayed almost no B cells, in 4 cases we detected the B cells to be around 2% of the PBMCs at T4. The average measured in the HC group was 8% (p=0.005). Due to the lack of cells, we decided not to further consider the B cells subpopulation and the memory subsets. Considering T cells, we observed the memory subsets (naïve, central memory, effector memory and TEMRA) to be comparable among the RTX-treated individuals and the HC. However, in some cases (n=2) we observed the TEMRA subpopulation to be particularly represented upon the second dose (T2). When observing the percentage of cytotoxic T cells expressing activation markers (such as CD69, CD107a, HLA-DRII and IFNg), the RTX-treated group showed percentages overall higher than the HC, although not significant. Finally, the RTX-treated group showed no neutralizing activity against SARS-CoV-2 (p=0.008), except for 3 out of the 4 subjects displaying B cells.

Conclusion: As expected, we found a minor/absent B cell SARS-CoV-2-specific response in RTX-treated subjects. However, they showed an overall functional T cell driven SARS-CoV-2 specific immune response, which was found to be even higher than the HC, with some traits associated to exhaustion. We believe that these preliminary observations might deliver a first insight on the SARS-CoV-2 vaccine effectiveness in Pemphigus Vulgaris bearing patients and, more generally, RTX-treated subjects. These results might help defining a proper management of such patients.

Immunological efficacy of COVID-19 vaccination in vulnerable populations

OP 117 SARS-COV-2 ANTIBODY RESPONSE IN SOLID ORGAN TRANSPLANT PATIENTS AFTER MRNA BNT162B2: DATA FROM AN OBSERVATIONAL PROSPECTIVE STUDY

F. Cogliati Dezza[1], F. Dominelli[1], M. Guardiani[1], E. Tortellini[1], G. Savelloni[1], M. Garofalo[2], A. Centofanti[3], C. Carillo[3], A. Gaeta[4], R. Pretagostini[2], G. Russo[1], C.M. Mastroianni[1]

[1]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome Italy, [2]General Surgery and Organ Transplantation Unit, Sapienza University of Rome, Rome, Italy, [3]Division of Thoracic Surgery and Lung Transplant, Sapienza University of Rome, Rome, Italy, [4]Department of Molecular Medicine, Sapienza University of Rome, Rome, Italy

Background: The impact of COVID-19 in Solid Organ Transplant (SOT) patients is still an open issue. A significant increased risk of complications, Intensive Care Unit (ICU) admission and mortality has been reported, however the real burden on the mortality rate is debated. Currently, SARS-CoV2 vaccination has become the standard of care to prevent COVID-19 hospitalization and mortality. In the SOT recipients, vaccine is strongly recommended as high-risk patients due to their immunocompromised status and underlying diseases. Unfortunately, the data described a lower seroprevalence after the second vaccine dose (between 22-54%) and the booster dose (between 33%-69%) compare to general population. The aim of the study was to assess overtime the antibody response in the Kidney and Lung Transplant Recipients (KTR and LTR, respectively) after the mRNA booster dose and the factors associated with humoral response.

Material and Methods: We conducted an observational, monocentric, prospective study including KTR and LTR that received the third mRNA BNT162b2 vaccine dose. We investigated clinical status and vaccine-induced humoral response of the study population before booster dose (T0), after 45 days (T1) and after 180 days (T2). At T0, T1 and T2 we performed a clinical questionnaire and collected blood samples to assess serum anti-Spike SARS-CoV-2 antibodies. LIAISON SARS-CoV-2 S1/S2 IgG chemiluminescent assay against a recombinant Spike (S) protein (S1/S2) was used. Results below 33.8 BAU/mL were considered negative. Patients with or without seroconversion were defined responder or no responder, respectively. Preliminary univariate analyses were performed in order to explore the factors associated with a no response to the booster dose.

Results: A total of 38 patients were included in the study, 29 (76%) KTR and 9 (24%) LTR, 14 (37%) females and 24 (63%) males. Overall, median age was 56 years (IQR 49-61), months from the transplant were 76 (55-169), days from 2nd to booster dose were 179 (172-204). No serious adverse effect was reported. Concerning maintenance immunosuppression regimen, 25 (66%) included an antimetabolite and 31 (82%) steroids. Generally, 20 (52%) were responder at T0, 28 (74%) at T1, 8 had a confirmed SARS-CoV-2 infection after T1 (Figure1). The T2 assessment is still on going. At T1 evaluation, no responder patients were more likely to be LTR (p: 0.02), no responder at T0 (p:0.02), aged > 60 years (p:0.01) and to receive the transplant within 48 months from T0 (p:0.03). Whereas, no differences were observed regarding sex, comorbidities and immunosuppression regimen.

Conclusions: In conclusion, SOT recipients still remain a vulnerable population with lower humoral vaccine response. In this population strict adherence to non-pharmacological interventions are mandatory. Further studies are needed in order to assess vaccine-induced humoral response, considering, above all, the ongoing fourth vaccine dose campaign.

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Immunological efficacy of COVID-19 vaccination in vulnerable populations

OP 118 DURABILITY OF SARS-COV-2 MRNA VACCINE IMMUNE RESPONSE IN PEOPLE LIVING WITH HIV

S. Cicalini[1], A. Cozzi-Lepri[2], A. Vergori[1], S. Meschi[1], V. Bordoni[1], S. Lanini[1], D. Lapa[1], D. Mariotti[1], L. De Pascale[1], V. D'Aquila[1], M. Fusto[1], C. Castilletti[1], A.R.Garbuglia[1], C. Agrati[1], E. Girardi[1], F. Vaia[1], A. Antinori[1]

[1]National Institute for Infectious Diseases Lazzaro Spallanzani, IRCCS, Roma, Italy, [2]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, UCL, London, UK

Background: Waning of vaccine protection against SARS-CoV-2 infection is currently a concern and durability of specific immunity after vaccination in people living with HIV (PLWH) is still to be defined. Aim of this study was to evaluate persistence of humoral and cell-mediated immune response to mRNA vaccines in PLWH.

Methods: PLWH enrolled in a SARS-CoV-2 vaccination program were evaluated at >90 days after 2nd dose of BNT162b2 or mRNA-1273 vaccine. Anti-Spike RBD-binding by CLIA, neutralizing antibody (nAb) titers by microneutralization assay (MNA90) and IFNγ production in response to Spike stimulation were assessed. Response was defined as having anti-RBD >7.1 BAU/mL, nAbs ≥1:10, IFNγ >12 pg/mL. PLWH were stratified by CD4 T-cell count at vaccination into severe immunodeficiency, SID, ≤200/mm3; minor immunodeficiency, MID, 201 -500/mm3; no immunodeficiency, NID, >500/mm3. Waning of humoral and cell-mediated immune response was evaluated in a subgroup of responders to vaccination for whom values at 1 month (T0) and >90 days (T1) after 2nd dose of vaccine were available. Paired t-test was used to test the overall decline. ANOVA and logistic regression analysis controlling for age, viral load, CD4 nadir and cancer were used for comparisons by CD4 groups.

Results: 314 pts were included (SID=50; MID=133; NID=131); 78% male; median age 56 yrs (IQR 50-61); median time from HIV diagnosis 9 yrs (4-21); 75% previous AIDS diagnosis; median CD4 nadir 58/mm3 (23-12). All pts receiving ART, 88% with HIV-RNA<50 cp/mL. After a median of 175 (IQR 166-186) days after 2nd dose, a detectable anti-RBD response was present in 72% of SID, 96% of MID and 99% of NID (P<0.0001); nAbs in 38% of SID, 79% of MID and 85% of NID (P<0.0001); and IFNγ in 65% of SID, 91% of MID and 93% of NID (P<0.0001). Mean level of humoral immune response at T1 was significantly lower in SID (Figure 1A). By logistic regression, risk of undetectability at T1 was higher in SID vs. NID for anti-RBD (aOR 19.76; 95% CI 1.42-275.6), and in SID (aOR 7.36; 95% CI 1.73-31.34) and MID (aOR 4.68; 1.48-14.76) vs. NID for nAbs; no evidence for a difference was found for IFNγ. Overall, a significant decline of immune response was observed for all immune parameters [mean log2 (SD)]: -2.89 (0.93), p<0.0001, for anti-RBD; -1.53 (1.44), p<0.0001, for nAbs; and -0.57 (2.06), p=0.004, for IFNγ, with no evidence for a difference between CD4 groups (Figure 1B/C).

Conclusions: A high proportion of PLWH with CD4 count <200/mm3 showed a lack of humoral response after a median of 6 months from vaccination compared to PLWH with CD4 count >500/mm3. All PLWH showed a significant rate of waning of immune response over time. These findings support the need for a three-dose schedule as primary vaccination in PLWH. Further studies are needed to establish the most appropriate dose intervals.

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Immunological efficacy of COVID-19 vaccination in vulnerable populations

OP 119 DECAY PATTERN OF ANTI–SARS-COV-2 ANTIBODIES IN PWH

J. Milic[1], A. Tili[2], S. Renzetti[3], F. Motta[1], M. Meschiari[2], R. Fogliani[2], F. Ferrari[2], B. Meccugni[2], S. Mimmi[2], S. Borsari[2], S. Calza[3], A. Cossarizza[1], C. Mussini[1,2], G. Guaraldi[1,2]

[1]University of Modena and Reggio Emilia, Modena, Italy, [2]Azienda Ospedaliero-Universitaria, Policlinico of Modena, Modena, Italy, [3]University of Brescia, Brescia, Italy

Background: We aimed to explore decay pattern of anti–SARS-CoV-2 antibodies titers after COVID-19 vaccination in PWH.

Methods: This observational study of PWH compared younger (<65 years) with older (>65 years) adults attending Modena HIV clinic. Inclusion criteria comprised PWH who received two doses of SARS-CoV-2 vaccine with at least one available serology two weeks after vaccination. Patients with SARS-CoV-2 prior or after vaccination and patients who did not complete vaccination were excluded. Anti–SARS-CoV-2 antibodies were detected with chemiluminescence immunoassay (LIAISON® TrimericS IgG). Antibody titers were expressed in BAU/ml. Antibody titers decay were analyzed in relation to interaction between age (> or <65 years), gender, and day post full vaccination. HIV variables and vaccine type were added as covariates the linear mix-effect regression model estimated through bootstrap.

Results: A total 563 PWH, 387 (68.7%) males, medial age was 56, 15.5% aged 65 were analyzed. Median duration since HIV diagnosis was 18.9 years, current CD4= 681.1 µL, 94% HIV viral load undetectable. 4.1% PWH experienced COVID prior vaccination, 0.9% after vaccination. PLWH received the following vaccine BNT162b2 in 528 (93.8%), mRNA-1273 in 22 (3.9%), ChAdOx1 in 13 (2.3%). Median follow-up was 10.8 weeks. On average, 1.5 antibody titers were analyzed per patient. Time interval from 2nd dose of vaccine and 1st available antibody titer (baseline) was similar in the 4 groups (mean 12±7 weeks, p=0.21). At baseline, a significant difference was observed in antibody titer in men and women (804 vs 1334.5, p<0.001) and in geriatric vs younger adults (678.6 vs 934.2, p=0.011). Baseline antibody titer differed by vaccine type: BNT162b2= 894 (Q1-Q3: 307-1838) BAU/mL, mRNA-1273= 2080 (Q1-Q3:1445-2080) BAU/mL, ChAdOx1=325 (Q1-Q3:179-840) BAU/mL (p<0.001). Figure 1 shows antibody decay according to sex and age interaction with time after correction for HIV variables and vaccine type. Significant weekly antibody decay differed by vaccine type. In detail, comparing ChAdOx1 vs BNT162b2 = -600.1 (-958.9, -231.7) BAU/mL and comparing mRNA-1273 vs BNT162b2=567.1 (322.4, 836.7) BAU/mL.

Discussions: Men and women aged >65 years showed lower baseline antibody titer and men displayed a lower decay over time compared to young men and women. Further studies are needed to understand mechanism of humoral and cellular response associated with SARS-CoV-2 vaccines in relation to age and sex in PWH.

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Open questions about ART efficacy

OP 120 BLOOD TELOMERE LENGTH GAIN IN VIROLOGICALLY SUPPRESSED PATIENTS SWITCHING TO DOLUTEGRAVIR PLUS LAMIVUDINE VERSUS MAINTAINING A TRIPLE REGIMEN: A PROSPECTIVE, LONGITUDINAL, MATCHED, CONTROLLED STUDY

F. Lombardi[1], A. Sanfilippo[2], M. Fabbiani[3], A. Borghetti[1], A. Ciccullo[4], S. Di Giambenedetto[1,2]

[1]Fondazione Policlinico Universitario A. Gemelli IRCCS, UOC Malattie Infettive, Roma, Italia, [2]Università Cattolica del Sacro Cuore, Dipartimento di Sicurezza e Bioetica, Roma Italia, [3]UOC Malattie Infettive e Tropicali, Azienda Ospedaliero-Universitaria Senese, Siena, Italia, [4]Unità di Malattie infettive, Ospedale San Salvatore, L'Aquila, Italia

Background: People living with HIV (PLWH) show accelerated aging, this may be a result of several factors, including HIV infection itself and the aging of the immune system. This immunosenescence is characterized by cells with short telomere length in the blood (BTL). Antiretroviral therapy (ART) determines both an immune reconstitution and viral suppression, enabling a reversal of immunosenescence with a BTL gain. In fact, PLWH recipients of long term ART who maintain virological suppression continue experiencing a BTL increase. However, ART containing nucleoside reverse transcriptase inhibitors (NRTIs), such as tenofovir disoproxil/tenofovir alafenamide (TDF/TAF) or abacavir (ABC), potent inhibitors of human telomerase activity, has been demonstrated to negatively impact on BTL increase.

Objectives: To assess in virological suppressed PLWH if treatment simplification from triple standard therapy with 2NRTI-backbone (one of which was TAF/TDF or ABC) plus a third anchor drug, to a dual regimen with one NRTI, lamivudine (3TC), plus one integrase inhibitor, dolutegravir (DTG) had an impact on BTL.

Patients and methods: This was a prospective, longitudinal, matched, controlled study. We enrolled virologically suppressed patients on stable three-drug ART who switched at baseline (BL) to dual therapy (DT group) or maintained triple therapy (TT group); subjects in the TT group were matched 1:1 with those in the DT group according to age, gender, years since HIV diagnosis, years on ART and anchor drug in the BL 3-drug regimen. BTL was assessed by a monochrome multiplex qPCR (MMqPCR) at BL and after 48 weeks (W48). A multivariate analysis to elucidate variable associated with BL BTL and BTL change over the time was performed.

Results: We enrolled 40 patients in each group; mostly males (80.0%), median age was 54 years (IQR 43-59). Two groups were homogeneous for all main characteristics (Table 1). At BL, the means of BTL were comparable between two groups: 1.02 (0.96-1.09) for DT and 1.02 (0.95-1.09), for TT (p=0.979). At W48, the viro-immunological status of patients was stable. The mean BTL from BL to W48 increased significantly in the DT group, +0.075 (0.022-0.127) (p=0.006), whereas it remained similar in the TT group, -0.005 (-0.057- 0.036) (p=0.817). In multivariable regression analysis, higher BL BTL was associated with younger age (per year increase -0.01, 95%CI -0.014/-0.007, p<0.001), female (vs male 0.153 95%CI 0.050/0.257, p=0.004) and higher CD4/CD8 ratio (0.071 95%CI 0.003/0.140, p=0.042). Lower BL BTL was the only factor associated with BTL change (-0.231 95%CI -0.231/-0.082, p=0.003).

Conclusions: These data showed that in this setting of virologically suppressed patients who switched to a dual therapy with 3TC as the only one NRTI, displayed a significant BTL gain, whereas no difference was observed in BTL for subjects who maintained triple therapy with two NRTIs. These data suggest a positive impact of dual therapy on BTL.

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Open questions about ART efficacy

OP 121 REAL-LIFE USE OF DORAVIRINE IN TREATMENT-EXPERIENCED PEOPLE LIVING WITH HIV: AN ITALIAN MULTICENTRE STUDY

M. Mazzitelli[1], M. Degli Antoni[2], F. Castelli[2], D. Ripamonti[3], G. Zuglian[3], G. Lapadula[4], M. Fabbiani[5], A. Ferraresi[6], C. Putaggio[1], A.M. Cattelan[1], E. Quiros-Roldan[2]

[1]Infectious and Tropical Diseases Unit, Padua University Hospital, Padua, [2]Department of Infectious and Tropical Diseases, ASST Spedali Civili General Hospital and University of Brescia, Brescia, [3]Infectious Diseases Unit, ASST Papa Giovanni XXIII, Bergamo, [4]University of Milan Bicocca, Monza, [5]Infectious and Tropical Diseases Unit, Azienda Ospedaliero-Universitaria Senese, Siena, 6Division of Infectious Diseases, Cremona Hospital, Cremona

Introduction: Doravirine (DOR) is a new-generation non-nucleoside reverse-transcriptase inhibitor (NNRTI). Recent clinical trials demonstrated and confirmed the efficacy and safety of DOR, but clinical evidence supporting successful DOR use in treatment-experienced people living with HIV (PLWH) is still scarce. We here describe the preliminary results of a multicentre real-life experience in switching patients to a DOR-containing regimen.
Methods: We retrospectively investigated the switch to DOR in HIV patients followed up in six Italian HIV centers. All PLWH (older than 18 years) who were switched to DOR since February 1, 2020, to December 31, 2021, were included. Demographical, clinical and viro-immunological data were recorded in an electronic database. The changes in virological, immunological and metabolic parameters at week 24 are described.
Results: A total of 132 subjects (68.9% males, median age 56 years) were started on DOR-based regimens. Table 1 shows the main baseline characteristics. The reasons for the switch to a DOR-containing regimen included the following: proactive switch (39.4%), dyslipidaemia (18.2%), virological failure (17.4%) and the management of drug-to-drug interactions (12.9%). Seven patients (5.2%) were switched to DOR-containing regimens for significant weight gain. Nine patients (6.8%) were switched for ongoing toxicity.
Doravirine was combined with integrase inhibitors in most cases (40%). Fifty-two patients were followed up for at least 24 weeks after DOR introduction. Table 2 summarizes the variations in parameters at week 24. No differences were observed regarding the proportion of subjects with virological suppression, CD4+ T-cell count or CD4/CD8 ratio and serum creatinine levels. In a sub-group of patients (52, 39.4%), a significant reduction in triglycerides and cholesterol levels was observed at week 24.
Conclusions: In 40% of cases DOR was combined with integrase inhibitors and the major reason for switching (80%) was the aim to decrease the metabolic impact of current ARVs and to manage the drug-to-drug interactions. Approximately 80% and 90% of patients had plasma HIV-RNA <50 copies/mL at baseline and week 24, respectively. More data are needed to assess the long-term efficacy and place in therapy of this new NNRTI in the real world practice.

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Open questions about ART efficacy

OP 122 FORGIVENESS TO IMPERFECT ADHERENCE TO BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE

F. Maggiolo[1], D. Valenti[1,2], R. Teocchi[3], L. Comi[1], E. Di Filippo[1], M. Rizzi[1]

[1]UOC Infectious Diseases, [2]FROM foundation, [3]Informatics department, ASST Papa Giovanni XXII, Bergamo Italy

Background: When applied to ART, forgiveness refers to the ability of a given regimen to maintain complete viral suppression despite a documented imperfect adherence. In contrast with most pharmacological parameters, forgiveness lacks an established, quantitative measure, but, despite this, the medical community has embraced the concept that some regimens are more forgiving than others, basing on this assumption therapeutic choices that are made every days in clinics. We explored forgiveness of bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF).

Methods: In this retrospective study, pharmacy drug refill was used to calculate PDC as a proxy of adherence. PDC is the number of days with medication available divided by the number of days in a specified time interval. If excess medication is collected or refills are made early, the excess is applied toward subsequent absences of drugs. Finally, we evaluated forgiveness defined as the sensitive therapeutic success (e.g. selected HIV-RNA threshold) achieved rate under a given level of imperfect adherence. Three different virologic cut-offs were used: target not detected (TND), that is a value of HIV-RNA current standard methods do not detect; HIV-RNA < 50 copies/ml as the gold standard to define therapeutic efficacy; HIV-RNA < 200 copies/ml as the value that prevents HIV transmission by sexual contacts. A probit model was applied to verify the impact of baseline variables and adherence on the virologic outcomes.

Results: 281 adult PLWH were included, 75% were males with a median age of 49 years (IQR 43-58). The median follow-up of the cohort under B/F/TAF was 590 days (IQR 381-685) for a total of 343 patient/years. Adherence was very high with a median of 98% (IQR 95-100%). Consequently, the virologic response was sustained: 41.8% of PLWH had HIV-RNA TND throughout the study period; 83.1% showed constant HIV RNA < 50 copies/ml and 96.8% of subjects had HIV-RNA always < 200 copies/ml (U=U level). A PDC as low as 70% was sufficient to obtain 100% of the desired virologic outcome irrespective of the cut-off (figure). Probit analysis indicated that adherence variation was not related to the possibility to obtain and maintain an HIV-RNA TND or < 50 copies/ml, but that PDC significantly correlated with the threshold of < 200 copies/ml differentiating non-responders from patients with eventual sporadic low-level viral blips. Adherence in non-responders was very low (median 67%; IQR 30-90%) compared to PLWH showing constant control of HIV replication (median 96%; IQR 95 -100%) (figure).

Conclusions: Adherence dynamics under B/F/TAF indicate that this regimen is highly forgiving and obtains desired virologic outcomes for adherence levels as low as 70%. Long-term success of ART needs well tolerated, effective regimens that are the least intrusive of the patient's lifestyle. In this context, an elevated forgiveness may be considered as an additional feature that can further improve long-term outcomes.

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Open questions about ART efficacy

OP 123 EVALUATION OF METABOLIC SAFETY PROFILE IN NAIVE AND VIROLOGICALLY SUPPRESSED HIV-1 INFECTED INDIVIDUALS STARTING/SWITCHING TO A BICTEGRAVIR SINGLE-TABLET-REGIMEN IN A REAL-LIFE SETTING

M. Trizzino, C. Gioè, E. Di Marco, A. Mancuso, M. Tolomeo, A. Cascio

Infectious and Tropical Disease Unit, AOU Policlinico "P. Giaccone", Palermo, Italy

Introduction: The STR BIC/FTC/TAF is a recommended regimen for adults and adolescents with HIV infections, with demonstrated safety, efficacy, and high barrier to resistance. Clinical trials data indicate that TAF is associated with greater increases in TC, LDL cholesterol and triglycerides relative to TDF based regimens. The aim of our study is to assess the effect of TAF on lipids in a cohort of PLWH switched to B/F/TAF and naïve-HIV population.

Material and Methods: We included all adult, treatment-naïve and treatment experienced PLWH starting BIC/FTC/TAF from December 2019 to March 2022. Outcomes of interest were viral suppression (HIV-RNA < 50 cp/ml) and treatment persistence in those patients who reached 6 and 12 months of follow-up. Also we evaluate metabolic profile (glycemia, T-Col, LDL-Col, TG) before BIC/F/TAF start and re-evaluation after 48 weeks. Retrospective cohort study including PLWH who switched to BIC/F/TAF while with HIV-RNA < 50 copies/mL and HIV-naïve population. Means, SD and medians were calculated. Paired Samples t Test was used to compare means of metabolic profile values in naïve and switch populations before BIC/F/TAF start and after 48 weeks.

Results: We included 152 PLWH, median age was 52 years, 23% were women and 91.5% were white. 31 (20.4%) pts were naïve and 121 pts (79.6%) switched from other regimens. The median of CD4 was 173 for naïve-pts and 244 for experienced-pts. In the switch population, 43/121 pts (35.8%) switched from a PI-based ART. For pts who completed follow-up at week 24 (126/152) and at week 48 (133/152) only 2 pts had virological failure. Comparing the metabolic parameters at baseline and after 48 weeks in the naïve population and in switch population, no statistical differences were found in both cases. Similarly, stratifying by previous PI therapy in the switch population, we found no statistically significant differences in the metabolic parameters analyzed. In switch population who complete entire study follow-up: mean glycemia was 92 ± 20.8 mg/dL and it increased to 92.3 ± 19 mg/dl at week 48 (P=.794); mean total cholesterol was 182.4 ± 33.8 mg/dL and it decreased to 182 ± 39.9 mg/dL (P=.918); mean LDL cholesterol was 105.5 ± 31.9 mg/dL and it decreased to 104.8 ± 39 mg/dL (P=.855); mean TG was 126.5 ± 51.8 mg/dL and it decreased to 119.3 ± 50.9 mg/dL (P=.170). In naïve population who complete entire study follow-up: mean glycemia was 88.4 ± 12.2 mg/dL and it decreased to 86.1 ± 11.5 mg/dL (P=.402); mean total cholesterol was 165.2 ± 44.2 mg/dL and it increased to 174.9 ± 32.7 mg/dL (P=.349); mean LDL cholesterol was 99.3 ± 36.8 mg/dL and it decreased to 97.4 ± 30.8 mg/dL (P=.885); mean TG was 114.7 ± 57.2 mg/dL and it increased to 119.3 ± 79 mg/dL (P=.805). Even in switch population with prior PI-b ART, there was no difference in metabolic values in follow-up period (P .942, .129, .110, .0432 for glycemia, T-Col, LDL-Col and TG respectively).

Conclusions: Data from this real-life Italian cohort confirmed the safety profile of B/F/TAF with no significant metabolic difference, both naïve and switch population. Our study demonstrated high virologic effectiveness of B/F/TAF regimen, with a low level rate of virological failure.

Open questions about ART efficacy

OP 124 REAL-WORLD EFFECTIVENESS OF SWITCHING TO BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE (BIC/FTC/TAF) IN WOMEN LIVING WITH HIV: SUBGROUP ANALYSIS FROM ICONA-BIC

A. d'Arminio Monforte[1], A. Tavelli[2], A. Cingolani[3], C. Mussini[4], S. Piconi[5], A. Calcagno[6], G. Orofino[7], S. Cicalini[8], A. Castagna[9], F. Ceccherini Silberstein[10], A. Gori[11], A. Antinori[8]

[1]Department of Health Sciences, Clinic of Infectious Diseases, 'San Paolo' Hospital, University of Milan, Milan, Italy, [2]Icona Foundation, Milan, Italy, [3]Infectious Diseases Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Department of Safety and Bioethics, Catholic University of the Sacred Heart, Rome, Italy, [4]Infectious and Tropical Diseases Unit, Azienda Ospedaliero Universitaria di Modena, University of Modena and Reggio Emilia, Modena, Italy, [5]Infectious Diseases, ASST Lecco, Lecco, Italy, [6]Unit of Infectious Diseases, Ospedale Amedeo di Savoia, Department of Medical Sciences, University of Turin, Turin, Italy, [7]"Divisione A" Unit of Infectious Diseases, Ospedale Amedeo di Savoia, ASL Città di Torino, Italy, [8]Clinical Department, HIV/AIDS Unit, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Roma, Italy, [9]Infectious Diseases Unit, IRCCS San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, Italy, [10]Department of Experimental Medicine, University of Rome Tor Vergata, Rome, Italy, [11]Clinic of Infectious Diseases, IRCCS Ca' Granda Ospedale Maggiore Policlinico, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy

Background: Sex-related factors can influence ART outcomes and the overall wellbeing of people living with HIV (PLWH). Women living with HIV (WLWH) are often under-represented in RCT and research studies. BIC/FTC/TAF is a widely used INSTI-based 3-drug regimen in WLWH. The aim of the present sub-analysis from ICONA-BIC study is to evaluate effectiveness of switching to BIC/FTC/TAF in virologically suppressed PLWH, focusing on ART-experienced women compared to men.

Methods: Observational study of PLWH enrolled in the Icona cohort switching to BIC/FTC/TAF while virologically suppressed (baseline). Study period: Apr2018-Dec2021. Exposure of interest: sex at birth (female vs male). Primary endpoint was treatment failure (TF) defined as treatment discontinuation (TD) for any reason or virological failure (VF, 2 consecutive HIV-RNA > 200 copies/ml or 1 HIV-RNA >1000 copies/mL). Four secondary endpoints were evaluated: TF excluding pregnancy as event (TFEP), TD regardless of the reason, TD excluding pregnancy (TDEP) and VF. Statistical analyses included descriptive statistics, and standard survival analysis. Cox-regression models were used to investigate the risk of primary and secondary endpoints in ART-experienced women compared to men.

Results: 1237 subjects have been included. 229 were women (18.5%), 84% Italian, median age 47 years (39-55), 50% MSM, 37% hetero-, median CD4 702 /mm3 (505-928), 86% previously on other 3-drug INSTI. After a median follow-up of 1.36 years (IQR 0.97-1.67) from switch, 112 PLWH (30 W and 82 M) had TF (9.1%) (14 VF and 98 TD). Overall, the KM-estimated probability of TF was 4.6% (95%CI 3.5-6.1) at 1-year, 7.5% (95%CI 4.7-12.0) in women and 4.0% (2.9-5.5) in men (Figure 1A, log-rank p=0.01). After fitting a Cox regression model adjusted for confounders, women showed 2-times higher risk of TF (AOR 2.01; 95%CI 1.17-3.44) (Table1). In the adjusted Cox model, after excluding the 6 pregnancies as events, women were no longer at higher risk of TF (AOR 1.69, 95%CI 0.93-2.90) (Table1).

100/1237 PLWH (26 W and 74 M) had a TD (8.1%): The 1-yr probability of TD was 4.1% (3.1-5.5): 6.6% (3.9-10.9) and 3.6% (2.5-5.0) respectively for women and men (log-rank p=0.03; Fig 1C). The independent risk of TD was higher in women (AOR 1.94, 95%CI 1.09-3.46), but again not after excluding TD due to pregnancy (AOR 1.53, 95%CI 0.82-2.82)(Table1). Details of reasons for TD are reported in Table 3. In the ITT analysis, VF occurred in only 15 PLWH: overall the 1-year probability of VF was of 0.7% (0.3-1.4), too few cases to infer in sex-related differences (Fig 1D).

Conclusions: In this large real-world study of ART-experienced PLWH switching to BIC/FTC/TAF, the regimen showedhigh effectiveness (4.6% TF and 0.7% VF by 1-year). The higher risk of TF and TD in females compared to males is related to discontinuation due to pregnancy. and after excluding these the success of BIC/FTC/TAF is similar in men and women. First case reports of BIC/FTC/TAF use in pregnancy are promising but more comprehensive studies need to be completed in pregnant women.

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Open questions about ART efficacy

OP 125 TOLERABILITY, VIRO-IMMUNOLOGICAL, METABOLIC EFFECTS, AND COSTS OF SWITCHING TO BIC/TAF/FTC IN A COHORT OF PEOPLE LIVING WITH HIV: A 48-WEEK ANALYSIS

M. Mazzitelli[1], M. Trunfio[2], D. Mengato[3], C. Putaggio[1], L. Sasset[1], D. Leoni[1], E. Castelli[1], A.M. Cattelan[1]

[1]Infectious and Tropical Diseases Unit, Padua University Hospital, Padua, Italy, [2]Infectious Disease Unit, Department of Medical Sciences at Amedeo di Savoia Hospital, University of Torino, Torino, Italy, [3]Hospital Pharmacy Department, Padua University Hospital, Padua, Italy

Integrase inhibitors combined with non-nucleos(t)ide retro-transcriptase inhibitors such as the bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) combination are recommended for the treatment of HIV-1 as first line or switch regimen. The objectives of this prospective analysis were: (I) to evaluate the viro-immunological efficacy of BIC/FTC/TAF regimen in a cohort PLWH who started this combination as switch, at the Infectious and Tropical Diseases Unit of the Padua University Hospital, (II) to assess its impact on body weight, lipids, and renal function parameters (from baseline to week 48), (III) to evaluate costs, level of adherence and the rate and causes of the discontinuation of the regimen.

We included all PLWH older than 18 years of age who switched to BIC/FTC/TAF combination from any previous regimen from February 1st, 2020 to December 31st, 2021 We collected demographic, clinical and HIV-related parameters from health record, as well as, all laboratory parameters, medications and comorbidities, level of adherence, dietary pattern and regular exercise. We assessed the rate of discontinuation of the study regimen during the follow-up and its reasons; in addition, patients who were lost to follow-up before or at W48 were considered as discontinuations.

Over the study period, 290 patients started the BIC/FTC/TAF as switch strategy (76.9% males, median age 52 years-IQR 44-58). Most patients (76.5%) were coming from another INSTI-based regimens. Overall 5.8% patients for toxicity/intolerance. Most common adverse events were gastrointestinal disorders (52.9%) and sleep disturbances (23.5%). Factors significantly ($p<0.05$) associated with discontinuation were coming from a dual regimen, suffering from neurological disorders, and length of HIV infection. At 48 weeks, we detected a significant increased for body weight, BMI, CD4 T cell count and CD4/CD8 ratio, with a significant reduction of triglycerides and costs (table 1). Factors associated with weight gain were having a higher BMI or belonging to a higher BMI category at the baseline.

Conclusions: Our results showed that switching to BIC/FTC/TAF was safe and virologically effective, and favour immunological recovery (even if increase of the absolute CD4+ T Cell count was mild). Even if we detected a significant reduction of triglycerides, it does not appear to be clinically relevant (-0.12 mmol/L). Similarly, we think that increase of body weight and BMI (+1 kg and +0.29 BMI), may be not clinically relevant over 1 year-time of follow-up because it is overlapping to that observed in the general population. In addition, this regimen seemed to be cost saving allowing to save -4.2 euro/day from baseline to week 48 with a mean saving of 1.533 euro/patient/year. Further studies are necessary to better understand the role of gastrointestinal/neuropsychological side effects in real-life setting.

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Immunological complexity in COVID-19

OP 126 DEVELOPMENT OF SARS-COV-2 IGM AFTER 1ST VACCINE DOSE PREDICTS LONGER IMMUNITY

A. Ruggiero[1], C. Piubelli[2], L. Calciano[1], G. Siracusano[3], M.T. Valenti[1], L.G. Delle Carbonare[1], T. Fantoni[1], L. Lopalco[3], S. Accordini[1], A. Beretta[4], Z. Bisoffi[2], D. Zipeto[1]

[1]University of Verona, Verona, Italy, [2]IRCCS Sacro Cuore Don Calabria Hospital, Verona, Italy, [3]Division of Immunology, Transplantation and Infectious Diseases, San Raffaele Scientific Institute, Milan, Italy, [4]Solongevity Research, Milan, Italy

Background: In our previous work, we demonstrated that individuals developing SARS-CoV-2 specific IgM following vaccination show higher levels of SARS-CoV-2 neutralizing IgG.
Aim: To study whether development of SARS-CoV-2 IgM following vaccination predicts longer immunity.
Methods: We analysed SARS-CoV-2 specific humoral response in 1873 health care worker (HCW) recipients of the BNT162b2, longitudinally: before administration (week 0, W0), at the second dose (W3), three weeks (W6) (W6) and 6 months (W27) after the second dose. The cohort included 1584 immunologically naïve subjects to SARS-CoV-2 (IN) and 289 individuals with a history of previous infection (PI). We measured IgG antibodies specific for the SARS-CoV-2 spike protein (S), specifically against the receptor binding domain RBD (IgG-S; Quant assay, Abbott, Ireland) and anti-S IgM (IgM-S; SARS-CoV-2 IgM-S assay, Abbott). For IgM-S, the patients were classified negative (<1 BAU/ml) or positive (≥1 BAU/ml) as indicated by the manufacturer. Two-level linear regression models were used to assess differences of IgG-S titers according to time of examination (W0-W27) and IgM-S group, separately for IN and PI subjects.
Results: In IN, we identified three patterns of responses: (a) IgG-S positive/IgM-S negative (36%); (b) IgM-S positive after the first dose together with IgG-S (38%); (c) IgM-S positive after the first dose and after IgG-S (26%). In PI, 41% were IgM-S negative at T0 (a); the remaining IgM-S positive developed IgM-S at T1(19%, b) or at T2 (2%, c); a proportion of patients had detectable IgM-S already at T0, probably as reflection of the recent infection (38%, d). In IN (Fig. 1A), expression of both IgM-S/IgG-S responses were associated with higher IgG-S titers at short (W6, $p<0.0001$) and long (W27, $p<0.001$) follow-up. In PI, although pre-existing immunity may differentially modulate antibody response, the generation of vaccine-induced IgM-S after the first vaccine dose was associated with a trend for higher IgG-S titres in subjects that developed Ig-M at follow-up (Fig. 1B).
Conclusion: SARS-CoV-2 vaccination induces (1) absence of IgM-S, (2) appearance of IgM-S after 1st vaccination dose and together with IgG-S, or (3) IgM-S following IgG-S appearance. The coordinated expression of IgG-S and IgM-S was associated with a more efficient response in both antibody titers and virus-neutralizing activity up to 6 months following vaccination schedule completion, representing a potential correlate of protection.

Immunological complexity in COVID-19

OP 127 AFFINITY MATURATION AND NEUTRALIZING ACTIVITY OF ANTI-SARS-COV-2 SPIKE ANTIBODIES

S. Caucci[1], R. Longo[1], B. Corvaro[1], A. Valenza[2], K. Marinelli[2], P. Bagnarelli[1,2], S. Menzo[1,2]

[1]Department of Biomedical Sciences and Public Health, Università Politecnica delle Marche, Ancona, Italy, [2]Virology Laboratory, Azienda Ospedaliera Ospedali Riuniti di Ancona, Ancona, Italy

Background: The ability to elicit anti-SARS-CoV-2 spike antibodies, capable of neutralizing different viral lineages, is a key factor for the efficacy of vaccination campaigns against COVID-19. It has been demonstrated that repeated antigenic stimulus improves both quantity and quality of the specific response, suggesting frequent multiple vaccine dose administrations to improve efficacy against refractory variants. As the issue of vaccine cross-efficacy against different variants is presently of the utmost importance, in the perspective of an rational vaccination strategy, we analyzed the data obtained in the context of the ongoing vaccination campaign in Italy.

Material and Methods: The isolation of 8 different lineages of SARS-CoV-2 and neutralization assay was performed on Vero E6 cells. Neutralization was performed in 96 well plates by challenging 100TCID50/well with serial dilutions of the sera. Five different populations were compared: COVID-19 convalescent patients (CCP); vaccinated naïve subjects receiving 2 doses of vaccine (NV2); subjects previously infected and subsequently vaccinated with either a single (IV1) or a double dose (IV2) of vaccine; subjects receiving the third dose (NV3).

Results: Sera from IV1 and IV2 displayed a significantly enhanced neutralizing power against all lineages compared to those from CCP or NV2, comparable to NV3. This difference was particularly striking against lineages most refractory to neutralization, notably beta, delta, or omicron. Interestingly, the titers obtained from subjects infected 6 months before vaccination and from subjects infected 1 year before were not statistically different. To further explore a possible role of antibody affinity maturation, we divided the neutralizing titer by the binding capability (BAU/ml) in each of the analyzed sera and lineage, a measure which can be considered as a value of specific Neutralizing Efficacy (NE). This index was typically lower in NV2 compared to CCP across all lineages. However, the highest values, across all lineages, were observed in IV1 or IV2, indicating an unquestionable improvement achieved by additional immunization even on CCP. In addition, NE value was significantly enhanced after 3rd dose.

Conclusions: These results, by demonstrating that IV1, IV2 and NV3 produce better antibodies rather than simply more antibodies, adds an important element to strengthen the hypothesis that affinity maturation, enhanced by repeated immunological stimuli over an extended period of time, is a fundamental contributor to the increased breadth of neutralizing power.

This improvement was observed in all subjects who had repeated immunological stimuli, independently from the nature of these stimuli. In conclusion, our study shows evidence that neutralizing efficacy of present vaccines, albeit based on an “obsolete” SARS-CoV-2 Spike sequence, may achieve a significant enhancement upon repeated immunization, in particular against neutralization-refractory viral lineages.

Immunological complexity in COVID-19

OP 128 CORRELATION BETWEEN CLINICAL ASPECTS AND SERUM/CSF CYTOKINE LEVELS IN EARLY VERSUS CLASSIC ONSET SARS-COV-2-RELATED GUILLAIN-BARRÉ SYNDROME

S. Boni[1], L. Benedetti[2], M. Feasi[1], A. Assini[3], E. Blasi Vacca[1], S. Grisanti[2,4], A. Parisini[1], D. Franciotta[2], F. Del Puente[1], F. Massa[2,4], N. Bobbio[1], T. Vigo[2], R. Prinapori[1], D. Giunti[2], E. Mobilia[2], D. Visigalli[2], A. Beronio[5], P. Rivera[6], F. Bandini[7], A. Granata[8], E. Narciso[7], A. Schenone[2,4], E. Pontali[1]

[1]Department of Infectious Diseases - Galliera Hospital, Genova, Italy, [2]IRCCS, Ospedale Policlinico San Martino, Genova, Italy, [3]Neurology Unit, Galliera Hospital Genova, Italy, [4]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genova, Genova, Italy, [5]Department of Neurology, Sant'Andrea Hospital, La Spezia, Italy, [6]Department of Neurology, Imperia Hospital, Imperia, Italy, [7]Department of Neurology, ASL3 Genovese, Genova, Italy, [8]Department of Neurology Santa Corona Hospital, Pietra Ligure, Savona, Italy

Background: Guillain–Barré syndrome (GBS) is a heterogenous immune-mediated peripheral neuropathy characterized by a typical post-infectious profile, but some post-Zika virus, post-SARS-CoV-2 and post-H1N1 influenza virus GBS cases manifested with very short intervals after infection. In SARS-CoV-2, a trigger for autoimmune reactions could be the release of a large amount of proinflammatory cytokines in the event known as "cytokine storm". In this study, we explored the hypothesis of a hyperacute immune response by dosing cytokines on cerebrospinal fluid (CSF) and serum samples of patients with SARS-CoV-2-related GBS.

Materials and methods: We consecutively enrolled SARS-CoV-2-patients in Liguria who subsequently developed GBS. We divided them into two groups based on time between onset of SARS-CoV-2 infection and onset of GBS symptoms: 1) patients who developed symptoms >7 days after onset of SARS-CoV-2 infection ("classic onset"), 2) patients who developed symptoms within 7 days from onset of SARS-CoV-2 infection ("parainfectious onset"). We dosed, SARS-CoV-2 RNA in CSF and cytokines (IL-1b, IL-6, IL-8, TNF-alpha) on CSF and serum (ELLA automated immunoassay) and compared the levels in both groups. The dosage of each cytokine was correlated with age, severity of COVID disease, clinical severity at the onset of GBS and at last follow-up (GBS disability scale – GBS-DS).

Results: We enrolled 26 patients; 15 in to the "classic onset" group (F = 6, mean age 62 years) and 11 in the "parainfectious onset" group (F= 4, mean age 62 yrs). Sixteen patients developed COVID-19-related pneumonia, 9 developed only symptoms of upper respiratory tract infection, one developed exclusively gastrointestinal symptoms. Out of 26, 7 were admitted in ICU and 8 had not been hospitalized. Mean GBS-DS at onset was 4, while mean GBS-DS at follow-up was 2. We found no difference in cytokines levels in serum and CSF between the 2 groups. In no case, SARS-CoV-2 RNA was detected in CSF. However, we found a statically significant correlation between younger age and para-infection onset (p=0.036). Furthermore, no correlation was found between levels of each individual cytokine and severity of SARS-CoV-2 infection, the GBS-DS at onset and the GBS-DS at follow-up.

Discussion: Our study did not detect significant differences in cytokines levels between patients with "parainfectious onset" of GBS and patients with "classic onset".

The most interesting finding is the correlation between early age and GBS onset within 7 days since SARS-CoV-2 infection, since this early presentation is generally unexpected and thus its diagnosis is challenging.

In conclusion, cytokine patterns in the two groups were not significantly different and no virus was isolated in CSF. Thus, the underlying mechanism is most probably immune-mediated, such as molecular mimicry and/or neuroinflammation. Larger cohorts are needed to better elucidate the complex relationship between SARS-COV-2 infection and GBS.

Immunological complexity in COVID-19

OP 129 A REAL-LIFE SINGLE-CENTER STUDY ON THE IMPACT OF ANTI-SARS-COV2 VACCINATION

C. Leanza, S. Covino, R.A. Valia, A. Destro, F. Petrucci, E. Motta, M. Aneuchoum, R. Donà, F. Cancelli, C.M. Mastroianni

Department of Public Health and Infectious Diseases, Sapienza University, Rome

Background: Aim of the study was to evaluate the clinical effectiveness of anti-SARSCoV2 vaccines.

Material and Methods: We conducted a real-life retrospective, single-center study at Department of Infectious Diseases (ID) (Sapienza University, Rome). Unvaccinated and fully vaccinated or up to date with their COVID-19 vaccination patients who had received vaccine for more than 15 days or less than 120 days hospitalized with a diagnosis of SARS-CoV2 infection in ID department from August 2021 to February 2022 were enrolled. Patients were divided in two groups: vaccinated (VP) and not vaccinated (NVP). To evaluate the role of comorbidities in COVID-19 mortality Veterans Health Administration COVID-19 (VACO) Index was used, it estimates risk of 30-day mortality after COVID-19 infection using pre-COVID health status. COVID-19 related pneumonia was diagnosed by computed tomography (CT scan) of the chest. Furthermore, we related severity of clinical picture to the worst P/F ratio in the higher oxygen demand. High level positive end expiratory pressure (PEEP) was administered with High flow nasal cannula (HFNC) and Continuous Positive Airway Pressure (CPAP) helmets. We evaluate the use of COVID-19 treatments: antiviral, anti SARS-CoV2 mAbs, steroids and immunomodulators. Primary outcomes were represented by ICU admission, length of stay and 30-day mortality.

Results: Overall, 139 patients were included in the study: 62 (44,6%) VP and 77 (55,4%) NVP. (Table 1) Regarding risk factor for development of severe COVID-19, VP were older than NVP (median 70,5 years vs 56 years, p=0,0022), arterial hypertension was the most represented comorbidity, higher in VP than NVP (23,74% vs 16,54%, p=0,0058), VACO index was higher in VP than NVP (median 12% vs 3,3%, p=0,0018). NVP tended to have a more severe clinical presentation and clinical course: pneumonia was higher in NVP than VP [63 (24,46%) vs 34 (45,32%), p=0,0008], higher level of PEEP was administered to NVP than VP (median 10 vs 3, p=0,0470). COVID-19 treatments such as steorids (52 vs 28, p=0,0098), remdesivir (52 vs 31, p= 0,0391) and mAbs anti-SARS-CoV2 for inpatients with severe COVID-19 (38 vs 13, p=0,0007) were administered highly in NVP than VP. Preventive mAbs anti-SARS-CoV2 for outpatients with non-severe COVID-19 were administered highly in VP than NVP (18 vs 4, p=0,0001). Regarding admission to ICU, length of stay and 30-day mortality no statically significant difference were noted between the two groups. (Table 2)

Conclusions: In our study NVP had worst severity clinical picture despite risk factor to develop severe COVID-19 pneumonia were higher in VP. Greater use of preventive dose antiSARS-CoV2 mAbs in VP and use of mAbs anti-SARS-CoV2 at treatment dose, remdesivir, corticosteroid in NVP confirmed this trend. Vaccination is valid strategy to prevent development and progression of severe COVID-19 pneumonia.

Attach: https://www.icar2022.it/public/abstract/Attach_ABS_253.jpg

Immunological complexity in COVID-19

OP 130 SHORT COURSE REMDESIVIR IN EARLY COVID-19 AS AN EFFECTIVE AND USEFUL OPTION IN BOTH OUT- AND IN-PATIENTS

C. Del Borgo[1], A. Gasperin[2], R. Marocco[1], D. Di Trento[2], S. Garattini[2], M. De Masi[1], A. Grimaldi[2], S. Corazza[2], S.G. De Maria[2], S. Gismondi[1], P. Fabietti[1], B. Bartolozzi[1], G. Bagaglini[3], G. Bonanni[3], M. Lichtner[1,2]

[1]Infectious Diseases Unit, SM Goretti Hospital Latina, [2]Department of Public Health and Infectious Diseases, "La Sapienza" University, Rome, [3]Pharmacy Service Unit, SM Goretti Hospital Latina

Background: It is already demonstrated that an early use of remdesivir (within 7 days from symptoms onset) in patients with Covid-19 determines a reduction of the risk of hospitalization or death. A three-days course is enough to reduce by 87% the risk of hospitalization or death in an unvaccinated population.
Since there is no clinical benefit from treatment in a late phase of the disease, the implementation of ambulatory day care or home- care services have a crucial role in the efficiency of preventive therapies.
Material and Methods: Since 07/01/22 the three-day course of remdesivir was added to armamentarium for treatment of early COVID inside a dedicated 7-day-service for anti-SARS CoV-2 MAbs administration and other antiviral therapies based on a medical-nurse-pharmacology team.
Patients are enrolled upon notification by general practitioners or service physician after confirmation of a positive nasopharyngeal swab and the infusion is made generally within 24-48h. If patients couldn't reach hospital independently, they were carried by the local transport team (no infusions were administered at home). Patients admitted to the hospital for other causes (inpatients) were also treated with short course of remdesivir to prevent the development of severe COVID-19. A descriptive analysis was performed comparing in and out-patients.
Results: During the 07/01-12/04/22 timeframe a total of 400 patients were treated. At the moment we have collected complete clinical data for 255. These were divided into two separate groups: outpatients (62,75%) and inpatients (37,25%). In the outpatient group we observed lower median age (p=0,0001), greater number of female (p=0,01), a greater prevalence of immunodeficiency (p=0,0001) and obesity (p=0,01) risk factors. On the other hand, in the inpatient group we found more patients with the following risk factors: a greater age (p=0,0002) and cardiovascular risk factor (p=0,0001). Moreover, it was compared the number of fully vaccinated patients (with a complete cycle) and non vaccinated ones in the two groups, with a greater number of vaccinated persons in the outpatients group (p=0,04).
Conclusions: In our preliminary results short course remdesivir were chosen frequently by clinicians as an option in both hospitalized and out-patients, covering a spectrum of different risk factors, and regarding even patients unable to assume oral therapy. Analysis are ongoing to define the rate of hospitalization or death in the outpatient group and the incidence of severe Covid or death in the inpatient group.
Further studies will be useful to understand the utility of early antiviral therapy in vaccinated patients with breakthrough infections.

Immunological complexity in COVID-19

OP 131 DENDRITIC CELL MATURATION AFTER INFECTION WITH A CLONE OF LEISHMANIA TARENTOLAE EXPRESSING THE SARS-COV-2 SPIKE PROTEIN AS A VACCINE VEHICLE

M. Garziano[1,2], I. Varotto-Boccazzi[3,4], C. Conforti[1], G.M. Cattaneo[3], B. Bisaglia[3], P. Gabrieli[3,4], M. Paroni[3,4], A. Manenti[5], D. Rubolini[6,7], M. Clerici[2,8], E. Montomoli[5,9], G. Zuccotti[1,4], C. Vanetti[1], S. Epis[3,4], M. Biasin[1], C. Bandi[3,4], D. Trabattoni[1]

[1]Department of Biomedical and Clinical Sciences, University of Milan, Milan, Italy, [2]Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy, [3]Department of Biosciences, University of Milan, Milan, Italy, [4]Pediatric CRC 'Romeo ed Enrica Invernizzi', University of Milan, Milan, Italy, [5]VisMederi, Siena, Italy, [6]Department of Environmental Science and Policy, University of Milan, Milan, Italy, [7]Water Research Institute-National Research Council of Italy, IRSA-CNR, Brugherio, Italy, [8]IRCCS Fondazione don Carlo Gnocchi, Milan, Italy, [9]Department of Molecular and Developmental Medicine, University of Siena, Siena, Italy

Background: Protozoa of the genus Leishmania are characterized by their capacity to target macrophages and dendritic cells (DCs). These microorganisms could thus be exploited for the delivery of antigens to immune cells. Leishmania tarentolae is regarded as a non-pathogenic species, already developed as a biofactory for protein production, and explored as a candidate vaccine or vaccine vehicle. However, results on the type of immune polarization determined by L. tarentolae are still inconclusive.

Methods: DCs were derived from human monocytes and exposed to live L. tarentoale, using both the non-engineered P10 strain, and the same strain engineered for expression of the spike protein from SARS-CoV-2. We analysed: 1) parasite internalization in the DCs (Giemsa staining); 2) the capacity of the assayed strains to activate DCs (Flowcytometry) and 3) the type of immune polarization (PCR Array).

Results: DCs effectively internalized protozoans from both strains resulting in a full pattern of maturation, in terms of MHC class II and costimulatory molecules expression (CD80, CD83). In addition, a mixed polarization profile was induced by Leishmania from both strains, with a production of cytokines such as TNF-α, IL-6, IL-9, IFN-ɣ, MCP-1. No significant differences were observed in the comparison between Lt-spike and Lt-wt, with the exceptions concern IL-12p70, whose levels are higher in the supernatant of DCs stimulated by Lt-spike, and MIP and IP-10, higher in presence of Lt-wt.

Conclusions: Our results shown that L. tarentolae is actually capable of targeting DCs, allowing the delivery to these cells of the heterologous protein antigen Spike from SARS-CoV-2, and capable of determining their maturation. Moreover, L. tarentolae results a nearly neutral agent and it could be used as a neutral scaffold for the production and delivery of antigens in vaccination, to be associated with immune-modulating molecules, suitable to skew the immune response on the desired direction.

The mixed cytokine profile suggests L. tarentoale as a neutral vaccine vehicle that could be administered in association with appropriate immune-modulating molecules.

Prevention and access to services during COVID pandemic

OP 132 NARRATIVES AT THE TIME OF SARS-COV-2 VACCINATION

M.G. Marini[1], E. Volpato[2,3], L. Reale[1], M. Portaro[4], A. Uglietti[4]

[1]Fondazione ISTUD, Milan (Italy), [2]Department of Psychology, Università Cattolica del Sacro Cuore, Milan (Italy), [3]IRCCS Fondazione Don Carlo Gnocchi, Milan (Italy), [4]Infectious Diseases&Vaccines Medical Affairs Department, Janssen-Cilag SpA, Cologno Monzese (MI) (Italy)

Background: SARS-CoV-2 is a new coronavirus causing COVID-19. Considering its mortality rate and rapid spread, effective vaccines have been generated to control the pandemic in record time.
The population was called to a choice: to accept or refuse vaccination. Large vaccination clinical trials have shown high efficacy and good safety. Meanwhile different variants of the virus have emerged and booster vaccinations are being implemented, while the polarization between the Pro Vax and the No Vax groups, with in between the Hesitant group, is growing. Narrative ethics is the approach that may help in finding solutions to different positions by being aware of the different narratives, while still working to increase the level of coverage of vaccination.
Material and methods: The main objective of this Cross-sectional Research of Narrative Medicine was to collect the views, social impact, emotional and physical experiences, perceived by the population about vaccination against COVID-19. The analysis was descriptive.
Narratives were read independently by two researchers to understand the dominant and peculiar features of the text. Both were evaluated in aggregate form by breaking down the text and identifying the recurrences and the main semantic clusters using NVivo 12 (QSR International®) software, and finally evaluated qualitatively.
Results: As of November 2021, 79.2% out of a total Italian population of 54,009,901 received at least one dose. Four hundred and twelve narratives were clustered as Pro Vax (86.4%), No Vax (8.3%) and Hesitants (4.4%). Results showed significant differences in length and mode of narratives on vaccination. People from large urban or metropolitan areas (37%) released narratives to a greater extent and were mainly Pro Vax, those who live in the smallest areas (25.2%) tended to participate and to express themselves less, and to be more Hesitant or No Vax.
According to sociological classification of Frank: Chaos, Restitution, and Quest, 147 narratives (49.2%) are related to Chaos among them are those who say a global NO: No Mask, No Social Distancing, No Vax, No Green Pass. Main attribution of Chaos was related to media messaging.
The Quest, 56(18.7%),goes from understanding the causes to being open to the new possibilities of living. The Restitution, 96(32.1%), the position was mostly registered in young people, who wanted to have their normality (78/96) and future back.
Conclusions: This research was able to explore and give voice to the views and perceptions of people from different socioeconomic and cultural backgrounds regarding COVID-19 vaccination. Summing up No Vax and Hesitant groups in this research (52/412) and comparing numbers with the entire Italian population, these results fit with the ~6.600.000 Italians that were not vaccinated in November 2021. Despite an unwillingness to vaccinate many narratives were testifying, hope for future either as restitution of lost normality or building a better new reality.

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Prevention and access to services during COVID pandemic

OP 133 VACCINE-PREVENTABLE DISEASES IN PLWH: ADHERENCE TO RECOMMENDATIONS IN A SINGLE CENTER IN NORTHERN ITALY

F. Pennati, V. Marchese, R. Zilocchi, S. Arsuffi, I. Polesini, F. Gaffurini, D. Castelli, E. Quiros Roldan, F. Castelli, E. Focà

Division of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili Hospital, Brescia, Italy

Background: People living with HIV (PLWH) are at increased risk of infection or can experience more severe morbidity following exposure to vaccine-preventable diseases. Immunization is recommended to prevent them, also in the case of live attenuated vaccines, to the availability of combined antiretroviral therapy (cART) which ensures adequate CD4+ cells recovery (at least >200 cell/μL). However, adherence to immunization is jeopardized between and within countries, due to low awareness of vaccine safety for PLWH among physicians, or vaccine hesitancy among patients. We analyzed the adherence to the recommended vaccines in a cohort of young-adult patients followed by an Infectious Disease Center in Northern Italy.

Material and methods: We performed an observational retrospective study, including all patients aged from 18 to 40 years old at the 31/12/2021 and in care for HIV infection in our Infectious Diseases Centre where a dedicated vaccination service is available. Data were retrieved from patient files and the regional system for vaccinations (SIAVR-Sistema Informativo Anagrafe Vaccinale Regionale). We selected young-adult patients to avoid the bias of vaccine administration due to age (as in case of pneumococcal vaccine and zoster vaccine) or due to recommendations for other diseases (i.e., cancer or cardiovascular diseases), more frequently detected in older patients.

Results: At the end of 2021, 481 patients aged 18-40 were followed in our HIV clinic: 254 (52.7%) Italians and 227 of foreigners, with Romania (6.9%), Nigeria (5.6%) and Brazil (5.2%) more represented. Males were 288 (59.8%). Overall, 163 males (54.3%) declared homo/bisexual activity, while only 20 (4.1%) patients were IDUs. 21 patients discovered HIV in 2021, median years of diagnosis was 7 (IQR 4-12). All patients were on cART, CD4+ T-cells were <200 cell/μL in only 4.4% of them. Pneumococcal immunization (recommended for all PLWH regardless of CD4+) was started in 24 (18.9%) and completed in 18 PLWH (4.9%). Lower rates were recorded for meningococcal immunization: 9 (1.9%) and 15 (3.1%) completed conjugate meningococcal ACWY and meningococcus B vaccine respectively while 20 (4.2%) were ongoing. Among MSM, 18 patients (4.9%) completed HAV immunization, 19 (11.6%) started it, while 30 (18.4%) had HPV vaccination ongoing and 44 (27%) completed it. HPV vaccination coverage was lower among females: only 9 (4.7%) had a complete immunization and 10 (5.2%) started it.

Conclusions: Despite international recommendations and indications of the Italian Ministry of Health, vaccine coverage remains low, with slightly higher rates for vaccination for which HIV disclosure is not required (HAV and HPV among MSM). Studies to assess hesitancy among patients, including possible role of stigma, awareness of physicians and service delivery strategies (HIV clinic dedicated immunization service vs general vaccination units) are needed to understand and address the issue.

Prevention and access to services during COVID pandemic

OP 134 IMPACT OF COVID-19 PANDEMIC ON SEXUAL EXPOSURE AND POST-EXPOSURE PROPHYLAXIS (PEP) PRESCRIPTION APPROPRIATENESS IN A LARGE HOSPITAL, NORTHERN ITALY

S. Arsuffi[1], D. Minisci[1], F.Pennati[1], I. Polesini[1], S. di Luglio[1], E. Quiros-Roldan[1], S. Calza[2], F. Castelli[1], E. Focà[1]

[1]Division of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili Hospital, Brescia, Italy, [2]Unit of Biostatistics and Bioinformatics, Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy

Background: In order to contain the spread of COVID-19 pandemic restrictive rules, based on limitation of social contacts, have been imposed since March of 2020. Access to all health care facilities was strongly reduced. It is unknown if these restrictions reduced sexual high-risk exposures, however HIV post-exposure prophylaxis (PEP) prescription and access to post-exposure surveillance and could be reduced. Our study hypothesis is that, since PEP is a time-dependent prophylaxis, its prescription could have been affected by COVID-19 restrictions.

Material and Methods: This is a retrospective monocentric study, conducted at the ASST Spedali Civili General Hospital. We performed the study relying on data gathered from the post-exposure surveillance program at the Infectious Diseases Unit between 01/01/2019 and 31/12/2021. Data collected included demographic characteristics, prophylaxis and surveillance prescribed and adherence to surveillance programs.

Results: The study population included all 166 subjects who were evaluated in our clinic because of a sexual exposure from 2019 to 2021. In 2019 patients evaluated were 67, in 2020 were 38 and in 2021 were 61. In the total of the record examined, in 145 cases (87.4%) the source has unknown serostatus, in 20 (12.0%) cases it was HIV+, in 1 case (0.6%) it was HIV+/HCV+. PEP was prescribed to 125 patients (76.7%): in 120 cases (96%) the selected regimen was TDF/FTC+RAL bid, while in 5 cases (4%) TAF/FTC/BIC.

Comparing PEP prescription with current guidelines, we found 13 cases (7.8%) in which it wasn't prescribed even if it would have been recommended, while in 14 cases (8.4%) it was prescribed even if there would have been no indication.

Considering sexually transmitted infections (STD) other than HIV, screening was prescribed in 90 cases (54.2%) and antibiotic prophylaxis in 42 cases (25.3%).

We also evaluated adherence to PEP through patients' compliance to drug dispensation: 4 patients (3.2%) refused PEP, 21 patients (16.8%) did not receive all the dispensations, in 99 cases (79.2%) the delivery was completed, while 1 patient (0.8%) received prophylaxis during hospitalization.

52 patients (31.3%) did not complete the surveillance program, in 10 cases (6.2%) it was not indicated, in 82 (49.3%) it was completed, 22 patients (13.2%) continued follow up in STD Service.

Conclusions: Our study evidences a significant reduction of access to post-exposure surveillance program during first waves of COVID-19 pandemic, with a normalization during 2021. Since the 16% of exposed subject received an inappropriate indication regarding PEP and we also found a high rate of subjects lost to follow up and who did not complete PEP when recommended, there is a need to standardize the PEP prescription and implement strategies to improve retention in care after first evaluation.

Prevention and access to services during COVID pandemic

OP 135 LOOKING FOR 90-90-90 GOALS: A REAL LIFE EXPERIENCE DURING SARS-COV-2 PANDEMIA

G. Brucci[1,2], S. Dettori[1,2], V. Busin[3], L. Taramasso[2], A. Vena[1,2], F. Mina[3], S. Beltramini[3], D. Malucelli[4], S. Mora[5], M. Giacomini[5], M. Bassetti[1,2], A. Di Biagio[1,2]

[1]Department of Health Sciences (DISSAL), University of Genoa, Genoa, Italy, [2]Infectious Diseases Unit, Ospedale Policlinico San Martino IRCCS, Genoa, Italy, [3]Pharmacy Unit, Ospedale Policlinico San Martino IRCCS, Genoa, Italy, [4]Deenova srl, Piacenza, Italy, [5]Department of Engineering and Informatics University of Genoa, Genoa, Italy

Background: The Joint United Nations Programme on HIV/AIDS (UNAIDS) goal is 90-90-90 treatment target for people living with HIV (PWH). The lockdown period due to severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic led to difficulties in the continuum of care of PWH, with possible issues on compliance to scheduled controls and treatment. The aim of this study was to evaluate UNAIDS goals in a tertiary care hospital before (period 1) and during (period 2) SARS-CoV-2 pandemic.

Material and Methods: A retrospective, observational study was conducted from January 2019 to April 2021. Period 1 was from Jan 2019 to Feb 2020; Period 2 from Mar 2020 to Apr 2021. Clinical and laboratory data were collected with electronic data capture system.

Data about antiretroviral therapy (ART) supply and withdrawal were analyzed and collected from an electronic therapy software. Primary objective of the study was to assess punctuality in ART refilling. A punctuality index (Pi) was created to assess ART adherence, calculated as ratio between number of days before or after planned supply and ART duration in days, ranging between -1 (early refill) and +1 (delayed refill), while 0 represented punctuality. Secondary objective was to analyze risk factors for low adherence and virological failure considered as a viral load > 50 cp/mL in one control even if on a second control viral load was suppressed.

Results: Data of 1360 PLWH attending our clinic were collected. In period 1 and 2 PWH on ART were 1290 (95%) and 1187 (100%) respectively. The average Pi was +0.002 (SD 0.18) in period 1 and +0.058 (SD 0.14) in period 2 ($p<0.001$), mainly due to a major delay at the beginning of the pandemic (figure). A lower Pi was found in period 1, in PWH who took single tablet regimens (STR) and in those who switched ART during the study period (table). 437 PWH switched regimen at least once during the two periods, of these 241 (55%) switched from EVG +COBI+FTC+TAF to BIC+TAF+FTC.

Regarding virological failure, 5058 HIV-RNA tests were performed: 2748 (54%) in period 1 and 2310 (46%) in period 2. Virological failure was identified in 188 PWH: 121 (9%) and 67 (6%) in period 1 and 2 ($p= 0.001$). A delay in ART withdrawal according to Pi (OR=2.78; 95%CI = 1.14–6.75; $p=0.04$) and being in multi-drug regimens (OR=1.79; 95%CI = 1.33–1.79; $p<0.001$) resulted associated to the probability of virological failure. Persistent successful virological suppression was found in 1169 (91%) and 1120 (94%) in period 1 and 2 respectively, while HIV-RNA was <50 copies/mL at the last available control in 95% and 96% PWH in each period.

Conclusions: These results emphasize how SARS-CoV-2 pandemic threatened adherence to ART, but, thanks to ART simplification strategies and reorganization of care models, the second and third 90 of UNAIDS goals were confirmed. The Pi allowed a reliable monitoring of PLWH adherence during pandemic and highlighted higher adherence in STR and after switching strategies.

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Prevention and access to services during COVID pandemic

OP 136 THE IMPACT OF COVID-19 PANDEMIC ON ACCESS TO HIV SERVICES AT URBAN CONTEXT-BASED HEALTH FACILITIES SUPPORTED BY CUAMM IN COLLABORATION WITH UNICEF, IN BEIRA MOZAMBIQUE

N. Ronzoni[1,2], C. Di Chiara[1], V. Casigliani[2], E. Barbieri[1], A. Agazzi[1], A. Zin[1], A. Merolle[2], F. Chenene[2], V. Cinturao[2], E. Occa[2], D. Donà[1], G. Putoto[3], C. Giaquinto[1]

[1]Department for Women's and Children's Health, University of Padua, Italy, [2]Doctors with Africa CUAMM, Beira 2100, Mozambique, [3]Operational Research Unit, Doctors with Africa CUAMM, Italy, [4]Department of translational research and new technologies in medicine and surgery - University of Pisa, Italy

Introduction: Since 2014, Doctors with Africa – CUAMM, is implementing in Beira, Mozambique health projects focused on: healthcare workers training, data collecting, health commodities supply and technical support to SAAJs (Serviço Amigo do Adolescente e Jovem), a network of primary health care centers promoting prevention and providing diagnosis, treatment, and retention in care of HIV patients. Starting from March 2020, the global spread of COVID-19 has been severely affecting public-health systems and economies worldwide. We describe the impact that COVID-19 had on the public-health projects supporting SAAJs in Beira, Mozambique.

Methods: Multi-center, retrospective observational study including HIV patients aged 10-24 years old attending SAAJs in Beira. Enrolled and lost to follow-up (LTFU) patients per month and HIV-viral load were considered indicators of CUAMM's implementing strategies. Four pandemic waves affecting Mozambique were identified: a first wave from September to November, 2020, second wave from January to March, 2021, third wave from June to September, 2021 and a fourth current wave started in December, 2021. Data were described with numbers and percentages. Mann-Kendall test was used to assess the monthly trend, and a linear regression model was applied.

Results: Data of eight SAAJs were analyzed from June 2019 to December 2021. The longitudinal evaluation of enrolled and follow-up subjects showed a significant increasing trend, with 35 new subjects per month treated with antiretroviral (ARV) in all SAAJs. The overall monthly number of patients on ARV therapy in December 2021 was five-fold higher than in June 2019 (1603 vs 328), with no decline or arrest after each wave (Fig.1). Moreover, the number of LTFU patients showed a decline of 3‰ each month across the analyzed period (Fig.2). To support these findings, has been found a coherent viral suppression achieved in most HIV-treated patients from March, 2021 to December, 2021.

Conclusions: All government health-centers involved and supported by CUAMM projects, treating youths living with HIV in Beira, presented with a higher number of treated patients at every time point of the follow-up. The ongoing pandemic seems not to have impacted health systems implementation programs in this country. Other studies are needed to support this encouraging hypothesis.

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Prevention and access to services during COVID pandemic

OP 137 HAV, HBV AND HPV VACCINATION COVERAGE RATE IN A COMMUNITY-BASED PRE-EXPOSURE PROPHYLAXIS PROGRAM IN MILAN

C. Muccini[1,2], A. Tavelli[1,3], R. Rossotti[1,4], D. Calzavara[1], P. Vinti[1], A. De Bona[1,3], S. Bossolasco[1,2], D. Canetti[1,2], D. Tesoro[1,3], G. Mulè[1,3], A. Foschi[1,5], R. Repossi[1], V. Ferrara[1], A. D'Arminio Monforte[1,3], M. Cernuschi[1,2]

[1]Milano Checkpoint, Milano, [2]IRCCS San Raffaele Scientific Institute, Milano, [3]ASST Santi Paolo e Carlo, Milano, [4]ASST Niguarda Hospital, Milano, [5]ASST Fatebenefratelli Sacco

Background: Community-based organizations that provide pre-exposure prophylaxis (PrEP) are crucial to promote health of people with risky sexual behaviors, such as men who have sex with men (MSM).
Aim of our study is to assess HAV, HBV and HPV vaccination coverage before and during a PrEP program in Milan and evaluate factors associated with missing vaccinations.
Methods: This is a retrospective study including people attending a community-based PrEP service who started prophylaxis between October 2017 and March 2022. Before starting PrEP, all the participants were screened for HAV and HBV infection. Data on HAV, HBV and HPV vaccinations were collected from questionnaires filled at each visit. Participants with at least one visit of follow-up were included; dropout was defined as person without any visit in the last 12 months.
We considered a person vaccinated/protected before starting PrEP based on serology (HAV IgG positive, HBsAb>10 mUI/ml and HbsAg negative) and self-reported questionnaire, and after starting PrEP if at least one dose of vaccination was recorded during the follow-up.
Characteristics were reported as median (interquartile range) or frequency (%). Poisson regression model was used to estimate incidence rate ratio (IRR) and 95% confidence intervals (CIs) for factors associated with missing vaccinations.
Results: The analysis included 566 participants with a median age of 36 (31-44) years; 494 (87.3%) were MSM and 460 (81.3%) Italian.
At the first visit, 224/534 (42.0%) PrEP users needed vaccination coverage for HAV infection, 132/543 (24.3%) for HBV infection and 256/470 (54.5%) for HPV infection. During the follow-up, 102/224 (45.5%) participants did not receive the recommended vaccination for HAV, 43/132 (32.3%) for HBV and 76/256 (29.7%) for HPV.
Dropout participants were 42 (32.0%) among 131 users who missed at least one vaccination and 8 (3.3%) among 246 who received one or more vaccinations. Others characteristics are reported in Table.
PrEP users who did not undergo vaccinations were less frequently older (IRR 0.74, 95%CI 0.61-0.90, p=0.003), MSM and bisexual (IRR 0.40, 95%CI 0.21-0.78, p=0.007) or sex workers (IRR 0.30, 95%CI 0.11-0.83, p=0.021) and more likely dropout (IRR 8.21, 95%CI 5.67-11.90, p<0.001).
In a multivariate model considering only participants currently linked to PrEP care, missing vaccinations were still less associated with older people (IRR 0.64, 95%CI 0.49-0.84, p=0.001) or sex workers (IRR 0.23, 95%CI 0.05 -0.98, p=0.047); MSM and bisexual were less likely to not receive the recommended vaccination (IRR 0.19, 95%CI 0.07-0.50, p=0.001) in a multivariate model including only dropouts.
Conclusions: Our findings showed that the majority of PrEP users received HAV, HBV and/or HPV vaccinations recommended by a community-based PrEP service. Although missing vaccinations were mainly associated with being dropout, further efforts need to be done to increase coverage rates, especially for younger PrEP users.

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SARS-CoV-2: from in vivo to in vitro

OP 138 CHARACTERIZATION OF SARS-COV-2 EPIDEMIC AND TRANSMISSION DYNAMICS IN CHILDREN OVER THE FOUR COVID-19 WAVES

R. Scutari[1,2], V. Costabile[1,2], L. Colagrossi[2], K. Yu La Rosa[2], V. Fini[2], A. Granaglia[2], E. Agolini[2], V. Lanari[2], S. Chiurchiù[4], L. Romani[4], A. Markowic[4], P. Bernaschi[3], C. Russo[3], A. Novelli[2], S. Bernardi[4], A. Campana[4], A. Villani[4], C.F. Perno[2,3], C. Alteri[1,2]

[1]Department of Oncology and Hemato-Oncology, University of Milan, Milan, Italy, [2]Multimodal Research Area, Bambino Gesù Children Hospital IRCCS, Rome, Italy, [3]Microbiology and Diagnostics in Immunology, Bambino Gesù Children Hospital IRCCS, Rome, Italy, [4]Academic Department of Pediatrics, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy

Background: No definite data were published so far regarding SARS-CoV-2 epidemic in children and potential correlation with clinical presentation. Here, we characterized viral diversity, transmission dynamic and clinical presentation of 1291 SARS-CoV-2 positive children over the four COVID-19 waves in Italy.

Material and Methods: This study included 1291 SARS-CoV-2 sequences, obtained from patients aged ≤12years referred for SARS-CoV-2 diagnosis at Bambino Gesù Children Hospital from March 2020, to February, 2022. To define the phylogenetic structure of the paediatric epidemic against SARS-CoV-2 diversity and time, Maximum Likelihood and Bayesian coalescent methods were performed. 722 SARS-CoV-2 sequences belonged to population aged >12years living in the same area of paediatric population were included.

Results: 722 (55.9%) paediatric patients were male, with a median age of 2 (IQR:1-6) years. Mild infections were the most prevalent (82.8%), followed by moderate/severe (10.9%), and asymptomatic infections (6.3%). 184 (14.3%) patients were hospitalized and 108 (16.1%) had comorbidities.

At least five clades circulated widely in the paediatric population during the four COVID-19 waves. 36.6% of sequences belonged to delta clade, followed by omicron (26.6%), EU (19.6%), alpha (9.8%) and gamma (2.7%) clades. At diagnosis, delta and gamma clades were characterized by higher viral load respect to omicron, alpha and EU clades (8.3 [7.3-8.7] vs 8.0 [6.1-8.6] vs 7.8 [7.1-8.3] vs 7.7 [6.2-8.5] vs 7.2 [6.1-8.4]copies/mL, respectively, P<0.0001). 12.6% of pediatric SARS-CoV-2 sequences were involved in local clusters, 6 of them large (≥10sequences) and involving mainly alpha and delta clades, and 5 small (5-7 sequences) clusters, involving only the omicron clade. No cluster was significantly associated with moderate/severe manifestations, and no cluster carried mutations able to increase pathogenicity, except for one delta chain, characterized by the Spike-Q677H known to enhance viral infectivity. Adult population was present exclusively in the 6 large chains.

Multivariate analysis showed that age <5, gamma and delta clades were positively associated with transmission clusters (adjusted odds ratio, AOR[95%CI]: 1.5 [1.3–1.8] P=0.008; 6.5 [2.7-15.6] P<0.0001; 2.7 [1.4-5.1], P=0.002). Comorbidities and alpha clade were positively and negatively associated with a moderate/severe COVID-19 presentation (AOR: 4.6 [2.7-7.8] P<0.001; 0.3 [0.1-0.9] P=0.034).

Conclusions: This study provides an increased knowledge of SARS-CoV-2 dynamic in children over the four COVID-19 waves, showing definite correlations among community transmission, children's age, and specific clade (also characterized by enhanced infectivity). These results also emphasise that the molecular surveillance in this partially vaccinated population will be essential to closely monitor SARS-CoV-2 evolution and to define potential correlations between SARS-CoV-2 variability and disease manifestations.

SARS-CoV-2: from in vivo to in vitro

OP 139 RAPID CHANGE IN EPIDEMIOLOGICAL AND CLINICAL CHARACTERISTICS OF SARS-COV-2 CIRCULATING VARIANTS IN ITALY IN APRIL-DECEMBER 2021

A. Bergna[1], A. Lai[1], C. Della Ventura[1], B. Bruzzone[2], F. Sagradi[3], F. Ceccherini Silberstein[4], A. Weisz[5], N. Clementi[6], G. Brindicci[7], I. Vicenti[8], V. De Pace[2], L. Lanfranchi[3], M.C. Bellocchi[4], G. Giurato[5], R. Ferrarese[6], A. Lagioia[7], D. Francisci[9], M. Lucente[2], M.R. Cappelletti[3], M. Iannetta[4], F. Rizzo[5], C.R. Santoro[7], C. Fraccalvieri[2], S. Testa[3], L. Carioti[4], T. Rocco[5], M. Clementi[6], L. Sarmati[4], S. Antinori[1], G. Zehender[1] and SCIRE-SARS-CoV-2 Italian research enerprise-collaborative group

[1]Department of Biomedical and Clinical Sciences Luigi Sacco, University of Milan, Milan, Italy, [2]Hygiene Unit, IRCCS AOU San Martino-IST, Genoa, Italy, [3]Unit of Infectious Diseases, Azienda Socio Sanitaria Territoriale Cremona, Cremona, Italy, [4]Infectious Diseases, Tor Vergata University, Rome, Italy, [5]Laboratory of Molecular Medicine and Genomics, Department of Medicine, Surgery and Dentistry 'Scuola Medica Salernitana', University of Salerno, Salerno, Italy, [6]Laboratory of Microbiology and Virology, Università "Vita-Salute" San Raffaele, Milan, Italy, [7]Infectious Diseases Unit, University of Bari, Bari, Italy, [8]Department of Medical Biotechnologies, University of Siena, Siena, Italy, [9]Department of Medicine and Surgery, Clinic of Infectious Diseases, "Santa Maria della Misericordia" Hospital, University of Perugia, Perugia, Italy

Background: Since the end of 2020,multiple SARS-CoV-2 variants have emerged worldwide potentially impacting the effectiveness of current vaccines. We studied epidemiological and clinical data obtained in several Italian regions involved in SARS-CoV-2 variant monitoring in April-December 2021.

Methods: Data were collected at the centers participating to the SCIRE group.We analyzed 2,001 samples obtained by RT-PCR variant screening assays (n=821), spike Sanger (n=213) and Next Generation Sequencing (n=43), and Whole Genome Sequencing (n=924).

Results: Samples were collected from centers located in Apulia (n=143), Basilicata (n=14), Campania (n=57), Calabria (n=26), Lazio (n=192), Liguria (n=375), Lombardy (n=1,145), and Umbria (n=49). In the first 3 months the Alpha variant (B.1.1.7/20I) was prevalent with a proportion of 70.2% (April), 67.7%(May) and 56.1%(June). Starting from June B.1.617.2/21A was firstly observed in Liguria and Lazio (16%) together with 1 and 2 cases of Delta sub-lineages in Apulia and Campania. The Delta variant and its descendants became prevalent from July. However, while in July clade 21A (67.7%) was predominant, 21J became prevalent in subsequent months. The Gamma variant (P.1-P.1.1/20J) was observed until July with a prevalence of 14.4%,24%,15.8%, and 1.4% in April, May, June and July ,respectively. The last case of Beta variant (B.1.351/20H) was reported in June, never reaching a prevalence >2%. A single case of Kappa (B.1.617.1/21B) and Mu (B.1.621/21H) variants was observed in May and July in Liguria and Lombardy, respectively; 5 cases of Iota (B.1.526/21F) were detected in June in Liguria. The first cases of Omicron variant were observed in the beginning and at the end of November in Lombardy (n=4) and in Umbria (n=1), overall increasing to 14.2% in December. We observed an increasing number of vaccinated subjects overtime, with the highest proportion in October (70%). Overall,40% of subjects were not vaccinated with a significantly lower median age compared to vaccinated subjects (45 vs. 61,p<0.001). Twelve patients reported previous exposure to COVID-19,11 were unvaccinated subjects. Most vaccinated subjects reported 2 doses (75.9%) of which 50.7% with BNT162b2 vaccine.

Stratifying patients according to viral variant, a largest proportion of symptomatic patients (56.4%) was observed among those carrying Delta variant.In the subset with known vaccination and clinical status,unvaccinated and vaccinated subjects had the highest proportion of death with Alpha (50%) and Delta descendent (66.7%), respectively. The Omicron variant was largely present (90%) in non-hospitalized vaccinated subjects,of which 60% were symptomatic.

Conclusions: This study provides insights into the rapid change in the epidemiological landscape of SARS-CoV-2 variants in Italy, reinforcing the need of continuous surveillance of viral variants. The association between genomic and clinical features allowed us to evaluate the role of vaccination with respect to severity of disease.

SARS-CoV-2: from in vivo to in vitro

OP 140 HIGHER VIRAL LOAD (VL) IN NASOPHARYNGEAL SWAB (NPS) OF INDIVIDUALS INFECTED WITH OMICRON BA.2 SARS-COV-2, COMPARED TO ALPHA, GAMMA, DELTA AND OMICRON BA.1 VARIANTS OF CONCERN (VOCS)

I. Mastrorosa[1], A. Cozzi-Lepri[2], F. Colavita[1], E. Lalle[1], V. Mazzotta[1], G. Matusali[1], C. Cimaglia[1], J. Paulicelli[1], L. Fabeni[1], F. Carletti[1], S. Rosati[1], S. Vita[1], G. Giannico[1], P. Piselli[1], E. Biliotti[1], S. Al Moghazi[1], S. Mosti[1], E. Girardi[1], E. Nicastri[1], A.R. Garbuglia[1], F. Vaia[1], A. Antinori[1]

[1]National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [2]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, UCL, London, United Kingdom

Background: SARS-CoV-2 has evolved, leading to the emergence of new VOCs with significant impact on transmissibility. Although the transmission process is complex, higher VL can be considered as a proxy for greater transmissibility. The aim of this analysis was to compare VL across a set of representative VOCs observed in mildly symptomatic patients (pts).

Methods: Observational single-center comparative analysis of pts with early mild-to-moderate COVID-19, enrolled within the monoclonal antibodies and antiviral access program at the National Institute for Infectious Diseases "Lazzaro Spallanzani" in Rome. Here, we considered the first visit at time of drug administration. Pts' characteristics, including vital signs, laboratory tests and self-reported symptoms were collected. Semi-quantitative estimation of VL in NPS was assessed by RT-PCR using DiaSorin Simplexa®COVID-19 Direct platform (DiaSorin, Italy) or ABBOTT ALINITY m SARS-COV-2 ASSAY (Abbott Laboratories,Germany), based on cycle threshold (CT) values. Identification of VOCs was conducted by Sanger sequencing of the Spike coding gene. CT values were compared between samples analyzed through the same platform. Main pts' characteristics were compared by VOCs using Chi-square or Mann-Whitney test. The average causal effect of VOCs (the exposure of interest/intervention) was estimated on the CT values fitted in the log2 scale. To adjust for the effects of the confounders, we modelled both the exposure (through inverse probability weighting) and the outcome (via regression) or both (doubly robust).

Results: Since March 2021, 706 pts was included in the analysis. VOCs were: 67 (10%) Alpha, 24 (3%) Gamma, 240 (34%) Delta, 241 (34%) Omicron BA.1, 134 (19%) Omicron BA.2. Compared to Omicron, pts identified with Alpha, Gamma and Delta showed more alterations in inflammatory parameters ($p<0.001$) and lower peripheral oxygen saturation ($p<0.001$), and a higher proportion with fever ($p=0.030$). No evidence for a difference in mean symptoms score was observed ($p=0.504$, Table). CT values for BA.1 and BA.2 were lower than Delta and BA.1, respectively ($p=0.031$ and $p<0.001$, Figure). After adjusting for calendar time, age, immunodeficiency and vaccination, CT values for Gamma and Delta were lower than Alpha ($p=0.003$ and $p=0.007$, respectively), for Delta were higher than BA.1 and BA.2 ($p=0.008$ and $p<0.001$, respectively), for BA.2 were lower than BA.1 ($p<0.001$) but we found little evidence for a difference between Gamma and Delta ($p=0.067$).

Conclusions: Our analysis provides evidence for higher VL of SARS-CoV-2 BA.2 compared to previous VOCs, even after considering factors potentially contributing to the amount of viral RNA in NPS. This finding suggests increased transmissibility of BA.2 but we cannot rule out residual confounding due to waning immunity of vaccination. Larger studies are necessary to clarify potential mechanisms for increased transmissibility and to provide guidance for public health measures.

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SARS-CoV-2: from in vivo to in vitro

OP 141 DOPAMINE REDUCES SARS-COV-2 REPLICATION THROUGH DOWNREGULATION OF D2 RECEPTORS AND UPREGULATION OF TYPE-I INTERFERONS

F. Limanaqi[1,2], D. Borana[2], S. Zecchini[2], G. Cappelletti[2], S. Strizzi[2], D. Trabattoni[2], M. Clerici[1,3], M. Biasin[2]

[1]Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy, [2]Department of Biomedical and Clinical Sciences L. Sacco, University of Milan, Milan, Italy, [3]Don C. Gnocchi Foundation, IRCCS Foundation, Milan, Italy

Background: Recent evidence suggests that SARS-CoV-2 may hinder immune responses via dopamine (DA)-related mechanisms. While DA receptors (DRs) were hypothesized to be exploited by the virus to improve its entry and life-cycle within cells, SARS-CoV-2 was documented to alter L-Dopa-Decarboxylase (DDC), the rate-limiting enzyme for the conversion of L-DOPA to DA. Nonetheless, studies addressing the specific role of DA in the frame of SARS-CoV-2 infection are still missing. Besides mere neurological manifestations associated with COVID-19, DA-related alterations may lead to a plethora of systemic effects, since DRs are expressed in a variety of immune cell subpopulations and organs targeted by SARS-CoV-2. In the present study we investigate the role of DA in SARS-CoV-2 replication along with potential links with innate immune pathways in CaLu-3 human epithelial lung cells.

Methods: CaLu-3 cells were pretreated with DA (10nm-100uM, 1h), D1/D2DR agonists and antagonists (10uM, alone or 30 min prior to DA administration), or Type-I IFNs (a,b, 100 IU/ml, 16h). Cells were infected with SARS-CoV-2 (MOI 0.05) for 3h and then washed in PBS. All the compounds were added post-infection. Supernatants were harvested at 24 and 48h to assess viral replication by RT-qPCR. At 48h, cells were either collected for RNA extraction, reverse-transcription and qPCR, or fixed in PFA 4% and further processed for double immunofluorescence against D2DR and SARS-CoV-2 Nucleocapsid protein. MTT was performed to assess cell viability.

Results: Administration of DA in the non-toxic 10-100 uM range, dose-dependently reduced viral replication in CaLu-3 cells. Such doses are known to act on high affinity DRs and induce agonist-dependent receptor internalization. Indeed, the anti-replicative effects of DA were associated with downregulation of D2DRs at both mRNA and protein levels while the amount of D1DRs was not significantly affected. The D2DR agonist produced robust anti-replicative effects which recapitulated those produced by DA and were instead reversed by the D2DR antagonist. Both DA and the D2DR agonist, by inducing D2DR internalization and downregulation, disrupted the dramatic co-localization that occurred between N-SARS-CoV-2 and D2DR proteins. This was associated with upregulation of DDC, Type-I IFNs, ISGs such as IRF3 and MX-A, and downregulation of NLRP3/IL-1b, HMGB1/TLR4, TNF-a, IL-6. In turn, administration of Type-I IFNs, while dramatically reducing SARS-CoV-2 replication, converged in strongly downregulating the expression of D2DR while augmenting DA synthetic enzymes.

Conclusions: Within lung epithelial cells, SARS-CoV-2 produces broad alterations in the DA system, which are bound to dysregulations of Type-I IFN pathways. Although the specific mechanisms bridging D2DR and IFNs remain to be elucidated, we disclose a previously unappreciated correlation among DA and Type-I IFNs which may be disrupted by SARS-CoV-2 for host cell invasion and replication.

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SARS-CoV-2: from in vivo to in vitro

OP 142 DEVELOPMENTAL SAFETY OF NIRMATRELVIR IN ZEBRAFISH EMBRYOS

S. Ferretti[1], E. Quiros-Roldan[1], F. Castelli[1], E. Massardi[3], G. Borsani[3], S. Storti[1], G. Tiecco[1], I. Zanella[2], D. Zizioli[3]

[1]Division of Infectious and Tropical Diseases, ASST Spedali Civili di Brescia, Brescia, Italy; Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy, [2]Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy; Clinical Chemistry Laboratory, Cytogenetics and Molecular Genetics Section, Diagnostic Department, ASST Spedali Civili di Brescia, Brescia, Italy, [3]Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy

Background: Nirmatrelvir (PF-07321332) is an orally bioavailable inhibitor of SARS-CoV-2 3C-like protease (3CLpro). FDA granted its emergency use for the treatment of non-hospitalized high-risk COVID-19 patients. Preliminary toxicology studies in animals (rats, rabbits and monkeys) demonstrated lack of adverse effects and genotoxicity and current published studies showed a good overall safety profile in humans. Zebrafish embryos has emerged as valuable models to study molecule toxicity since their transparency allow easy observation of morphology during developmental processes. Here, we used zebrafish embryos to evaluate developmental effects of nirmatrelvir exposure during early embryonic phase.

Methods: Embryos were generated from AB wild-type zebrafish line. Treatments were conducted at least 3 times with 30 embryos/treatment at gastrula stage (4 hours post fertilization, hpf), with nirmatrelvir exposure at 2, 5, 10, 20 and 25 μM (Cmax 5 μM in humans). A control group treated with fish water was maintained parallelly. Mortality after drug exposure at each dose was recorded at 48 hpf. Embryo length was measured at each dose at 72 hpf. Total weight of 30 embryos was measured at each dose at 72 hpf. Data are expressed as mean ± SEM. The statistical significance was analyzed with Student t-test.

Results: Following nirmatrelvir exposure, mortality and morphological changes in zebrafish embryos were visually assessed at 48 and 72 hpf. We evaluated at 48 hpf the percentage (%) of dead embryos. Nirmatrelvir exposure of zebrafish embryos at gastrula stage did not affect the survival rate in the dose range of 2-10 μM, that is in the range of human therapeutic dosage (Cmax 5 μM), while the drug induced higher mortality at higher doses (20-25 μM) (Figure 1). At 72 hpf, we observed lower fetal length and lower fetal weights only at the highest doses. Till 72 hpf, we also analyzed the embryo morphology to evaluate possible developmental effects of the drug exposure. Nirmatrelvir treated embryos showed normal morphology throughout all the exposure periods.

Conclusions: In zebrafish embryos, nirmatrelvir exposure at gastrula stage caused no evident developmental defects, adding further information to the recent work of Catlin et al. demonstrating early embryonic developmental safety of nirmatrelvir in rats and rabbits. Our results also confirm the observations of Catlin et al. that describe lower fetal weights at very high dosages (1000 mg/kg/day) and further suggested a slight reduction in embryo length at the same high doses. Since pregnant women are at increased risk for severe illness with COVID-19 and COVID-19 in pregnancy is more likely associated with complications that can affect pregnancy (preeclampsia/eclampsia, infections and maternal mortality) or developing baby (preterm birth, severe infants' morbidity/mortality), our data add further information for the drug potential safety during pregnancy and embryonic development in a vertebrate model.

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SARS-CoV-2: from in vivo to in vitro

OP 143 PEPTIDOMIMETIC COVALENT REVERSIBLE INHIBITORS EXHIBIT BROAD-SPECTRUM INHIBITION OF COVS MAIN PROTEASE AND CELLULAR ACTIVITY AGAINST SARS-COV-2: DESIGN, SYNTHESIS, BIOLOGICAL EVALUATION, AND STRUCTURAL BIOLOGY

R. Cannalire[1], F. Esposito[2], I. Stefanelli[1], A Corona[2], C. Cerchia[1], E. Cassese[1], S. Improta[1], P. Storici[3], E. Costanzi[3], E. Tramontano[2], V. Summa[1]

[1]Dipartimento di Farmacia - Università degli Studi di Napoli Federico II, Napoli, Italy, [2]Dipartimento di Scienze della vita e dell'ambiente, Università degli Studi di Cagliari, Cittadella Universitaria di Monserrato, Cagliari, Italy, [3]Elettra-Sincrotrone Basovizza, Trieste, Italy

Background: The pandemic outbreak of SARS-CoV-2 causing COVID-19 represents one of the major health scourges of our time. More than 11 billion doses of vaccines have been administered especially in industrialized countries helping to control of pandemic. However, emerging SARS-CoV-2 variants undermine vaccines and the search for new complementary treatments is mandatory. Optimized oral direct-acting antivirals (DAAs) will improve patient management and may represent another prophylactic option for subjects at high risk. Despite huge repurposing and focused medicinal chemistry efforts, only one iv and two oral DAAs have been approved, but with moderate efficacy or suboptimal pharmacokinetic. Targeting conserved enzymes essential for SARS-CoV-2 and other coronaviruses (CoVs) may create a valuable arsenal for current and future epidemics.
Mpro is a highly conserved cysteine protease with an almost unique P2−P1 specificity for Leu-Gln (1). Compounds targeting the Mpro of different CoVs were repurposed against SARS-CoV-2 and Nirmatrelvir, the first in class provisional approved inhibitor, resulted in a broad-spectrum activity with potent inhibition also against Omicron.
Material and methods: Starting from literature data indicating that known Mpro inhibitors share a Gln mimetic γ-lactam, we designed by combining structure-based approach and molecular modelling different peptidomimetic reversible covalent inhibitors by modifying P2-P3 residues, the electrophilic warhead, and the cap group. The compounds were obtained by convergent solution synthesis and tested in an antiviral screening funnel composed of biochemical (SARS-CoV-2 and MERS Mpros) and cell assays to assess inhibition of SARS-CoV-2 replication and cytotoxicity. X-ray structural biology studies were carried out to validate the molecular modelling predictions and fully characterize the compounds interaction with SARS-CoV-2 Mpro.
Results: Proline was inserted at P2 of the peptidomimetic sequence in order to generate a beta-turn for stabilizing the bioactive conformation and several functionalized proline residues were investigated in order to explore their binding mode and the effect on the antiviral activity (2). The most promising compounds showed low nM/pM potency against the Mpro of SARS-CoV-2 and MERS-CoV and inhibited SARS-CoV-2 replication in different cell lines in the nM range without detectable cytotoxicity. Some inhibitors were co-crystallized with SARS-CoV-2 Mpro showing the formation of the covalent complex and elucidating the binding interactions in the enzymesubstrate pockets.
Conclusions: A series of potent peptidomimetic covalent reversible inhibitors broadly active against different CoVs Mpro and able to block SARS-CoV-2 replication in cells has been discovered. Data herein presented will help in the development of new candidates for COVID-19 treatment.

1) Cannalire R. et al. J. Med. Chem. 2022, 65, 2716.
2) Summa V. et al. 35th ICAR, Seattle (WA, USA), March 21-25, 2022, 046.

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Immunopathogenesis of HIV

OP 144 DISTINCTIVE FEATURES OF IMMUNE MARKERS OF ACTIVATION AND EXHAUSTION IN ADOLESCENTS AND YOUNG ADULTS PEOPLE LIVING WITH HIV INFECTED PERINATALLY VS. ADULT AGE

L. Taramasso[1], C. Dentone[1], D. Fenoglio[2,3], T. Altosole[2], A. Parodi[2], I. Cama[4], C. Campi[4,5], S. Garbarino[4], M. Piana[4,5], S. Mora[6], M. Giacomini[6], L. Labate[7], G. Filaci[2,3], M. Bassetti[1,7], A. Di Biagio[1,7]

[1]Infectious Disease Clinic, IRCCS Policlinico San Martino Hospital, Genoa, Italy, [2]Department of Internal Medicine-Centre of Excellence for Biomedical Research (CEBR), University of Genoa, Italy, [3]Biotherapy Unit, IRCCS Policlinico San Martino, [4]MIDA, Dipartimento di Matematica, Università degli studi di Genova, Genova, Italy, [5]LISCOMP, IRCCS Ospedale Policlinico San Martino, Genova, Italy, [6]Department of Informatics, Bioengineering, Robotics and System Engineering (DIBRIS), University of Genova, Genova, Italy, [7]Department of Health Science (DISSAL), University of Genova and Infectious Disease Clinic, Policlinico San Martino Hospital, Genova, Italy

Background: The aim of this study was to compare the level of activation and exhaustion immune markers in perinatally HIV-infected young adults (PHIV) and patients with similar age, but becoming infected in adulthood (AHIV) and to evaluate which immunological features might better differentiate the two populations.

Methods: This was a cross-sectional study including HIV-infected patients aged ≥18 and <40 years, with HIV-RNA < 50 copies/mL and on ART since at least 12 months. We compared the expression of immune exhaustion measure (PD-1, TIM-3, EOMES), activation markers (CD38+ DR+), and maturation status (naïve, Central Memory [CM], Effector Memory [EM], Terminal EM [TEM]) on CD4+ and CD8+T cells and the frequency of Treg CD4+ and CD8+. The frequency of monocyte populations and their homing markers expression were also measured by flow cytometry. Values were expressed as medians (interquartile range) and compared by Mann Whitney U test. Principal component analysis (PCA) approach and k-means cluster analysis were used to investigate which combination of immunological features better associated with perinatal vs. adult timing of HIV acquisition.

Results: We analyzed 26 PHIV and 18 AHIV with median age of 26 (8.0) and 28 (6.8) years (p 0.080) and history of 20 (9.0) and 2.5 (2.8) years of ART. Patients with PHIV showed significant higher percentages of naïve CD4+ and CD8+ cells and lower percentages of TEM CD4+ and CD8+ cells (Table 1). AHIV consistently exhibited higher expression of exhaustion markers on both CD4+ and CD8+T lymphocytes (PD-1, TIM-3, and EOMES). The analysis of CD4+Treg showed a higher percentage of activated CD4+Tregs (CD45RA-FOXP3high) in AHIV.

PCA was performed for 75 immune markers in 25 PHIV and 17 AHIV. The two vector components obtained by PCA, accounted for 16.9% and 13.9% of the variability of the data. PCA was repeated including only the 10 features whose distribution showed at the same time the highest inter-group difference that were: frequency of TEM CD4+, PD-1+CD4+T cells, TEM CD8+, naïve CD8+T-cells, EOMES+CD8+, PD1+TregCD8+, TIM-3 +TregCD8+, FoxP3+EOMES+CD8+ cells, total CD14+ monocytes and CD11b expression on non-classical (CD14dimCD16+) monocytes.

The two vector components obtained by PCA accounted for 39.9% and 14.3% of the variability of the data. Using these 10 features, we were able to group subjects automatically in two clusters based on the studied markers (Figure 1). The two identified clusters showed a predictive positive value of 1.0 and a predictive negative value of 0.77 for identifying PHIV vs. AHIV.

Conclusions: These data seem to highlight the maturation process of T lymphocytes in PHIV, as compared to AHIV, despite HIV infection since birth. A greater immune-activation was seen in AHIV, and the expression of some immune exhaustion and activation markers seemed allow to discern cellular and innate immunity expression between perinatal vs. adult timing of HIV infection

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Immunopathogenesis of HIV

OP 145 LACK OF HIV TYPE 1 ANTIBODY SEROCONVERSION IN ACUTELY INFECTED INDIVIDUALS TREATED WITH EARLY ANTIRETROVIRAL THERAPY

A. Bertoldi[1], A. Primavera[1], M. Tamburello[2], A. Morellini[2], V. Ferraro[2], S. Vituliano[2], V. D'Urbano[2], T. Lazzarotto[1], L. Calza[3], I. Bon[1]

[1]Microbiology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy, [2]Section of Microbiology, Department of Experimental, Diagnostic and Specialty Medicine, University of Bologna, Bologna, Italy, [3]Clinics of Infectious Diseases, Department of Medical and Surgical Sciences, School of Medicine, University of Bologna, Bologna, Italy

Background: Patients exposed to HIV-1 typically develop HIV-1-specific antibodies within several weeks of primary infection. Rare cases have been reported of patients who are persistently seronegative despite virological markers of HIV-1 infection. We described 2 cases of failure of HIV seroconversion in patients with acute HIV infection in early TARV: a 25-years-old male (Pt1) and a 58-years-old woman (Pt2) who came to our attention on January and September 2021 respectively due to a sexual risk occurred 5 days earlier. We studied the dynamic of viral infection, focusing on the expression of restriction factors (RFs), cellular proteins belonging to innate branch of the immune system, providing an early line of defense against viruses

Methods: Blood samples of Pt1 and Pt2 were collected at T0 (time of first serological testing), T1 and T2 (4 and 16 weeks after starting therapy with BIC/TAF/FTC). Serological (HIV-1 Ag/Ab ECLIA and ELFA test) and virological analysis (HIV-RNA and HIV-DNA) were performed at all time points. RNA and DNA, extracted from PBMCs, were analyzed for expression profile variations of ten RFs (APOBEC3G, MX2, BST, SAMHD1, SERINC3, SERINC5, IFI 16, TRIM11, TRIM5α, STING) by qRT-PCR, comparing the expression profile variation with the results obtained from PBMCs isolated from anonymous healthy donors and from 14 naïve HIV positive patients with long-lasting infection

Results: At baseline, both Pt1 and Pt2 were screened for HIV-1 Ag/Ab with a fourth-generation immunoassay resulting respectively Ab negative and Ag p24 reactive. The HIV-RNA was 3498copies/ml and 575261copies/ml respectively: both patients were infected with HIV-1 B subtype wild type virus. At T1, Pt1 and Pt2 were again HIV-1 Ag/Ab negative with two different immunoenzimatic assays, with a plasma viral load (HIV-RNA) of 216copies/mL and 166copies/mL respectively. At T2, the HIV screening was negative with ELFA test for both patients, although the ECLIA test performed in Pt1 displayed a weak reactivity. At this time, HIV-RNA was TNR (target not detected) and <20copies/mL respectively. The HIV DNA quantification was <35copies/10^6 PBMCs and 753copies/10^6 PBMCs at T0 respectively and under the limit of detection at T1 and T2. Among the RFs analyzed, Pt1 and Pt2 exhibited a statistically significant increment from T0 to T2 of APOBEC3G, MX2, BST and SERINC3 ($p<0.1$). Finally at T0 APOBEC3G, MX2, BST and SERINC3 expression in Pt1 and Pt2 showed a statistically significant downregulation compared to naïve patients with long-lasting infection ($p<0.05$).

Conclusions: Rapid and effective virologic suppression due to early cART may result in levels of antigenic stimulation that are inadequate for developing and maintaining HIV-1–specific antibody responses. The study of these extremely rare cases is fundamental as they underscore the potential unique immunologic effect of early cART in patients with primary HIV-1 infection along with the role of RFs in modulating viral replication.

Immunopathogenesis of HIV

OP 146 EVALUATION OF HCMV SPECIFIC T-CELL RESPONSES IN PLWHIV AND THEIR CORRELATION WITH THE IMMUNE-VIROLOGICAL STATUS AND CLINICAL PARAMETERS

M. Iannetta, A. Lodi, L. Ferrari, A. Imeneo, A. Di Lorenzo, I. Fato, B. Massa, I. Spalliera, B. Rossi, M. Zordan, L. Campogiani, L. Coppola, V. Malagnino, E. Teti, M. Andreoni, L. Sarmati

Department of System Medicine Tor Vergata University, Rome

Chronic human cytomegalovirus (HCMV) infection significantly impacts T-cell immunity in people living with HIV (PLwHIV), eliciting immune senescence, and limiting T-cell capacity to recognise novel antigens. HCMV coinfection has been associated with an increased risk of non-acquired immune deficiency syndrome (AIDS)-defining events.

The HCMV proteins pp65, and Immediate Early-1 (IE1) are targets of the CD8 T-cell response against HCMV. IE1 is expressed early during HCMV replication, therefore T-cells specific to this antigen may be important for protection against HCMV reactivation from latency.

PLwHIV and healthy donors (HD) were included in the study. Epidemiological and clinical data were recorded in an ad hoc database. T-cell responses were assessed with an Interferon (IFN)-γ release assay (IGRA), after overnight stimulation of heparin whole blood with pools of lyophilized peptides, covering the complete sequence of the HCMV IE1 protein and 65 kDa lower matrix phosphoprotein (pp65). For each stimulation a negative and positive control were included. IFN-γ production was assessed with a commercial enzyme linked immunosorbent assay (ELISA). Statistical analysis was performed with GraphPad Prism.

15 PLwHIV and 18 HD were enrolled: M/F: 12/3 and 8/10, respectively; median [interquartile range, IQR] age: 49 [46-62] years and 41 [31-48] years, respectively. 12 PLwHIV were classified as C3 at HIV diagnosis; on enrolment, median [IQR] CD4, CD8 cell counts and CD4/CD8 ratio were 357 [215-682] cells/μl, 820 [584-1390] cells/μl and 0,30 [0,15-0,66], respectively. All patients were under highly active antiretroviral therapy (HAART) since at least 6 months, with at least 3 drugs. Considering HIV-RNA detection, 7 PLwHIV were classified as target non detected (TND), while 8 as target detected, below 50 copies/ml (TD). 5 patients were positive for HBV anti-core antibodies (HBcAb+) and were on tenofovir. Concerning HCMV serology, specific HCMV IgG were detectable in 12/15 PLwHIV, undetectable in 1/15 PLwHIV and the serostatus was unknown in 2/15 individuals. At the CMV-IGRA, IFN-γ was increased in PLwHIV supernatants only upon IE1 stimulation, compared to HD (p=0,014). This result was confirmed after normalising for IFN-γ production in the PHA condition (p=0,004). In PLwHIV, increased IFN-γ production upon IE1 stimulation was associated with C3 classification (p=0,01). No associations with CD4, CD8 counts, CD4/CD8 ratio were found. A positive correlation with age was also identified (p=0,017) (Figure).

Increased production of IFN-γ by T-lymphocyte after IE1 stimulation was shown in PLwHIV compared to HD, and was associated to alder age and CDC C3 stage. HCMV chronic infection can drive T-cells to replicative senescence and increased HCMV-specific T-cell responses have been associated with non-AIDS related events. Further studies are needed to understand the role of increased HCMV-specific T-cell responses in predicting non-AIDS related events in PLwHIV.

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Immunopathogenesis of HIV

OP 147 CROSSTALK BETWEEN GUT MICROBIOTA AND T CELL RESPONSES IN ART-TREATED HIV-1 INFECTED PATIENTS

L. Santinelli[1], L. Maddaloni[1], A. Lazzaro[1], P. Vassalini[1], F. Frasca[2], C.M. Lofaro[1], S. Caiazzo[1], G. Ceccarelli[1], G. Antonelli[2,3], C.M. Mastroianni[1], C. Scagnolari[2], G. d'Ettorre[1]

[1]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Italy, [2]Virology Laboratory, Department of Molecular Medicine, Sapienza University of Rome, Italy, [3]Microbiology and Virology Unit, Sapienza University Hospital "Policlinico Umberto I", Rome, Italy

Background: A complex alteration of the immune cell-mediated responses in intestinal mucosa and peripheral blood deeply affect the pathogenesis and the outcome of HIV-1 infection. These events reflect the damage of gut barrier integrity and changes of gut microbiota composition that are linked with the progression of inflammatory symptoms. A comparison between the CD4+ and CD8+ T cells responses in the gut and peripheral districts and an evaluation of their association with gut microbial composition in ART-experienced HIV-1 patients were the main purposes of this study.

Material and Methods: Twenty-eight long-term ART treated HIV-1 infected individuals and ten age-matched healthy volunteers (HC) were enrolled. Peripheral Blood Mononuclear Cells (PBMCs) and Lamina Propria Lymphocytes (LPL) were isolated from peripheral blood samples and gut biopsies collected from five different intestinal sites by pancolonoscopy, respectively. The expression of markers of immune activation (CD38, HLADR) and of IFN-γ and IL-17A in naïve, central memory (TCM) and effector memory (TEM) CD4+ and CD8+ T cells was evaluated by multi-parametric flow cytometry. The analysis of faecal microbiota composition was performed in a subgroup of HIV-1 infected patients (n=10) by 16S rRNA gene sequencing.

Results: HIV-1 infected individuals (19 males and 9 females) had increased frequency of intestinal and peripheral CD4+ and CD8+ T cells subsets expressing CD38 and HLADR as compared to healthy subjects ($p<0.05$). On average, T cell immune activation levels showed a higher value in the gut than in the blood ($p<0.05$). Differences in the frequencies of CD4+ and CD8+ T cell subsets (naïve, TCM, TEM) expressing IFN-γ and/or IL17-A were recorded between HC and HIV-1 infected patients, who exhibited lower levels of these T cell subsets in the blood as compared to the intestinal district ($p<0.05$). Also, HIV-1-infected individuals differed in the fecal microbiota composition, exhibiting a reduction in the levels of Bifidobacteriacae ($p=0.03$) and Ruminococcaceae ($p=0.03$) families compared to uninfected controls. A correlation between the gut frequency of CD4+ and CD8+ T cells expression of IFN-γ/IL-17A and the levels of distinct bacterial families (e.g., Bifidobacteriacae, Prevotellaceae, Lactobacillaceae, Clostridiales) was observed.

Conclusions: This comparative analysis of the frequency, phenotype, activation, and functional status of CD4+ and CD8+ T cells between intestinal mucosa and peripheral compartments of long-term HIV-1-infected patients provides insights into the role of mucosal T cell response in HIV-1 immunopathogenesis and emphasize the intriguing association between microbiota and alterations in mucosal levels of T cell activation, Th1 and Th17.

Immunopathogenesis of HIV

OP 148 LARGE PROPORTION OF NEW HIV DIAGNOSES SUSTAINED BY NON-B SUBTYPES – CLINICAL AND IMMUNOLOGICAL CORRELATES

G. Bozzi[1], P. Saltini[1], G. Butta[2], C. Bobbio[1], A. Muscatello[1], S. Ludovisi[1], A. Gori[1,3], A. Bandera[1,3], L. Manganaro[1,2]

[1]Infection Diseases Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico - Milan, Italy, [2]Virology Unit, INGM-Istituto Nazionale di Genetica Molecolare - Milan, Italy, [3]Department of Pathophysiology and Transplantation, University of Milan - Milan, Italy

Background: Non-B subtypes, once rare in the European HIV-1 epidemic, are nowadays becoming established in Italy. While of epidemiological interest, clinical correlates of such diffusion are yet to be understood. For subtype C, altered susceptibility to RT inhibitors has been described, and CD4 T cell subsets that express more CCR5 have been shown to be more susceptible to infection; other subtypes are not equally characterized. We conducted a sub-analysis of a still-enrolling monocentric study dedicated to better understand latency in stem memory T-cells, comparing features of newly diagnosed individuals carrying B and non-B subtypes.

Methods: Sub-analysis of the GR-2018-12365699 study. A cohort of naïve outpatients newly diagnosed with HIV from 11/2019 at IRCCS Policlinico, Milan was studied. Characteristics of individuals with B vs. non-B subtypes were compared with Mann–Whitney test for quantitative variables and Fisher test for categorical variables. Pre-ART CD4 T cell immunophenotype was determined after staining with membrane antibodies allowing discrimination among different CD4 T cell subsets. After membrane staining cells were acquired on the BD-Symphony machine and data were analyzed on FlowJo Software.

Results: A total of 25 new diagnoses were analyzed, 13 with primary infection (compatible Western blot, known time of seroconversion and/or clinical syndrome) and 12 with chronic infection. Median age was 36 [IQR 30.5 - 42], sex was male in 24/25 (96%) cases. Country of birth was Italy in 19/25 (75%), foreigners were European in 2/6 and South American in 4/6 cases. Route of transmission was HO in 21/25 cases (84%) and HE in 4/25 cases (16%). Median CD4 count was 427/mcL [295 - 653] and median plasma HIV RNA was 58400 cp/mL [34950 - 161500] at diagnosis. A total of 7/25 (28%) patients harbored non-B subtypes: 4 had CRF02_AG; 2 had A1; 1 had C. None had transmitted drug resistance (TDR) to antiretrovirals, while 3 with clade B had TDR. Carrying non-B subtypes did not show association to having acute infection, to route of transmission, to country of birth or CD4 count at diagnosis. It was instead associated to plasma HIV RNA values at diagnosis (p=0.04), in particular with higher loads for non-B patients. At immunophenotyping, while we observed a decrease in peripheral CD4 Central Memory, Effector memory and Temra subsets in HIV patients infected with non-B strains compared to healthy individuals, we observed a statistically significant decrease in Effector Memory subset in HIV-positive individuals infected with non-B subtype compared to individuals infected with a B subtype.

Conclusions: Our monocentric cohort confirms that non-B subtypes are sustaining large shares of new HIV-1 diagnoses and becoming endemic. Significantly different proportions in the Effector Memory subset might reflect subtle discrepancies in natural history and even impact drug susceptibility. A cohort expansion and 1-year post-ART timepoint analysis are underway.

Antiretroviral therapy

Issues on antiretroviral therapy

P 1 REAL-WORLD DATA ON THE EFFECTIVENESS AND SAFETY OF BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE (B/F/TAF) IN PEOPLE LIVING WITH HIV: 12-MONTH RESULTS OF THE ITALIAN BICSTAR COHORT

A. Antinori[1], S. Rusconi[2], D. Canetti[3], V. Esposito[4], E. Quiros-Roldan[5], B. Candelaresi[6], A. D'Arminio Monforte[7], M. Andreoni[8], A. Saracino[9], A. Marongiu[10], L. Albini[10], R. Caldera[11], G. Forcina[10], G. Di Perri[12]

[1]HIV/AIDS Department, National Institute of Infectious Diseases, L. Spallanzani, IRCCS, Rome, Italy, [2]Infectious Diseases Unit, ASST Ovest Milanese – University of Milan, Milan, Italy, [3]Clinic of Infectious Diseases, IRCCS San Raffaele Scientific Institute, Milan, Italy, [4]Infectious Diseases and Gender Medicine Unit D. Cotugno Hospital-A.O. dei Colli, Naples, Italy, [5]Division of Infectious and Tropical Medicine, ASST Spedali Civili, Brescia, Italy, [6]Infectious Diseases Clinic, Department of Biological Sciences and Public Health, Marche Polytechnic University, Ancona, Italy, [7]Clinic of Infectious Diseases, Department of Health Sciences, University of Milan, "ASST Santi Paolo e Carlo", Milan, Italy, [8]Infectious Diseases Clinic, University Hospital "Tor Vergata", Rome, Italy, [9]Division of Infectious Diseases, Bari University Hospital, University of Bari, Bari, Italy, [10]Gilead Sciences Europe Ltd, Stockley Park, Uxbridge, UK, [11]Gilead Sciences Srl, Milan, Italy, [12]Department of Medical Sciences, Infectious Diseases, University of Turin, Turin, Italy

Background: BICSTaR (GS-EU-380-4472) is an ongoing, multi-country, observational cohort study evaluating the effectiveness and safety of B/F/TAF in routine clinical practice in antiretroviral therapy (ART)-naive (TN) and ART-experienced (TE) people living with HIV. Here we present the month 12 (M12) results from the Italian cohort.
Material and methods: M12 evaluation included data from participants with either a M12 visit or discontinuation prior to M12 at data cut (Aug2021). Outcomes of interest included treatment persistence, viral suppression (HIV-1 RNA <50 cp/mL; missing=excluded), weight change, and drug-related non-serious and serious adverse events (DRAEs, DRSAEs).
Results: The analysis set consisted of 94 PLWH (88 TE, 6 TN): 81% male, 43% ≥50 years of age. Baseline (BL) demographic and HIV-related characteristics are shown in Table 1. Comorbidities were documented in 67% of participants (≥10%: hyperlipidemia [30%], musculoskeletal disorders [21%], hypertension [17%], and cardiovascular disorders [11%]); 52% received concomitant medication/supplements (≥10%: vitamins [28%; cholecalciferol (26%)], lipid-modifying agents [15%], and agents acting on the reninangiotensin system [13%]).
Main reason for switch to B/F/TAF in TE participants was simplification of ART (97%). TE had a median of 3 previous antiretroviral regimens (Q1, Q3 [2, 6]); 19% had a history of virologic failure, 11% had prior evidence of resistance-associated mutations (RAMs); 97% of TE were on suppressive ART, most commonly elvitegravir/cobicistat/F/TAF (56%), dolutegravir+F/TAF (11%) and rilpivirine/F/TAF (7%).
Of participants with available HIV-1 RNA data at M12 (n=86), HIV-1 RNA was <50 cp/mL in 100% (81/81) TE and 100% (5/5) TN. No major RAMs to components of B/F/TAF were reported.
M12 persistence on B/F/TAF was 99% (1 B/F/TAF discontinuation at investigator's discretion). Two participants discontinued the study without B/F/TAF discontinuation; moreover, two were lost to follow-up.
In total, 4 DRAEs (insomnia [2], tongue disorder [1], paraesthesia [1]) were reported in 4 (4%) participants. In TE (70 with data at BL and M12), the baseline weight was 76 kg (Q1, Q3 [68, 83]), and the median weight change at M12 was 0.0 kg (Q1, Q3 [-3.0, +3.0], p=n.s.). Weight gains of >5% and >10% in TE were reported in 16% (11/70) and 3% (2/70), respectively. Weight loss of >5% and >10% were reported with the same frequency: 16% (11/70) and 3% (2/70), respectively. Median BL BMI in TE was
24.6 kg/m2 (n=70; Q1, Q3 [22.3, 26.2]). At M12, there was no change in BMI (0.0 kg/m2, median (Q1, Q3 [-0.9, +0.9])).
Conclusion: The Italian BICSTaR cohort showed high persistence on B/F/TAF after one year with no discontinuation due to DRAEs or virologic failure. B/F/TAF achieved high rates of viral suppression at M12 without emergence of resistance to its components. This supports real-world evidence of the safety and effectiveness of B/F/TAF, including TE participants with a history of multiple regimen changes.

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Antiretroviral therapy

Issues on antiretroviral therapy

P 2 ANTIRETROVIRAL THERAPY IN NAÏVE PATIENTS: PERUGIA'S COHORT DURING COVID PANDEMIA

A. Lanzi, G. De Socio, E. Schiaroli, S. Benedetti, P. Milani, E. Stolaj, D. Francisci

Clinic of Infectious Diseases, Department of Medicine and Surgery, University of Perugia, "Ospedale Santa Maria della Misericordia", Perugia, Italy

Background: The impact of SARS-CoV-2 pandemic on outpatient activity has yet to be fully understood. The aim of this study was to investigate in HIV-infected patients diagnosed between 2019 and 2021, naive to Anti Retroviral Therapy (ART), the efficacy of ART and retention in care.

Methods: New HIV diagnosed patients between 2019 and 2021, naïve to ART, have been enrolled by the "Infectious Diseases outpatient clinic" of Perugia. Data from those patients have been gathered from electronic health records and inserted in a cohort retrospective monocentric study. The laboratory response to ART has been evaluated by comparing the baseline limphocyte T CD4 cell count and plasmatic HIV-RNA at the latest data available at march 2022. A percentage of patients lost to follow-up had to be taken into account for retention in care analysis.

Results: 72 patients, diagnosed in the past 3 years, were enrolled. Among these, 12 (16.6%) were lost to follow-up, including 4 who never withdrew their test, 3 transferred to another center, 5 who did not show up for visits. Clinical and demographic characteristics were reported in the table. 70.6% (48/68) of analyzed patients were male, with a mean age of 41.06 (SD 15.0 years). At diagnosis of HIV infection, 27/63 (42.9%) patients presented with CD4 <200 cells-ul, of these 13 (20.6%) with AIDS defining diseases. The most represented among the opportunistic pathologies (7/63 - 11.1%) was Pneumocystis Jirovecii Pneumonia, followed by disseminated Cytomegalovirus infection (3/ 63 - 4.8%) and Kaposi's sarcoma (2/ 63 - 3.2%). All patients who showed up for medical examination (87.5% - 63 of 72) have undergone ART and the mean follow-up period has been 19 months (SD 10.8 months, range 2.3-37.13). An immuno-virological improvement was observed with reduction of mean viremia from 895,073.5 cp/ml (SD 1,829,676.7) to 37.3 cp/ml (SD 120.5) ($p<0.001$, t-test); the patients with viral suppression after at least 6 months of ART were 56/63 patients (88.9%). The increase in the mean of CD4 was from 335.4 (SD 270.0) cell-ul to 576.3 (SD 384.4) cell-ul ($p<0.001$, chi square). By analyzing the characteristics of poorly compliant patients (5/72, 6.9%) and patients lost to follow-up (9/72, 12.5%) have been assessed that these were mainly represented by foreign people (7 of 14).

Comparing the current data with those obtained by analyzing patients in the pre-pandemic era from our Infectious Diseases clinic (from 2005 to 2017) we found an improvement both in terms of retention in care (from 70.3% to 83.3%) and in terms of suppressed viremia (from 82% to 88.9%).

Conclusions: Naïve HIV patients diagnosed in the past 3 years have shown a retention in care of 83.3% and undetectable HIV-RNA of 88.9% both below the expected level of 90% even if close to being reached. Foreign patients were reported among those lost to follow-up. Further efforts will be made to be able to understand and intervene on the social causes of this therapeutic ineffectiveness.

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Antiretroviral therapy

Issues on antiretroviral therapy

P 3 DURABILITY OF DORAVIRINE CO-FORMULATED WITH LAMIVUDINE AND TENOFOVIR DISOPROXIL FUMARATE IN PEOPLE LIVING WITH HIV (PLWH)

F. Alberton[2], D. Ceccarelli[1], R. Lolatto[1], S. Nozza[1], S. Bossolasco[1], V. Spagnuolo[1], E. Bruzzesi[2], M. Chiurlo[2], A. Castagna[1,2], N. Gianotti[1]

[1]Unit of Infectious and Tropical Diseases, IRCSS San Raffaele Scientific Institute, Milan, Italy, [2]Vita-Salute San Raffaele University, Milan, Italy

Background: Doravirine (DOR) co-formulated with lamivudine (3TC) and tenofovir disoproxil fumarate (TDF) approval is based on data from the phase 3 DRIVE-AHEAD and DRIVE-FORWARD studies, in which DOR demonstrated non-inferior efficacy compared with efavirenz and superiority in neuropsychiatric tolerability and lipid profile. Aim of this study was to evaluate durability of DOR/3TC/TDF.

Material and methods: Retrospective cohort study including people living with HIV (PLWH) who started DOR/3TC/TDF. Outcomes during follow-up were evaluated at month 3, 6 and 9 and they included viral load and the main chemistry and metabolic parameters. Cumulative probability of being free of discontinuation, without virological failure or with virological success were estimated by Kaplan-Meier curves. The primary endpoint of this study was to evaluate the therapy discontinuation (TD) defined as discontinuation of at least one drug for any reason. Secondary endpoints were virological failure (VF) and virological success (VS), defined as two consecutive observations of HIV-RNA ≥ 50 copies/mL or just one ≥ 1000 copies/mL and HIV-RNA < 50 copies/mL, respectively.

Results: 89 PLWH with HIV-RNA load at baseline (BL) were evaluated (full details of baseline characteristics and causes of start with DOR/3TC/TDF are reported in figure 1, panel A): 85 of them were experienced and 4 naïve, 76 had HIV-RNA < 50 copies/mL at BL, 13 had HIV-RNA ≥ 50 copies/mL at BL. 52 individuals had at least a follow-up observation. Median follow-up was 151 (IQR 55; 295); among individuals with < 50 copies/mL at BL was 162 (IQR 57.2; 307) and 92.0 (IQR 23.0; 193) among people with HIV-RNA ≥ 50 copies/mL (p= 0.223). 5 (5.62%) experienced TD; 3 had HIV-RNA < 50 copies/mL at BL and 2 (15.4%) of them had HIV-RNA ≥ 50 copies/mL at BL. The probability of being free of TD at 365 days was 94% [95% CI (confidence interval) = 88%-99%] (figure 1, panel B). TD occurred after a median of 4 days [(interquartile range) IQR 2.00; 21.0], in particular 21 days (IQR 11.0; 73.0) among the PLWH with HIV-RNA < 50 copies at the BL and 3 days (IQR 2.50; 3.50) in individuals with HIV-RNA ≥ 50 copies/mL at BL (p= 0.564). Overall, switches from DOR/3TC/TDF were due to: drug interaction (1), patient's wish/decision (1), side effects-predominantly from gastrointestinal tract (2) and predominantly from nervous system (1). VF occurred in 1 (2.27%) case; VS was seen in 7(87.5%) individuals and the median time to success was 67 days (IQR 32.0; 98.0. Among 26 individuals, significant 6-month changes from BL were observed in white blood cells (p= 0.03), total lymphocytes (p= 0.04), HDL cholesterol (p= 0.003) and LDL cholesterol (p= 0.03) (figure 1, panel C).

Conclusions: The majority of the individuals (94.4%) of our sample have continued DOR/3TC/TDF over five months of follow-up.

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Antiretroviral therapy

Issues on antiretroviral therapy

P 4 EVALUATION OF SWITCH THERAPY TO ANTIRETROVIRAL REGIMENS WITH DORAVIRINE IN PEOPLE LIVING WITH HIV

C. Candela[2], D. Ceccarelli[1], R. Lolatto[1], D. Canetti[1], M. Cernuschi[1], P. Cinque[1], M. Ranzenigo[2], F. Badalucco[2], A. Castagna[1,2], N. Gianotti[1]

[1]Unit of Infectious and Tropical Diseases, IRCCS San Raffaele Scientific Institute, Milan, Italy, [2]Vita-Salute San Raffaele University, Milan, Italy

Background: Doravirine is a nonnucleoside reverse transcriptase inhibitor with demonstrated efficacy in treatment of HIV infection. The aim of this study was to evaluate the switch therapy to doravirine associated with other antiretrovirals (excluding doravirine/lamivudine/tenofovir disoproxil fumarate combination) in a real-life setting.
Methods: This retrospective cohort study includes treatment-experienced PLWH who switched to antiretroviral regimen with doravirine, with HIV-RNA load at start of treatment (baseline, BL). Primary endpoint was therapy discontinuation(TD) defined as discontinuation of at least one drug of the regimen for any reason. Secondary endpoints were virological failure and virological success defined as two consecutive values of HIV-RNA≥50cps/mL or one value ≥1000cps/mL and achievement of HIV-RNA<50cps/mL, respectively. Results were described by medians with interquartile range(IQR) and frequencies with percentage(%) for continuous and categorical variables, respectively. Mann-Whitney U test and Chi-square test were applied. Kaplan-Meier analysis was used to assess TD-free survival.
Results: Overall, 82 PLWH (59 with HIV-RNA<50cps/mL and 23 with HIV-RNA≥50cps/mL) switched to doravirine-including regimen. Patient's characteristics at BL are summarized in Panel A. Reasons for therapy switch were cardiovascular disease in 4(5%) people, dyslipidemia in 9(11.1%), Panel B drug interactions in 14(17.3%), more effective/simplified drugs in 30(37%), toxicity in 12(14.8%) and viral failure in other 12(14.8%). Median age was 58.4 years, with median duration of HIV infection of 27.9 years. Median follow-up was 162 days (IQR 90;399). Metabolic profile at baseline and variables changes at 6 months are reported in Panel B. Overall, 5 patients experienced TD. Of these, at BL 2 had HIV-RNA<50cps/mL and 3 had HIV-RNA≥50cps/mL. TD occurred at a median of 90 days, specifically 50(IQR 37;64) and 176(IQR 133;277) days for people with HIV-RNA<50cps/mL and HIV-RNA≥50cps/mL at BL, respectively. Reasons for TD were death, simplified treatment available and virological failure in 1 individual each, and toxicity/side effects (predominantly from CNS) in the remaining 2 individuals. The estimated 365-day probability of no discontinuation was 93% (95%CI: 87%;100%), as illustrated in Panel C. HIV-RNA values during follow up were available in 71 patients. We observed 2(4%) virological failure among 49(69%) PLWH starting with HIV-RNA<50cps/mL and 15(68%) achieved virological success among 22 (31%) PLWH starting with HIV-RNA≥50cps/mL.
Conclusion: In our cohort, the discontinuation rate of doravirine was low during a median of 6 months of follow-up.

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Antiretroviral therapy

Issues on antiretroviral therapy

P 5 SWITCHING TO BICTEGRAVIR IN ELDERLY PEOPLE LIVING WITH HIV-1 UNDER VIROLOGIC CONTROL: WEEK 96 RESULTS FROM THE BICTEL COHORT

A. Lazzaro[1], D. Bianchini[1], E. Gentilini[1], E.N. Cavallari[1], C. Fimiani[1], I. Mezzaroma[2], C.M. Mastroianni[1], G. d'Ettorre[1]

[1]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Policlinico Umberto I of Rome, Rome, Italy, [2]Department of Translational and Precision Medicine; Sapienza University of Rome, AOU Policlinico Um-berto I of Rome, Rome, Italy

Background: We present an interim data analysis on week 96 from the BICTEL cohort, a real life observational retrospective cohort of people living with HIV (PLWH) 55 years who were switched to a bictegravir/emtricitabine/tenofovir alafenamide fumarate (BIC/FTC/TAF) single tablet regimen, independently from the previous antiretroviral therapy (ART).

Method: Data were collected from medical records.

Primary objective was long-term efficacy [changes in HIV-RNA levels from baseline (BL) to week 96 (w96)]. Secondary objectives were virological failure (serum HIV-RNA >50 copies/mL), changes in immune and metabolic profile, safety and tolerability.

Data are shown as median values (interquartile range) and simple frequencies (percentage). Longitudinal analysis was assessed by the paired Wilcoxon test for pair-wise comparisons between BL, week 48 (w48) and w96 (p values showed in text), and by the Friedman test for overall comparison (p values showed in figure). p-value < .05 was considered statistically significant, with FDR correction for multiple comparisons. All data were analyzed using RStudio (Version 1.3.1056, 2009-2020 RStudio, PBC).

Results: On March 2022, 88 participants had completed the 96 weeks follow-up: among them 62 were over 55 years old. Only 1 virological failure was detected, because of lack of adherence to ART. Participants with HIV-RNA <50 copies/ml increased from 85 (95%) at BL to 87 (99%) at w96.

From BL to w96, CD4+ T cells count (cells/μL) increased from 570 (311) to 787 (392) (p <.001); CD8+ T cells count increased from 750 (448) to 827 (541) (p .248); CD4+/CD8+ T cells ratio increased from .72 (.29) to .96 (.67) (p <.001).

After a significant slope from BL to w48 (p .009), median total cholesterol levels (md/dL) raised again on w96 and no significant changes were detected between BL and w96 [from 190 (44) to 188 (51) (p .538)]. From BL to w96, HDL and LDL components and ALT did not change significantly. A statistically, yet not clinically, significant increase from BL to w96 was observed for both AST level from 21 (7) to 22 (7) (p .005), and creatinine levels from .93 (.21) to 1.02 (.28) (p <.001), with values within the healthy range. A not significant increase in body weight was detected between BL and w48 from 76.5 (15.5) to 78 (16.5) (p .06), but this trend was not confirmed at w96 when median body weight was 78 (19.6) (w48 versus w96, p .17).

No adverse effects attributed to BIC/FTC/TAF use were reported in the medical records, including signs or symptoms related to CNS disorders.

Conclusions: BIC/FTC/TAF is well tolerated, also in PLWH ≥ 55 years. We observed an overall safe profile on lipidic, renal and hepatic metabolism, without a significant increase in body weight. All but one participant maintained the virological suppression with a significant improvement of CD4+ T cells count and CD4+/CD8+ ratio from BL.

The project has been partially supported by an unrestricted grant from Gilead Sciences for the 48 weeks part.

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Antiretroviral therapy

Issues on antiretroviral therapy

P 6 REAL LIFE EXPERIENCE WITH DORAVIRINE: IMPACT ON METABOLIC ASPECTS AND IMMUNE-VIRAL CONTROL

C. Papalini, A. Lanzi, C. Pallotto, D. Francisci

Infectious Diseases Clinic, Santa Maria della Misericordia Hospital, Università degli studi di Perugia, Perugia, Italy

Background: Doravirine (DOR) is the latest licensed Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI) and is available singly or co-formulated with Tenofovir Diproxil Fumarate/Lamivudine (TDF/3TC) as single-tablet-regimen (STR). According to guidelines, DOR is considered first-line drug in antiretroviral therapy (ART) due to the high genetic barrier and the lower impact on weight gain and lipid metabolism in comparison to Integrase Inhibitors and to Protease Inhibitors, respectively.

Materials and methods: Observational retrospective study focused on PLWH visited at Infectious Diseases Clinic of Santa Maria della Misericordia Hospital of Perugia, Italy, and assuming DOR at the 1st March 2022. From clinical records we collected data about: gender, nationality, age, CDC classification, co-morbidities (hypertension and diabetes), smoking, immune-viral status, biochemical parameters (cholesterol, glycaemia, triglycerides, creatinine, gamma-glutamyl transpeptidase, glutamate pyruvate transaminase), weight, ART, atherosclerotic cardiovascular disease (ASCVD) risk score calculated according to the American College of Cardiology. The immune-viral values and the biochemical ones were collected twice, before and 6 months after starting DOR therapy.

Results: Study population included 40 individuals: 62.5% males, 60% Italians, mean and median age 50.6 and 51 years, respectively. Concerning clinical aspects of HIV infection: 30% were C3 according to CDC classification, 97.5% patients assuming DOR as switch from previous ART and 55% as STR. About the 38/40 non-naïve patients, 15% have switched to DOR because of metabolic problems, 20% to up to date to the latest guidelines, 22.5% because of viral resistance, 7.5% and 22.5% for adverse effects and weight gain with previous ART, respectively. After switching to DOR, viral suppression has been kept and no statistically relevant differences with the previous ART were noticed analyzing ASCVD score, weight and metabolic parameters except for triglycerides, total and HDL cholesterol which resulted lower after DOR starting.

Conclusions: DOR represents a suitable ART showing excellent capacity to keep HIV viremia under control. Analyzing our little study sample, its effect on metabolic issue has demonstrate statistically relevant benefits in term of lowering triglycerides and cholesterol in comparison to previous ART assumed by patients.

Antiretroviral therapy

Issues on antiretroviral therapy

P 7 **STRENGTH OF 2DR-HIV-THERAPY IN HEAVY POLY-PHARMACOLOGICAL TREATMENT OF MULTI-COMORBIDITY PATIENTS**

L. Pagnucco, R. Gulminetti, R. Bruno

UOC Malattie Infettive 1, Dipartimento di Scienze Mediche e Malattie Infettive, Fondazione IRCCS Policlinico San Matteo - Università degli Studi di Pavia. Pavia

Background: Modern combination antiretroviral therapy (cART) has prolonged the life expectancy for pts with HIV infection. Furthermore, compared to their peers, people living with HIV (PLWH) are more likely to suffer from comorbidities that often require the use of numerous medicines with a consequent increased risk of therapeutic failure or poor tolerability. Italian and international guidelines for the Use of Antiretroviral Agents in PLWH, recommend the use of two-drug regimens (2DR) both in naïve patients and, in switch, in experienced pts. It is therefore relevant, in the era of 2DR, to evaluate the efficacy, safety and durability of these therapeutic regimens in polypathological pts with polypharmacy, hemodialysis treatment and pts receiving immunosuppressive therapy.
Methods: We conducted a retrospective cohort study, from December 2015 to February 2022, in pts on 2DR with dolutegravir plus lamivudine (DTG+3TC) or dolutegravir plus rilpivirine (DTG+RPV) and multiple comorbidities The primary endpoint was to assess the efficacy of a 2DR in these pts. Variables collected were sex, age, VL, CD4, comorbidities and concomitant medication. Follow-up accrued from the date of 2DR initiation to the date of treatment discontinuation or to the date of last available visit.
Results: 72 patients, without documented resistance for studied drugs, HBsAg negative, were enrolled; 63% in DTG/3TC and 37% in DTG+ RPV. The presence of polypharmacy was defined as the use of 4 or more medications other than cART. They took overall 199 non-ARV drugs for 67 different comorbidities of cardio-vascular system, bone, kidney, liver, CNS, lung or lipids and glucose homeostasis comorbidities. 3 pts were organ transplant recipients (1 liver, 2 kidney) and 1 bone marrow transplant recipient, 5 pts were on dialysis and, among the 33 pts with a neoplastic disease, 29 pts underwent chemotherapy or immunotherapy (Table 1). The pts had a median follow-up of 42.3 months after treatment switch. During the follow-up no virologic failure occurred. 3 pts presented a viral blip during follow-up in the DTG+ 3TC group (> 200cp/mL) and 2 in the DTG+RPV group (>200 cp/mL) that returned negative at the following control without modifying the antiretroviral treatment. 5 subjects discontinued the treatment because of death (1 neoplastic diseases and 2 cirrhosis in the DTG/3TC group and 1 neoplastic disease in DTG/RPV) and 1 pts was lost to follow-up (DTG/3TC). CD4 mean increment was of 113cells/mcl without a significant change in the CD4/CD8 ratio (values relating to immunosuppressed/neoplastic patients were not considered). A slight improvement of the lipid profile was observed.
Conclusions: 2-DR appears to be safe, effective and well tolerated alternative cART in polypathological pts and in hemodialysis treatment or with severe immunosuppression. Maintenance of virologic suppression was kept in all pts, although 5 temporary viral blips emerged that returned negative at the following control.

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Antiretroviral therapy

Issues on antiretroviral therapy

P 8 **USE OF DORAVIRINE IN EXPERIENCED PEOPLE LIVING WITH HIV: A REAL-LIFE EXPERIENCE**

A. Bitti, A. De Vito, M. Fois, A. Colpani, B. Zauli, M.C. Meloni, S. Bacciu, S. Babudieri, G. Madeddu

Unit of Infectious Diseases, Department of Medical, Surgical, and Experimental Sciences, University of Sassari, Sassari, Italy

Introduction: Doravirine (DOR) is a new non-nucleoside reverse transcriptase inhibitor (NNRTI) that exerts its antiviral effect through a non-competitive inhibition of HIV-1 reverse transcriptase. Comparing with other NNRTIs, it has a higher genetic barrier, better drug interaction profile, an improved efficacy and metabolic safety profile. DOR joins treatment options for people with HIV infection since 2018, and it is recommended by 2019 EACS guidelines as first-line regimen. However, few data are present about its uses in a real life-setting. The focus of our study is to evaluate the efficacy and safety of DOR in clinical practice.

Methods: We performed a retrospective study including all PLWH who started an antiretroviral regimen containing DOR. We collected demographical (age, gender, risk factor for HIV infection, country of origins), clinical (HBsAg, HCV status, data of HIV diagnosis, last detectable HIV-RNA, zenith of HIV-RNA, nadir CD4, CDC stage), viro-immunological data (HIV-RNA, CD4 cell counts), and pharmacological treatment (years of starting antiretroviral treatment, previous treatment).We aimed to evaluate the virological efficacy, safety, and durability of DOR.

Results: We included 32 patients who started a treatment with DOR between 01/06/2021 and 31/12/2021. The mean age was 53.1 ± 8.67 year; the majority of patients were Italian-born, and male.

The majority of patients had a long HIV history, with a median age of duration of infection equal 20 (IQR 12-24.5) years. Eleven (37.5%) patients were inCDC stage C, and only sixwere in A. Despite the duration of HIV infection, the median time of virological suppression was 4.95 (IQR 1.47-11.4) years. The main cohort characteristics are summarized in Table 1.

At the moment of switch, five patients had a detectable HIV-RNA, sign of virological failure. The most common previous regimens were 2NRTI plus nevirapine, followed by 3TC/DTG, TAF/FTC/DRV/c, and DTG+DRV/c (Figure 1).

The majority of PWH started a treatment with TAF/FTC+DOR (12, 37.5%), or TDF/FTC/DOR (21.2%) (Figure 2).

During the follow-up, no adverse events have been reported, and all the patients had an undetectable HIV-RNA.

At six months after switch we observed a significant reduction of median total cholesterol (205[IQR173-225] vs. 198[IQR 168.5-207], p=0.0317), and median LDL cholesterol (124[IQR 104-144] vs. 119[IQR 95-128.5] p=0.0075). No differences regarding creatinine, HDL cholesterol and triglycerideshave been observed(Figure 3).

Conclusions: Our data confirm the efficacy and safety of DOR in a real life setting in long term treated PWH. Furthermore, the switch to DOR resulted in an improvement of lipid profile, especially regarding total and HDL cholesterol.

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Antiretroviral therapy

Issues on antiretroviral therapy

P 9 STATIN INDUCED ANTI-HMGCR MYOPATHY IN A PATIENT UNDERGOING ARV THERAPY: A CASE REPORT

A. Destro[1], R.A. Valia[1], D. Fago[1], R. Aronica[1], V. Mauro[1], F. Cancelli[1], M. Candy[1], S. Valeri[1], M. Ridolfi[1], P. Pasculli[1], P. Guariglia[2], A. Brogi[2], A. Lazzaro[1], C.M. Mastroianni[1], G. d'Ettorre[1]

[1]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Policlinico Umberto I of Rome, Roma Italy, [2]Departmnet of Infectious Diseases, Azienda Ospedaliera Universitaria Policlinico Umberto I of Rome, Roma Italy

Background: The association between statin use and myopathies has long been established, as well as the interaction between this class of drugs and cobicistat based antiretroviral (ARV) therapy, the latter increasing plasma concentration of statins by inhibition of CYP3A4 and transmembrane transporters as breast cancer resistance proteins (BCRP) and organ anions transporter proteins (OATPs). Although the exact pathogenesis of the adverse effect has not been fully understood, the damage is due to direct toxicity of the drug and finishes with its discontinuation. The persisting of muscular damage despite the withdrawal of statins has in the last decades been associated with an immune mediated condition, defined by the development of anti-3-hydroxy-3-methyl-glutaryl-coenzyme A reductase (HMGCR) autoantibodies.

Material and Methods: We describe the case of a 64-years-old-man, living with HIV-1 since 2001, under ARV treatment with DRV/c/FTC/TAF for 1 year, a newly diagnosed HCV infection, and a colon adenocarcinoma. Two months after beginning of rosuvastatin, he presented to the Emergency Department for increasing muscle fatigue and loss of sensation in the lower extremities. Laboratory results showed extremely increased levels of CPK (30334 UI/l), which slightly decreased but remained elevated (over 7000 UI/l), despite the interruption of statin-therapy and massive intravenous hydration. No elevations in autoimmune markers or cryoglobulins were found in the blood, and the specific autoimmune myositis antibodies panel resulted negative. Electromyography showed signs of active myogenic damage and muscular biopsy showed necrosis and regeneration of muscular fibres. To stop the suspected drug-drug interaction with cobicistat, we decided to switch current ARV to BIC/FTC/TAF, although the value of HIV-RNA was undetectable and the count of CD4 T cells was 600 cell/mmc. Because of persisting myositis after the switch, the patient started therapy with methylprednisolone 500mg daily, with a slight reduction of CPK levels and improving muscular strength. Meanwhile HMGCR autoantibodies were detected in the blood, giving the diagnosis. Our patient presented all the classical features of this condition: markedly elevated (cut off 2000UI/l) CPK levels in plasma, proximal muscular weakness, presence of HMGCR antibodies, and a consistent muscular biopsy, with necrosis and regeneration but absence of inflammatory infiltrates.

Conclusions: It is possible that the enzymatic inhibition due to cobicistat led to a marked and persistent elevation of statin concentrations in the blood, causing an extreme overexpression of HMGCR in muscular tissue, triggering the auto-immune response. Specific immunogenic alleles have been described in literature as possible facilitating factors, as well as HCV infection. Genetic screening should be warranted in all patients with risk factors for anti-HMGCR myopathy before beginning therapy with statin, as well as a close follow up afterwards.

Antiretroviral therapy

Issues on antiretroviral therapy

P 10 CARDIOVASCULAR RISK IN PLWHS WITH IP-BASED ARV

N. Leoni, A. Leonardi, M. Garau, F. Ferrari, S. Perra, S. Bergamin, M. Buffa, F. Cabras, G. Caligaris, M.F. Nurchi, G. Sanna, G. Angioni

SC Malattie Infettive, Cagliari; Università degli Studi di Sassari, Sassari

Backgrounds: The increase in the average age of HIV-positive patients is a well-established trend. The management of the experienced and naive patient must take into account the cardiovascular (CVD) risk, amplified by both infection and antiretroviral therapy, as well as the age and inflammatory state. The EACS and the Italian guidelines suggest the evaluation of CVD risk of the HIV patient through different 10-year cardiovascular risk scores: the use of Framingham, widely used and studied for the general population, and the D:A:D score, specific for PLWHs. This score takes into consideration sex, age, smoking, family history of cardiovascular diseases, diabetes, mean systolic blood pressure, total cholesterol and HDL, also specific parameters for the HIV patient: the number of CD4, the exposure years a NRTI and PI, treatment with Abacavir.

Materials and Methods: A cohort of 30 patients practicing ARV with two NRTIs and a boostered IP was considered, compared with a second cohort of 30 patients practicing ARV with two NRTIs and one INI. All patients undergo regular blood tests (last checks January-March 2022), have been virologically suppressed for at least three years and have continued their current therapy from the same time.

In the court of patients who use IP, the average age is 49 years, 26.6% are women, 43% smoke, and have an average of 184 mg/dl of total cholesterol and 47 mg/dl of HDL; 26.6% have Abacavir being treated, and 20% are familiar with cardiovascular diseases. In the cohort of patients using INI, the mean age is 52.6 years, 23.3% are women, 30% are on abacavir therapy, 30% smoke, 16,7% are familiar with cardiovascular diseases, and have an average of 174 mg / dl of cholesterol and 47 of HDL. The analysis continued by calculating 2 scores: Framingham and D:A:D.

Results: Patients who practice ARV with IP have a Framingham score of 11.84% and a D:A:D score of 12.67%. On the other hand, patients treated with INI have a mean Framingham score of 11.6% and a D:A:D score of 8.86%. For the Framingham score, statistical significance was not demonstrated in the comparison between the two cohorts. Instead, the comparison of the D:A:D score was statistically significant (p-value: 0.039).

Conclusions: Cardiovascular risk assessment should be an important routine in the management of the HIV patient and could influence therapeutic approaches. The use of IP-based ARV, due to its effects on the metabolic structure, requires frequent and careful monitoring of the patient, considering switching to therapeutic regimens that affect this aspect less and reducing the CVD risk in a population with a higher average age. The limitations of our study are mainly represented by the small number of the sample examined, and it would be appropriate to extend the case series to other classes of drugs and other pharmacological associations.

Antiretroviral therapy

Issues on new anti-HIV drugs

P 11 **REAL-LIFE OUTCOMES OF DORAVIRINE-BASED DUAL REGIMENS AS SALVAGE AND SIMPLIFICATION THERAPY FOR MULTIDRUG-RESISTANT HIV IN A SERIES OF SEVEN CASES IN LECCO HOSPITAL**

V. Morena[1], F. Conti[1], C. Molteni[1], M. Bottanelli[1,2], L. Bradanini[1], G. Castaldo[1], L. Donghi[1], A. Pandolfo[1], S. Pontiggia[1], S. Piconi[1]

[1]Infectious Diseases Unit, A. Manzoni Hospital, ASST Lecco, Lecco, Italy, [2]Infectious Diseases Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy

Doravirine (DOR) is a NNRTI recently approved for the treatment of HIV-1. DOR in combination with two NRTIs is approved for use in naïve HIV-positive individuals or for ARV simplification in patients with suppressed viral load and no genotypic mutations. When compared with other NNRTIs, DOR has better tolerability, less DDIs and a higher genetic barrier; DOR is also active in vitro against most common NNRTI-resistant variants. Combination of DOR and integrase inhibitors (INI) like raltegravir (RAL) and dolutegravir (DTG) and darunavir/cobicistat (DRV/cobi) are not currently contemplated as associations by guidelines, because of lacking of specific studies. However, efficacy of dual regimens containing either DTG or a boosted PI plus another NNRTI, such as rilpivirine, has been proven and small case series of patients successfully treated with DTG+DOR have already been published. DOR, overcoming some NNRTI-resistance mutation, may also be the ideal companion in dual regimens for patients with multidrug-resistant virus, who have failed first-line ARV regimens.

We present a small retrospective case series of 7 treatment-experienced patients who started dual therapies with DOR+INIs or DOR+DRV/cobi after viral failure to standard triple therapy. Some of the patients were transitioned to off-label DOR-based regimen because of viral failure to the directly previous regimen, while the remaining were already on viral suppression with other unconventional ARV-combination and were switched to DOR in order to reduce toxicity, DDIs and pill burden.

Results are showed in Table 1. 5 patients were male (71%) with median age of 57 (IQR 51-60). Median duration of HIV disease was 25 years (16-31). Genotype analyses were available for 6 patients. 5/6 patients had NRTIs-associated mutations; between them, 4/5 showed also PI-resistant variants, 1/5 INI-resistant variants and 2/5 major NNRTI-resistant variants (written in bold in Table 1). Patient n°6 showed only one mutation associated with NNRTI resistance (E138A) but experienced persistent low-level viremia under a 4 drug-regimen. 3 patients were virological suppressed prior to switch. Most patients (6/7) switched to a dual-regimen containing DOR+INI (4 DOR +DTG and 2 DOR+RAL) while patient n°7 (who had viral failure under INIs) was put on DOR+DRV/cobi. 6/7 patients maintained or achieved virological suppression while patient n°7 did not: despite genotype showed full susceptibility to DRV/cobi and DOR, his viral load was > 100 copies/ml after 3 month of treatment. None of the patients reported any adverse event related to DOR.

Doravirine's unique resistance profile makes it an interesting companion for RAL, DTG and DRV/cobi in simplification and salvage therapy for experienced patients who failed multiple ARV regimens, even if these combinations are not yet contemplated by guidelines. This is only a small case series with a brief follow-up and results need to be taken with caution until more data will be available.

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Clinical HIV

Late presenters for HIV/AIDS infection

P 12 IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME ASSOCIATED WITH KAPOSI'S SARCOMA IN THE ERA OF HAART: A CASE REPORT

M. Trizzino, S. Bonura, L. Pipitò, P. Di Carlo, G. Boncori, A. Cascio

Infectious and Tropical Disease Unit, AOU Policlinico "P. Giaccone", Palermo, Italy

Background: Despite the benefits of ART, some patients experience immune reconstitution inflammatory syndrome (IRIS), an exaggerated inflammatory response that can mimic the presentation of an active opportunistic infection. This is a case report of disseminated Kaposi's sarcoma (KS) in the context of IRIS in an HIV-infected patient on an INI-based cART regimen.

Case Report: A 29-year-old homosexual man accessed our ID unit in October 2020 following a positive ELISA HIV test. CD4 lymph at onset were 330/mmc, HIV viremia was 136,000 copies/mL. cART with DTG and TAF/FTC was promptly initiated. After 30 days HIV viremia was less than 20 copies/mL with an increase in the CD4 count (659 cells/mmc). After 2 months the patient reported the appearance of purplish, fusiform, slightly raised elements, localized on the whole skin, in particular on the face and limbs, associated with facial edema. HHV-8-DNA was performed and resulted positive. Histological examination of skin lesions showed proliferation of vascular elements lined by endothelium with a fusiform appearance, compatible with the diagnosis of KS. Gastroscopy/colonoscopy were performed, which showed gastrointestinal and mucosal ileocolic lesions compatible with KS, confirmed by the histological diagnosis carried out attributable to visceral localization of KS. Whole-body CT revealed a widespread picture of KS, with the presence of multiple hypervascular lesions in the facial, cervical, thoracic, abdominal subcutaneous, at the level of parotid gland, and suspicious lesions in liver and spleen. The patient started chemotherapy with liposomal doxorubicin 20 mg/m2 once every 21 days for a duration of 6 months. cART was simplified with a PI based single-tablet-regimen containing DRV/c/TAF/FTC. At the end of the 6 months of chemotherapy cycles, a new whole-body CT showed the disappearance of the previously reported hypervascular lesions. The face edema was completely resolved, the viremia for HHV-8 was also negative. KS-IRIS flare completely recovered in 6 months.

Conclusion: Although the incidence of HHV-8 KS has declined in the past years thanks to the introduction of cART, KS remains to date the most frequent HIV-associated malignancy. The impact of cART is believed to be mainly due to the suppression of HIV replication and the recovery of the immune system thus leading to the control of HHV8 replication. Some evidence suggests that PIs may have effects against on KS that are independent of their action on HIV infections. A protective role of PIs against HHV8 should not be neglected especially in populations at high risk of contracting the virus, namely MSM sexually active. In our case, HHV8 load in plasma was useful to identify the patient who experienced a KS-IRIS. Risk factors for developing KS-IRIS include advanced KS tumor stage, pre-treatment HIV viral load, and detectable pre-treatment plasma HHV-8. Thus, we recommend measurement of HHV8 load in plasma, especially in HIV late-presenter patients.

Clinical HIV

Late presenters for HIV/AIDS infection

P 13 **A FATAL CASE OF DIFFUSE LARGE B-CELL LYMPHOMA WITH INTESTINAL PERFORATION IN AIDS PATIENT: A CASE REPORT**

M. Trizzino, R. Rubino, A. Medaglia, G. Valenti, M. Alfonzo, V. Garbo, A. Cascio

Infectious and Tropical Disease Unit, AOU Policlinico "P. Giaccone", Palermo, Italy

Background: Non-Hodgkin lymphoma is the most common malignancy affecting people living with HIV infection. Among its several subtypes, diffuse large B-cell lymphoma (DLBCL) is an important manifestation. DLBCL is the most common aggressive lymphoma irrespective of HIV status.

Case Report: In September 2021, a 39-year-old man accessed our ID-unit for a recent positive HIV ELISA test performed in the context of differential diagnostics for diffuse lymphadenopathy. In anamnesis, Beçhet syndrome with uveitis in treatment with steroids and immunosuppressive drugs and paroxysmal atrial fibrillation in therapy. HIV-RNA at baseline was 1.150.000 copies/mL, CD4 lymph were 47 cells/mmc. QuantiFERON-TB Gold PLUS Test was negative. Antiretroviral therapy with BIC/TAF/FTC was promptly initiated. In consideration of marked leukopenia and the symptoms reported by the patient (fever, weight loss, asthenia), PET/CT examination was performed which confirmed the suspicion of lymphoproliferative disease with high metabolic activity in the supra- and sub-diaphragmatic and pulmonary, hepatic, lymph node splenic and skeletal. Bone marrow and lymph node biopsy was also performed, with histological profile attributable to diffuse large B cell lymphoma EBV + with "T-cell-rich histiocyte-rich B-cell lymphoma" pattern, associated with signs of hemophagocytosis. Culture for atypical lymph node mycobacteria was negative. The patient was initiated on R-COMP chemotherapy (rituximab, cyclophosphamide, non-pegylated liposomal doxorubicin, vincristine and prednisolone). For the onset of acute abdomen and septic shock secondary to diffuse peritonitis from perforation of the mid-distal ileum, the patient underwent emergency surgery and a right lateral ileostomy. In the following weeks there was a progressive worsening of the general clinical conditions, with severe leukopenia not responsive to steroid therapy and G-CSF, together with a severe impairment of liver function indices, with jaundice and hyperbilirubinemia with values higher than 15 mg/dL. The patient died after an episode of shock unresponsive to infusion of amine and fluid resuscitation.

Discussion: As the life expectancy of HIV-positive individuals has increased in the cART era, malignancies have become an important cause of morbidity and mortality. PLWH had a 113-fold higher risk of developing NHLs than uninfected counterparts. Even in the post-HAART era, NHLs are still reported as the most common neoplasia in PLWH. Among the numerous subtypes of NHLs, DLBCL and Burkitt lymphoma are the most frequent manifestations in PLWH. Regarding DLBCL treatment, main option is chemotherapy. Different adverse events are observed during this treatment (adverse events related to the infusion, hematologic events, cardiovascular events, infections). Perforations of the stomach and small intestine are rare but life-threatening complications of DLBCL immunochemotherapy, and is more frequently associated with aggressive lymphomas.

Clinical HIV

Late presenters for HIV/AIDS infection

P 14 **CLINICAL MANAGEMENT OF AN ELDERLY PATIENT, LATE PRESENTER, WITH KAPOSI'S SARCOMA AND MYCOBACTERIOSIS**

G. Panto', S. A. Sofia, G. Strano, C. Iacobello

Unit of infectious diseases Cannizzaro Hospital, Catania

Background: Today, one in two HIV-positive people receives the diagnosis in the late stage of infection and this is of particular concern because the later the diagnosis, the more complex the management of HIV infection will be.
Materials and methods: The clinical case of a 77-year-old man, MSM, who reported arterial hypertension in treatment with ace inhibitors.
For about a year he presented nodular skin lesions, partly ulcerated, on the lower limbs associated with a lymphedema and he also reported asthenia and weight loss.
He had already undergone a biopsy of one of the above lesions with a diagnosis of Kaposi's sarcoma HHV8+, followed by radiotherapy without any benefit, even with extension of the lesions to other skin districts. Despite the presence of these lesions, the patient was not advised to perform HIV testing.
After one year from the onset of the skin lesions and from the diagnosis of SK, the diagnosis of AIDS was made with HIV-RNA of 47377 cp/mL, and CD4 421 mm3 (33%), (CDC 2 clinical stage).
It was decided to undertake ART with FTC/TAF/DAR/COBI, also because some evidence suggested that IP might have an antineoplastic.
The patient underwent:

- CT scan showing enlarged lymph nodes, with a partially colliquated appearance, at laterocervical, nuchal and thoraco-abdominal level;
- EGDS and colonoscopy that excluded visceral lesions of SK;
- Lymph node biopsy negative for SK but whose cultural examination was positive for the presence of Micobacterium fortuitum.

On the basis of ACTG he was classified as T1I0S1.
After two months from the start of ART the patient presented acute renal failure for which the therapy with ace inhibitors was suspended. The antiretroviral therapy was modified by selecting DTG + DOR. Chemotherapy for SK was postponed.
For mycobacteriosis antibiotic therapy was undertaken with minocycline, levofloxacin, and Sulfamethoxazole +trimethoprim.
The following month, paclitaxel therapy was started weekly for 18 cycles.
Results: Six months after the start of HAART, the clinical conditions improved, with remission of neoplastic manifestations, virosuppression and good immunological recovery; the control PET scan documented the near complete regression of lymphadenopathies, with persistence only at the laterocervical level.
Conclusions: In this clinical case, the risk factor and the typical Kaposi's lesions did not arouse the suspicion of doctors who treated the patient before the diagnosis of AIDS. This confirms the low attention that in the health professions area is paid to HIV pathology.
Epidemic SK remains one of the most encountered AIDS-defining malignancies. HAART is essential in treatment, alone or in combination with systemic chemotherapy or local therapy.
Although ART alone could represent the only treatment for SK, in this case the evolving lesions and the lymphedema in the lower limbs induced us to start a systemic chemotherapy.
Our patient's outcome was favorable despite his age and delayed diagnosis.

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Clinical HIV

Management of HIV infections

P 15 **RESOLVED HEPATITIS B VIRUS (HBV) INFECTION AND LOWER NADIR OF CD4+ ARE RISK FACTORS FOR PROGRESSIVE INCREASE OF CD8+ T-CELLS ABSOLUTE COUNT IN COURSE OF ANTIRETROVIRAL THERAPY (ART)**

T. Mulas, V. Malagnino, E. Teti, M. Compagno, L. Ferrari, G. De Simone, F. Caldara, D. Checchi, A. Crea, S. Tedde, L. Dori, M. Iannetta, M. Andreoni, L. Sarmati

Università degli Studi di Roma Tor Vergata

Background: An increase in CD8+ T-cells can occur despite antiretroviral therapy (ART) initiation and CD4+ T-cells count recovery in People living with HIV (PLwHIV). The mechanisms that regulate the CD8+ T-cell trends (ΔT-CD8+) during ART is not fully understood.

Material and methods: A single-center, retrospective study was conducted including PLwHIV on ART who achieved virologic suppression (VS, defined as HIV-RNA<200cp/ml). PLwHIV who experienced a virologic failure were excluded. Based on the 75th percentile value of median ΔT-CD8+ during follow-up (defined as the variation of CD8+ T-cells count from last value in 2021 and baseline), two populations were identified. Uni- and multivariable odds ratios (OR) associated with increased CD8+ T-cells counts during follow-up were assessed using logistic regression.

Results: 401 patients were included: median age 49 (IQR 39-58) years, mostly males (288 [72.7%]), Caucasian (331 [83,5%]) and with sexual transmission risk factor (342 [50,3%]). Almost a quarter of the population was AIDS-presenter (100 [25.2%]), with a CD4+ nadir median value of 234 cells / mmc [IQR 88-104]). ΔT-CD8+ was 18/mmc (IQR -258-350). Based on 75th percentile, we identified 165 (41.1%) patients with ΔT-CD8+≥350/mmc and 236 (58.9%) <350/mmc. Patients with the highest increase in CD8+ T-cells were found to have: advanced age (51 [42 -60] vs 47 [37-56], p=0.0047), CDC stage C (59 [37.1%] vs 41 [17.6%], p<0.0001),and lower CD4+ nadir (142/mmc [38-306] vs 278/mmc [106-441], p=0.0001). No differences in the frequency of detectable viremia during ART (21 pts [13%] vs 26 pts [11%], p=0.81) were found in the two groups of subjects. At the multivariable analysis the risk of having ΔT-CD8+≥350 cells/mmc was associated to the time necessary to reach VS after starting ART (per month aOR 1.02 [95%CI 1.01 - 1.4], p 0.029) and to HBcAb+ status (resolved HBV infection) (aOR 2.84 - 95% CI 1.1 - 7.32, p 0.03).

Conclusion: An increase in CD8+ T-cells during ART is common in patients with a delay in VS achievement during ART. We have shown that HBcAb-positivity is associated with greater increase of CD8+ trend, arguing that a possible occult hepatitis B condition may have implications on the immune regulation during ART.

Clinical HIV

Management of HIV infections

P 16 **DOES CD4+ T-LYMPHOCYTES COUNT OVER 200 CELL/MM3 AFFECT THE EPIDEMIOLOGY OF AIDS DEFINING ILLNESSES? AN OVERVIEW FROM A LARGE ITALIAN CLINICAL CENTER**

V. Iannone[1], A. Dusina[1], D. Farinacci[1], F. Lamanna[1], R. Passerotto[1], A. Borghetti[1], E. Visconti[1], E. Tamburrini[1], S. Di Giambenedetto[1], A. Ciccullo[2]

[1]Fondazione Policlinico Universitario A. Gemelli IRCCS, UOC di Malattie Infettive, Roma, [2]Ospedale San Salvatore Unità di Malattie Infettive, L'Aquila

Background: Measures of CD4+ T-lymphocytes are used to guide clinical and therapeutic management of people living with HIV (PLWH). According to CDC classification system, renewed in 1993, and to the pathogenesis of HIV -1 infection in human, as the number of CD4+ T-lymphocytes decreases, the risk and severity of opportunistic illnesses increase, revealing the strong association between the development of opportunistic illnesses and the absolute number (per microliter of blood) or percentage of CD4+ T- lymphocytes, with the established cut off of CD4+ 200 cell/mm3. In our study we aimed to describe the epidemiology of AIDS-defining illnesses (ADI) in our cohort, evaluating possible differences due to a higher CD4+ cell count at time of ADI diagnosis.
Materials and Methods: We analyzed data from our center's database, collecting all ADI diagnosed in the last five years. We also collected patients' clinical history and viro-immunological parameters and analyzed data via parametric and non-parametric tests, as appropriate.
Results: We analyzed 160 PLWH with at least 1 ADI: 127 were males (79.4%), with a median age of 43 years (IQR 36-53). The most observed ADI were: Pneumocystis pneumonia (PCP, 33, 20.6%), CMV infection (21, 13.1%), Kaposi sarcoma (20, 12.5%) and Candidiasis (18, 11.3%). In our cohort, 62 PLWH (38.8%) were on a ARV regimen at time of ADI diagnosis, with 38 of them (61.3%) on a regimen composed of 2NRTI+INI. Thirty-five PLWH (21.9%) had a CD4+ cell count over 200 cell/mm3 at ADI diagnosis. We observed a significant difference in terms of type of ADI observed between individuals with a CD4+ cell count below or over 200 cell/mm3 (p=0.001): in PLWH with over 200 CD4/mm3, lymphomas (14.3% vs 6.4%) and wasting syndrome (11.4% vs 2.4%) were most commonly observed compared to individuals with a lower CD4+ count. Conversely, CMV disseminated infection was less common in PLWH with a higher CD4+ count (2.9% vs 16.0%). We observed 21 deaths due to ADI during our observation time; having a higher CD4+ cell count at ADI diagnosis was not correlated with difference in mortality (p=0.372).
Conclusions: In our cohort we observed a significant difference in terms of the epidemiology of ADI relating to CD4+ cell count. Lymphomas have been showed to be the most recurrent ADI in individuals with CD4+ over 200/mm3, while CMV disseminated infection was rare in this group. PCP rate remained stable in both groups.

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Clinical HIV

Opportunistic infections (OIs)

P 17 **VISCERAL LEISHMANIASIS COMPLICATED BY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS ASSOCIATED TO IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME IN A HIV-INFECTED PATIENT**

A. Forniti, C. Caroselli, F. Almerigogna, S. Verdenelli, R. Iapoce, G. Tiseo, M. Falcone

Infectious Disease Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy

Immune reconstitution inflammatory syndrome (IRIS) is a well-known consequence of the restoration of pathogen-specific immune responses following the initiation of antiretroviral therapy (ART). A few cases of IRIS-related leishmaniasis, mostly occurring in high-endemicity areas, are reported. Here we describe a case of visceral leishmaniasis, complicated by hemophagocytic lymphohistiocytosis (HLH), associated to IRIS in a patient who had recently started ART after he was diagnosed with HIV infection.

A 56-year-old man living in Fivizzano, Tuscany, was admitted to the primary-care hospital of Fivizzano in January 2020 for a three-month history of intermittent fever, asthenia, weight loss and a maculo-papular rash. He was found with mild anemia and thrombocytopenia, marked hypergammaglobulinemia and splenomegaly (14 cm). After discharge, he tested positive for HIV and came as an outpatient to the tertiary-care University hospital of Pisa. CD4+ T-cell count and HIV viral load at diagnosis were 11% (169/μL) and 1650000 copies/mL (Log 6,2), respectively. ART with emtricitabine/tenofovir + dolutegravir was started two days after the diagnosis. A week later, the patient complained of profound asthenia and high-grade fever. On the 9th February he was admitted to the Infectious Diseases Unit of Pisa hospital. Laboratory exams revealed bicytopenia (Hb 11,8 g/L, platelets 52000/μL), together with hypergammaglobulinemia (37%) and increased C-reactive protein (9,12 mg/dL) and ferritin (5026 μg/L). AST, ALT, and coagulation studies were normal. CD4+ T-cell count and HIV-RNA two weeks after starting ART were 208 copies/mL (Log 2,3) and 21% (149,2/μL), respectively. An abdominal CT scan showed increasing splenomegaly (17 cm). A serologic test for Leishmania spp. proved positive, so bone marrow aspiration and biopsy were performed. Histologic examination with Giemsa staining showed activated histiocytes containing hemosiderin and cellular debris without amastigotes, but the PCR assay for Leishmania spp. was positive, thus liposomial amphotericin B 4 mg/kg according to the FDA-approved regimen for immunosuppressed patients was initiated. Despite treatment, fever persisted and the bicytopenia rapidly worsened; moreover, a marked rise in ferritin (18025 μg/L), increased AST and ALT and reduced fibrinogen were observed. Therefore, suspecting HLH complicating visceral leishmaniasis, dexhametasone 20 mg per day was started. In the following weeks fever and laboratory exams improved and dexhametasone was gradually tapered. The patient was discharged on 10th March 2020, completed therapy with liposomial amphotericin B as an outpatient and fully recovered.

Although visceral leishmaniasis is a rare manifestation of IRIS, it should be suspected in endemic regions, including some Italian islands and coastal areas. The clinical course can be further complicated by hemophagocytic lymphohistiocytosis due to uncontrolled T-cell and macrophage activation in the context of IRIS.

Coinfections and Hepatitis

Bacterial and fungal infections in immunocompromised host

P 18 **HANSEN'S DISEASE, A NEGLEATTED DISEASE? CASE REPORT OF A PATIENT WITH HIV AND MYCOBACTERIUM LEPRAE INFECTION**

L. Alessio[1], S. De Pascalis[1], C. Curatolo[2], V. Pattapola[2], M. Pisaturo[2], N. Coppola[2]

[1]Luigi Vanvitelli Hospital - Naples (Italy), [2]University of Campania, luigi Vanvitelli - Naples (Italy)

Background: Hansen disease is an infectious disease caused by Mycobacterium leprae, primarily affecting the skin, peripheral nerves, mucous membranes of the upper respiratory tract and eyes. It is transmitted from person to person, with a close and prolonged contact, and has a long incubation period. Leprosy is common in Asia, Africa, Central and South America, largely concentrated in 6 countries representing 88% of cases and these countries are India, Brazil, Nepal, Myanmar, Madagascar and Mozambique.
Case(s) description: This case report describes a 38-year-old, Brazilian, MSM patient in Italy from 10 years and with HIV infection, category B2 (diagnosis in 2015) and in treatment from 2019 with TAF/FTC/BICnwith poor adherence to therapy. Upon access to our infectious disesase unit, patients showed numerous nodular formations on the face, ears, nape and abdomen; and loss of substance localized to the nose and upper lip; involvement of the distal extremities of the limbs with ulcerative lesions of the distal phalanges. Blood tests showed anemia with Hb 9 g/dl, a CD4 count of 225 cells /Ul and a CD4/CD8 ratio of 0,78, TPHA and VDRL positive with 1/640 title, Hbcab positivity. Specific therapy for Syphilis was performed. For nodular lesions, TNF for mycobacterium leprae was used for suspected leprosy with negative results and excision biopsy for histological and cultural examination.
Histological examination showed the followed results: "skin with thin epidermis orthokeratosis, dermal infiltration consisting of histiocytes with cytoplasm foamy, with associated share of plasma, interesting the dermis in its entire thickness: probable infectious etiology, compatible with Hansen's disease". Diagnosis of Hansen's disease virchowiana with type 2 reaction was therefore made. In July the patient began treatment with a multi-drug-therapy schedule lasting 24 months, including Rifampicin 600mg (1 time/month), Clofazimine 300mg (1 time/month) and 50mg (per day), Dapsone 100mg (per day), with clinical improvement of lesions (attached images).
Discussion: This case has taught us that the universe of infectious diseases has no borders and globalization along with migratory flows could affect the epidemiology of infectious diseases.

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Coinfections and Hepatitis

Bacterial and fungal infections in immunocompromised host

P 19 **TROPHERYMA WHIPPLEI INFECTION IN HIV: REPORT OF TWO CASES AND LITERATURE REVIEW**

F. Raumer[1], A. Ferrari[1], M. Trevenzoli[1], M. Fassan[2], M. Cola[1], A.M. Cattelan[1]

[1]Azienda Ospedale-Università di Padova, Department of Infectious Disease, Padova, [2]Azienda Ospedale-Università di Padova, Department of Pathological Anatomy, Padova

Background: reports of Whipple's disease in HIV positive patients are rare, but the prevalence of Tropheryma whipplei colonization in this population is higher than in HIV negative subjects. A damage of cell-mediated immunity, as the one caused by HIV infection, may be a predisposing factor for the development of symptomatic Whipple's disease. We report two cases of T. whipplei infection in HIV positive patients treated at the Infectious Diseases Unit of Padova's Hospital.

Case reports and review of the literature: A 35-year-old man and a 43-year-old woman, both HIV positive patients, have been diagnosed with Whipple's disease in 2011. At the time of diagnosis, the man had been taking HAART for 6 years with viral suppression and good immunological response (CD4+ T cell count 340/mm3 – 22%). The woman had been taking HAART for 20 years with partial compliance; she had 1003 copies/mL of HIV-RNA in a blood sample and 4 CD4+/mm3 (6%). They both complained of chronic diarrhea for the last 2 years. Moreover, both suffered from conjunctivitis and arthralgia. Diagnosis was reached in the first case with DNA sequencing for T. whipplei in blood sample, in joint fluid and in small-bowel's biopsy and confirmed by histological detection of PAS-positive foamy macrophages within duodenal biopsies; in the second case typical histology and positive T. whipplei PCR in the small-bowel's biopsy confirmed the diagnosis. Both patients were treated with prolonged antibiotic therapy with cotrimoxazole. The man had a favorable evolution and maintained a good immunological control and undetectable HIV-RNA. The woman instead developed a relapse of the disease two years after first diagnosis and four months after discontinuation of therapy with cotrimoxazole, defined by recurrence of diarrhea and arthralgia and confirmed by histology of the duodenal biopsy; at the time of relapse she had 0 CD4+/mm3 and 27662 copies/ml of HIV-RNA.

We performed a Pubmed search and found 9 case reports and three observational studies which demonstrated a higher prevalence of T. whipplei colonization in HIV positive subjects compared to HIV negative subjects in stool samples and bronchoalveolar lavage samples.

Discussion: These reports confirm the presence of Whipple's disease in HIV positive patients. In particular, earlier studies showed that the prevalence of T. whipplei colonization was higher in ART-treated HIV positive subjects than in the HIV negative control group.

In our two case reports the patient who was taking the HAART therapy regularly and who had high CD4+ T cell count and undetectable HIV-RNA had a complete recovery, while the patient who suspended the antiretroviral therapy had a relapse of Whipple's disease. This observation suggests that a good immunitary system may help eradicate Tropheryma whipplei infection. Further research is needed to clarify the possible immunological deficiencies involved in the development of Whipple disease.

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Coinfections and Hepatitis

HCV elimination

P 20 **HEPATITIS C INFECTION AMONG PEOPLE WHO USE DRUGS: A RETROSPECTIVE COHORT STUDY USING ADMINISTRATIVE HEALTH RECORDS**

G. Moretti[1], L. Ceccarelli[1,2], M. Vainieri[1], L. Tavoschi[2]

[1]Sant'Anna School of Advanced Studies – Management and Healthcare Laboratory, Pisa, Italy, [2]University of Pisa – Department of Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy

Background: Drug use is a major driver of the hepatitis C virus (HCV) epidemic in Italy, with an estimated prevalence up to 64.3% and evidence of ongoing transmission. Direct-acting antivirals (DAAs) can cure HCV in about 95% of patients after 8−12 weeks of treatment. This study aimed to describe the features of chronic HCV infection among people who use drugs (PWUD) in Tuscany and evaluate the impact of regional policies.

Methods: A retrospective analysis of administrative health records was performed to identify all PWUD resident in Tuscany in the period 2015-2020 using two sources: exemption codes for problematic substance use and prescriptions for opioid agonist treatment. Data linkage was performed with HCV treatment prescriptions over the same period. PWUDs were stratified by gender and age.

Results:

In the period 2015-2020, 1734 PWUD have been treated for HCV with DAAs in Tuscany (12.6% out of all patients treated), 1.386 males (79.9%) and 348 females (20.1%); 33-53 age group was the most represented (69.8%) in both genders with 983 males (70.9%) and 228 females (65.5%). On average, 289 (range 113-504) PWUD patients started DAA treatment each year during 2015-2020, with a peak of 504 both in 2018 and 2019.The annual increase rate of treatment coverage among PWUD reached a peak in 2018 with a +284%, while the increase rate of all patients treated in the same year was lower (+123%). Alongside, regional testing capacity increased from 154 PWUD tested for HCV-Ab in 2015 to 1028 tested in 2020, with a peak of 1271 in 2019.

Conclusions:

Regional HCV elimination strategy plan was successful in optimizing health services effectiveness in treating HCV patients in Tuscany, even though COVID-19 pandemic hindered progress in 2020. PWUD remain a priority group to be identified and treated, therefore strategies towards the elimination of HCV must focus on tailored screening campaigns.

Conflict of interest: The authors declare no financial support. No pharmaceutical grants were received in the development of this study.

Coinfections and Hepatitis

HCV elimination

P 21 **HCV PREVALENCE IN A OVER 65 YEARS OLD POPULATION ATTENDING GENERAL PRACTITIONER**

A. Di Fraia[1], M. Pisaturo[1], V. Messina[2], M. Starace[1], C. Minichini[1], L. Occhiello[1], L. Onorato[1], N. Coppola[1]

[1]Infectious Diseases Unit, Department of Mental Health and Public Medicine, University of Campania "Luigi Vanvitelli", Naples, Italy, [2]Department of Infectious Diseases, Sant'Anna Hospital, Caserta, Italy

Aim: to evaluate the prevalence of HCV infection in a over 65 years old population attending general practitioner to performe flu vaccination.
Patients and Methods: a multicenter perspective interventional choort study was conducted between November and December 2019 involving 12 general practitioners operating in Campania, Southern Italy to find HCV infection in a population over 65 years old attending general practitioner to performe flu vaccination and to obtain linkage-to-care program. Screening for anti-HCV antibodies was performed with HCV rapid tests using acupuncture.
Results: 305 patients were enrolled. 259 (84.9%) accepted HCV rapid test screening. Table 1 showed epidemiological characteristics of enrolled patients. Patients included in the study had a median age of 71 (IQR:11), 179 (58.6%) were male, 302 (99.1%) were of Italian nationality, 190 (62%) patients had less than 8 years of schooling.
The most frequent comorbidities found are hypertension in 102 (33.4%) patients, diabetes mellitus in 59 (19.3%), cardiovascular disease in 14 (4.5%) and 8 (2.6%) patients had BPCO. 2 (0.6%) patients reported a history of PWID, 5 (1.6%) patients had a history of prison, 37 (12%) patients had a history of familiarity of HCV infection. 6 (1.9%) patients were HCV Ab positive. Table 2 showed the epidemiological characteristics of screened patients compared to non-sreened patients. Table 3 showed the characteristics of HCV Ab positive patients compared to HCV Ab negative. There is no difference in the two groups for age, sex, years of schooling, PWID and history of prison but there is statistical significance for family history for HCV (p=0.004).
Conclusions: We used this study model to screen a populaton over 65 years old for HCV infection. It can also be extended to the key populations (PWID, prisoners, migrants, sex workers, etc.) this would limit new infections and would allow HCV eradication.

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Coinfections and Hepatitis

HDV cure

P 22 **BULEVIRTIDE MONOTHERAPY AT LOW AND HIGH DOSE IN PATIENTS WITH CHRONIC HEPATITIS DELTA: 24 WEEKS INTERIM DATA OF THE PHASE 3 MYR301 STUDY**

H. Wedemeyer[1], S. Aleman[2], P. Andreone[3], A. Blank[4], M. Brunetto[5], P. Bogomolov[6], V. Chulanov[7], N. Geyvandova[8], G. Hilgard[9], N. Mamonova[10], U. Merle[4], M. Viacheslav[11], O. Sagalova[12], T. Stepanova[13], J. Schulze zur Wiesch[14], S. Zotov[15], S. Zeuzem[16], P. Lampertico[17,18]

[1]Klinik für Gastroenterologie, Hepatologie und Endokrinologie, Medizinische Hochschule Hannover, Hannover, Germany, [2]Karolinska University Hospital/Karolinska Institutet, Department of Infectious Diseases, Stockholm, Sweden, [3]Internal Medicine, University of Modena and Reggio Emilia, Italy, [4]University Hospital Heidelberg, Clinical Pharmacology and Pharmacoepidemiology, Heidelberg, Germany, [5]U.O. Epatologia - Azienda Ospedaliero Universitaria Pisana, Pisa, Italy, [6]State budgetary institution of health care of Moscow region “Moscow regional research clinical institute after M.F. Vladimirsky", Moscow, Russian Federation, [7]Federal Budget Institute of Science "Central Research Institute for Epidemiology" of Federal Service on Consumers Rights Protection and Human Well-Being Surveillance, Moscow, Russian Federation, [8]Stavropol Regional Hospital, Stavropol, RussianFederation, [9]Universitätsklinikum Essen (AöR), Klinik für Gastroenterologie und Hepatologie, Essen,Germany, [10]FSBI National Research Medical Center for Phthisiopulmonology and Infectious Diseasesof the Ministry of Health of the Russian Federation, Moscow, Russian Federation, [11]LLC MedicalCompany “Hepatolog”, Samara, Russian Federation, [12]Federal state-funded institution of highereducation "Southern Ural State Madical University of Ministry of Health of the Russian Federation" of Ministry of Health of the Russian Federation, Chelyabinsk, Russian Federation, [13]Limited liability company “Clinic of Modern Medicine”, Moscow , Russian Federation, [14]Universitätsklinikum Hamburg-Eppendorf Medizinische Klinik Studienambulanz Hepatologie, Hamburg, Germany, [15]State budgetaryinstitution of health care "Specialized Clinical Infectious Diseases Hospital" of Ministry of Health of Krasnodar Region, Krasnodar, Russian Federation, [16]University Hospital Frankfurt, Department of Medicine , Frankfurt am Main, [17]Foundation IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Division of Gastroenterology and Hepatology, Milan, Italy, [18]CRC “A. M. and A. Migliavacca” Center forLiver Disease, University of Milan, Department of Pathophysiology and Transplantation, Milan, Italy

Aims: 24-week interim analysis of the MYR301 phase 3 study in chronic HDV patients receiving 2mg/qd or 10mg/qd dose of bulevirtide monotherapy compared to observation.

Method: 150 patients were randomized 1:1:1 to no antiviral treatment for 48 weeks followed by BLV 10mg/qd for 96 weeks (arm A, n=51), treatment with BLV 2 mg (arm B, n=49) or BLV 10 mg (arm C, n=50) for 144 weeks with a treatment-free follow-up of 96 weeks. The combined primary endpoint is defined as undetectable HDV RNA (<LoD) or decrease by ≥2log10 IU/ml and ALT normalization at week 48.

Results: 57.3% were male, 82.7% were White and mean age was 41.8 years. Baseline HDV RNA levels were 5.05 log10 IU/mL and ALT mean levels were 110.9 U/L. BLV was well tolerated during the first 24 weeks: overall, 421 treatment emergent adverse events (TEAE) were reported; 55 TEAE in 26 patients in the arm A, 121 TEAE in 32 patients in the arm B and 245 TEAE in 36 patients in the arm C. 48 TEAE in arm B and 100 TEAE in arm C were assessed as possibly related to BLV. At week 24, 36.7% of patients in arm B and 28.0% in arm C achieved combined virological and biochemical response (vs. 0% in arm A, p<0.0001). HDV RNA decrease by ≥2 log10 IU/mL at week 24 from baseline was observed in 55.1% of patients in arm B and 68% in arm C (vs. 3.8% in arm A, p<0.0001). ALT normalization was achieved in 53.1% of arm B, 38% of arm C (vs. 5.9% in arm A, p<0.0001).

Conclusion: Monotherapy with BLV is safe and well tolerated in patients with chronic HDV. 24-week treatment with BLV was associated with significant HDV RNA declines and improvements in biochemical disease activity.

Coinfections and Hepatitis

Hepatitis epidemiology

P 23 **SEROPREVALENCE OF HCV-AB AND AWARENESS IN PEOPLE WHO INJECT DRUGS (PWID) FROM ADDICTION SERVICES**

C. Marcia[1], E. Prinčič[1], G. Seu[2], L. Denti[1], M. Fois[1], S. Babudieri[1], I. Maida[1]

[1]Department of Medical, Surgical and Experimental Sciences, University of Sassari, [2]Addiction Services of Sassari

Seroprevalence of HCV-Ab and Awareness in People Who Inject Drugs (PWID) from Addiction Services

Background: HCV infection is the main cause of cirrhosis, HCC and liver failure. World Health Organization (WHO) estimated that, globally, around 71 million people live with hepatitis C virus (HCV) infection and they aimed to eliminate hepatitis C virus by 2030.

In our countries HCV infected people, except People who inject drugs (PWID), are treated in hepatology centre with Direct-acting antiviral (DAA) that have, by now, proven to be higly effective.

Now the resevoir of HCV infection is mainly in PWID. Some papers estimate that the infection prevalence in PWID is about 63-64%, but the exact prevalence is not really known.

In May 2019 a partnership between Infectious Disease Depratment of University and Addiction Services of Sassari started. The goal of this collaboration is to screen for HCV infection all people followed by the Addiction Services (SERD) and create a smart diagnostic and therapeutic path.

The goal of this study is to describe seroprevalence and awareness of the infection in our PWID population.

Material and Methods: We studied PWID in Opioid Substitution Treatament (OST). To collect our data we looked in medical records stored in SerD of Sassari and found previous laboratory tests from the regional clinical management software, in addiction we offered to test all the patients for Anti-HCV antibodies.

Demographic and epidemiological characteristics of the population were recorded (age, sex, opioid substitution treatment, duration of drug dependence, seroprevalence and awareness of the infection).

Results: The study includes 961 PWID in OST whose characteristics are summarised in table 1. We screened 716 users for anti-HCV antibodies, Of these 574 (80.1%) were positive.

170 users referred their previous positivity to the test. In 77 of those (45,2%) the positivity was confirmed, the remaining are still waiting to be screened.

All the users aware of their infection before our screening was confirmed to be infected with HCV. 263 people had no knowledge of HCV infection before the screening.

Conclusion: Seroprevalence in this population was 80%.

Only 4.2% of PWID in OST refused serological screening for anti-HCV antibodies some of them referred previous positivity as a motivation. No patient who referred previous positivity was found negative in our determination, showing a good awareness on HCV infection.

This partnership between Infectious Disease Depratment of University and Addiction Services improved the knowledge about our local submerged, letting us to treat them and getting closer to the WHO 2030 goal.

Coinfections and Hepatitis

HIV-associated tuberculosis

P 24 **SOCIO-DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF HIV-ASSOCIATED TUBERCULOSIS IN TOR VERGATA HOSPITAL, ROME: A 9-YEAR ANALYSIS**

B. Rossi, M. Zordan, A.M.A. Crea, M. Compagno, M. Iannetta, L. Campogiani, L. Coppola, L. Sarmati, M. Andreoni and the PTV group

Infectious Diseases Department, Tor Vergata Hospital, Rome, Italy

Background: Alongside with HIV infection, tuberculosis (TB) is still one of the major global health problems worldwide. Among all new cases of TB in Europe, 12% were people living with HIV (PLWH). TB represents also a serious health threat because is one of the leading causes of death especially among PLWH. We present a case series of TB/HIV co-infected patients.

Material and methods: We conducted a retrospective, single-center observational study including data from patients with an active TB diagnosis, admitted to the Infectious Diseases Department of the Tor Vergata Hospital, Rome, Italy, from 2013 until 2021. Further analysis was restricted to patients who tested positive for HIV.

Results: The study included 210 patients with a median age of 38 years (IQR 36-46), 77% were male, 74% were foreigners. After obtaining informed consent, all included patients were tested for HIV, and 13 patients (6,2%) tested positive.

Among TB/HIV co-infected patients, 92% were male, 92% were foreigners (4 Asians, 4 Latin Americans, 4 Africans, 1 East European). 2 were sex workers, 3 were injection drug users, 1 was an alcohol abuser. 3 patients had also an HCV infection, 1 had a Pneumocystis jirovecii pneumonia. 5 patients knew their HIV-positive status before the TB diagnosis; two were already on ART and 3 had a CD4 cell count below 200 cells/mm3. Median time from HIV to TB diagnosis was 7 years (IQR 7-10). Eight patients received TB/HIV diagnosis at the same time; 3 patients had a prior TB diagnosis, but were lost to follow-up, for both HIV and TB. Overall, at the time of TB diagnosis, median CD4 count was 149 (IQR 24-391) cells/mm3, median HIV-RNA was 165000 (IQR 44885-323142) copies/ml. 6 patients had a PPD test >5mm, while Quantiferon-TB Gold resulted positive in 6, indeterminate in 3 and negative in 4 patients. 8 patients (66.6%) presented with extrapulmonary tuberculosis (EPTB); among these 6 were lymph node TB, 2 pleural TB, 2 abdominal TB, 1 bone TB and 2 was a disseminated TB. Among the pulmonary tuberculosis (PTB), 3 were miliary forms, 2 had a tree-in-bud presentation. Mycobacterium tuberculosis complex (MTC) was identified in 92% of cases; phenotypic resistance analysis was performed and showed 1 MDR-TB and 1 case of rifampicin resistance.

All patients with a new diagnosis of HIV were started on ART after at least 2 weeks of antitubercular therapy. No one presented IRIS and only 2 patients presented adverse effects related to TB treatment. (Table 1). Successful treatment was accomplished in 5 patients, 3 are still treating TB, 5 were lost to follow-up, no one died.

Conclusions: One of the most relevant data in our cohort is that 41% of patients were lost to follow-up. Nowadays one of the biggest challenges is to implement comprehensive social and healthcare interventions to improve access to diagnosis and care, and strengthen educational programs among population to improve patient's compliance and adherence to treatment.

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Coinfections and Hepatitis

Management and treatment of viral hepatitis

P 25 **IMPROVING ORGANIZATIONAL EFFECTIVENESS FOR CHRONIC HEPATITIS C LINKAGE TO CARE AND TREATMENT: A CASE REPORT**

L. Ceccarelli[1,2], I. Corazza[2], M. Vainieri[2], L. Tavoschi[1]

[1]University of Pisa, Department of Translational Research and New Technologies in Medicine and Surgery, Pisa, Italy, [2]Sant'Anna School of Advanced Studies, Management and Healthcare Laboratory, Pisa, Italy

Background: In the frame of WHO's Global Health Sector Strategy to eliminate hepatitis C virus (HCV) infection as a public health threat by 2030, Italy has launched a national effort. The Italian Medicines Agency has approved direct-acting antivirals (DAAs) for the treatment of HCV in 2015, providing universal access since 2017. DAAs can cure HCV in about 95% of patients after 8–12 weeks of treatment, however early diagnosis and linkage to care remain a challenge. This study aimed to describe the organizational and managerial features of HCV chronically infected patients' care pathways.

Methods: Within the context of an ongoing project aiming to optimize HCV care and treatment pathways in Tuscany region, semi-structured on-site interviews were delivered to 11 specialists of 7 hospitals accredited for providing DAA treatment (accredited hospitals, AH) between 14th October 2021 and 13th January 2022, to gather information about 3 main domains: 1) referral and linkage to care; 2) patients' care pathway; 3) patients' follow-up. Particular attention was dedicated to highlighting facilitators and barriers to access HCV care services and throughout the patients' care pathway.

Results: Referring to the first domain, most of the AH received patients directly from general practitioners (<50% of patients reported by 4; >50% by 3 out of 7 AH) followed by addictions services (<30% reported by 6 out of 7 AH) and prisons (>30% reported by 4 out of 7 AH); community-based testing services were usually not involved in the formal referral processes. Most of the patients accessed to AH services by booking the first visit independently while fewer could benefit from a direct referral. Concerning the second domain, patients had to spend less than an hour in 4 out of 7 AH to complete pre-treatment assessment (specialist visit, ultrasound/elastography, blood tests) and 2 out of 7 AH offered all HCV services in the same visit. Referring to the third domain, all the AH effectively rescheduled the follow-up visit directly with the patients at the end of the first one. One of the main barrier highlighted was a complaint towards the too long waiting lists for accessing the first visit, an aspect that may lead to dropouts and the absence of preferential routes for hard-to-reach patients (e.g., people who inject drugs and people who live in prisons); on the other hand, the presence of a dedicated regional number to call in order to book the first HCV specialist visit was considered a facilitator, even if it was deemed that awareness was low among general population.

Conclusions: The organization and implementation of patients' HCV care's pathways were very heterogeneous in Tuscany region. This might be partly related to sub-regional health system set-up and to local needs, including HCV epidemiology. However, similar facilitators and barriers emerged from the interviews across the region, including for linkage to care. Standardization of the care pathways would be recommended.

Coinfections and Hepatitis

Management and treatment of viral hepatitis

P 26 **ANALYSIS OF PATIENTS CHARACTERISTICS AND TREATMENT PROFILE OF PERSONS WHO USE DRUGS (PWUD) WITH AND WITHOUT A CO-DIAGNOSIS OF VIRAL HEPATITIS C: A REAL-WORLD RETROSPECTIVE ITALIAN STUDY**

F. Nava[1], A. Mangia[2], M. Riglietta[3], L. Somaini[4], F.G. Foschi[5], E. Claar[6], I. Maida[7], C. Ucciferri[8], F. Frigerio[9], C. Hernandez[10], D.D. Ancona[11], M. Andretta[12], A. Barbieri[13], F. Bartolini[14], A. Ciaccia[15], A. Costantini[16], S. Dell'Orco[17], R. Moscogiuri[18], E. Mosele[19], C. Procacci[11], F. Santolieri[16], M. Dovizio[20], D. Sangiorgi[20], V. Perrone[20], L. Degli Esposti[20], M. Puoti[21]

[1]U.O. Sanità Penitenziaria e Area Dipendenze, Azienda ULSS 6 Euganea, Padova, Italy, [2]UOS Epatologia, Istituto di Ricovero e Cura 'Casa Sollievo della Sofferenza', S. Giovanni Rotondo, Italy, [3]UOC Dipendenze, ASST Papa Giovanni XXIII, Bergamo, Italy, [4]Servizio per le Dipendenze, SERT di Cossato, Biella, Italy, [5]UOC Medicina Interna, Ospedale di Faenza, Faenza, Italy, [6]UOC Medicina Interna, Ospedale Evangelico Villa Betania, Napoli, Italy, [7]UOC Malattie Infettive e Parassitarie, Azienda Ospedaliera Universitaria, Sassari, Italy, [8]Clinica di Malattie Infettive Ospedale "SS Annunziata " Chieti, Italy, [9]Gilead Sciences, Milano, Italy, [10]Gilead Sciences, Global Medical Affairs, Stockley Park, London, UK 16, [11]Pharmaceutical Department, Local Health Unit BAT, Andria, Italy, [12]UOC Territorial Pharmaceutical Service, Azienda ULSS 8 Berica, Vicenza, Italy, [13]Territorial Pharmaceutical Complex Structure, Local Health Unit VC, Vercelli ,Italy, [14]Pharmaceutical Department, Local Health Unit Umbria 2, Terni, Italy, [15]Territorial Pharmaceutical Service, Local Health Unit Foggia, Italy, [16]Hospital Pharmacy, "Santo Spirito" Hospital, Pescara, Italy, [17]Local Pharmaceutical Service, Roma 6 Local Health Unit, Albano Laziale RM, Italy, [18]Pharmaceutical Department of Taranto Local Health Unit, Hospital SS. Annunziata, Taranto, Italy, [19]U.O.C. Territorial Pharmaceutical Assistance, ULSS 7 Pedemontana, Bassano del Grappa, Vicenza, Italy, [20]CliCon S.R.L. Società Benefit, Health Economics and Outcomes Research, Bologna, Italy, [21]SC Malattie Infettive, ASST Grande Ospedale Metropolitano Niguarda, Milano, Italy

Background: People who use drugs (PWUDs) are a population characterized by an increased risk of hepatitis C (HCV) infection, along with the associated morbidity and mortality. Limited data are available on their clinical and therapeutic management. This study aimed to evaluate characteristics of PWUD, with and without HCV, profiling their comorbidities and pharmacological treatments in a real-world setting in Italy.

Material and Methods: A retrospective study was conducted using administrative databases of Italian Local-Health Units, covering 3.9M of health-assisted individuals. During 01/2011-06/2020, PWUD individuals [identified by exemption code or hospitalization discharge diagnosis] were included. HCV was identified by the presence of a discharge diagnosis or exemption code or direct anti-viral agents (DAAs) prescription. PWUD, with and without HCV, were allocated into PWUD-HCV+ and PWUD-HCV- cohorts. Among PWUD-HCV+, DAA-treated or untreated patients were identified. The date of PWUD/HCV first diagnosis or DAA first prescription was the index date (ID). Patients were characterized for demographic and clinical(Charlson comorbidity index, CCI) variables, during all available periods before ID. All prescribed treatments (excluding DAA) were evaluated after the ID during the first year of follow-up. PWUD with alcohol dependency were also identified.

Results: Overall, 3,690 PWUD were included: 1,141 (30.9%) PWUD-HCV+ and 2,549 (69.1%) PWUD-HCV- patients. The mean age of PWUD-HCV+ and PWUD-HCV- was 43.6±9.0 and 38.5±10.7 years ($p<0.001$), respectively, and 82.7% and 81.9% were males. PWUD-HCV+ had a significantly higher CCI value than PWUD-HCV- (0.8±1.6 vs. 0.4±0.9, $p<0.001$). Untreated PWUD-HCV+ had significantly higher CCI (0.9±1.9) compared to DAA-treated cohort (0.6±1.3, $p=0.003$). During the first year of follow-up, the number of prescribed treatments in PWUD-HCV+ was higher versus the counterpart cohort (4.0±4.6 vs. 3.6±4.3, $p=0.011$). In both PWUD-HCV+ and PWUD-HCV-cohorts, among the most prescribed treatments there were those belonging to ATC class A02 (drugs for acid related disorders, 22.4% average), N03 (antiepileptics, 25.9%), N05 (psycholeptics, 26.3%), N06 (psychoanaleptics, 24.6%), and the consumption of cardiovascular treatments accounted in an average of 15.3% of patients. Among PWUD, 436 (11.8%) had a co-diagnosis of alcohol dependence (128 were PWUD-HCV+ and 308 PWUD-HCV-).

Conclusions: This real-world analysis among Italian population depicted the demographic and clinical profile of PWUD patients with a without a co-diagnosis of HCV. PWUDs are characterized by elevated comorbidity and number of concomitant treatments. PWUD-HCV+ patients were characterized by a more severe comorbidity profile, especially those untreated, and by a complex therapeutic management characterized by a high number of prescribed medications. These data could be supportive for the optimization of medical care setting of PWUD patients with HCV infection.

Comorbidities
Cancers in HIV

P 27 **RARE BONE INVOLVEMENT OF KAPOSI'S SARCOMA IN HIV LATE PRESENTER: A CASE REPORT**

V. Crosato[1], S. Arsuffi[1], F. Pennati[1], V. Ferrari[2], M.A. Forleo[1], E. Quiros-Roldan[1], A. Berruti[2], F. Castelli[1], E. Focà[1]

[1]Division of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili Hospital, Brescia, Italy, [2]Division of Medical Oncology, University of Brescia at ASST Spedali Civili, Brescia, Italy

Background: Kaposi sarcoma (KS) is a multifocal, angioproliferative neoplastic disease of the blood vessels promoted by HHV-8 infection. It usually involves the skin and mucosal surfaces such as the oral cavity or genitalia and is frequently associated with spread to lymph nodes and respiratory or gastrointestinal tract.
Although several reports of unusual localizations of KS have been made, bone involvement of classic KS is exceptional. Metastatic spread of KS to the bones is known to worsen the prognosis, but shows promising response to treatment if diagnosed early.
This is a case of a HIV late presenter with KS of the skin and multiple and extensive bone metastasis.
Case report: The patient is a 41-year-old Italian man who presented to the emergency department in September 2021 for cough and fever.
He had no medical history and was otherwise in good conditions. He was immediately tested negative for SARS-CoV-2; his chest X-ray showed bilateral infiltrates.
Further diagnostics with CT scan resulted compatible with the suggestion of P. jirovecii pneumonia (PJP), which led to the diagnosis of HIV infection.
His baseline viro-immunological parameters revealed HIV-RNA with a viraemic load of 972,878 cp/mL and CD4+ 89 cell/uL (8.7%), CD4+/CD8+ 0.13.
The patient was successfully treated for PJP and began combined antiretroviral therapy (cART) with bictegravir/emtricitabine/tenofovir alafenamide.
Further examination led to the finding of a violaceous skin lesion on his leg. Its bioptical analysis confirmed the diagnosis of cutaneous KS. Stadiation MRI, colonoscopy and gastroscopy excluded visceral metastasis but showed lesions of the vertebral spine, thus originating the suspicion of bone localization.
Targeted MRI showed the presence of multiple osteolytic lesions at T1, T2, T5, T9-12, L1, S1, S2, S4, C2, C4 and C7 and at the right iliac crest, all consistent with secondary localizations of disease.
Histologic examination of bone biopsy of the right iliac wing confirmed bone involvement of KS.
The patient is currently undergoing chemotherapy with doxorubicin and follow up is still ongoing.
Conclusions: Skin and mucosal KS is a relatively common finding in individuals with severe immunodeficiency and has a particular relevance in HIV/AIDS patients.
However, bone metastasis of KS can be considered a rarity and it is known to worsen the prognosis, but shows promising response to treatment if it is diagnosed at an early stage. Therefore, it needs to be suspected and excluded in case of osteolytic bone lesions of unknown origin, especially in late presenters, to provide the correct treatment and prevent further spread of the disease and a worsening of the patients' prognosis.

Comorbidities

Cancers in HIV

P 28 **OUTCOMES IN HIV CARRIERS WITH OR WITHOUT RECURRENCE OF HEPATOCELLULAR CARCINOMA AFTER INVASIVE THERAPY**

C. Bertoni[1], L. Galli[2], E. Messina[2], H. Hasson[2], A. Siribelli[2], S. Bagaglio[2], A. Castagna[1], C. Uberti-Foppa[1], G. Morsica[2]

[1]Vita-Salute University, Milan, Italy, [2]Dept. of Infectious Diseases, San Raffaele Hospital, Milan, Italy

Background and Aims: to address the overall survival (OS) and recurrence (RE) in HIV-carriers treated with invasive therapy (IT) for hepatocellular carcinoma (HCC). **Methods**: retrospective cohort study on HIV-carriers with HCC diagnosed between 2002-2021. The study outcomes were OS and RE, investigated by use of Kaplan-Meier curves.

Results: the analysis included 41 HIV-carriers with HCC who underwent IT [liver resection (LR, N=6) orthotopic liver transplantation (OLT, N=11) radiofrequency thermo ablation (RFTA N=6) chemo/radioembolization (CRE, N=18)].

Barcelona clinic liver cancer (BCLC) stage was 0/A in 20, B in 8, C/D in 13 pts. Characteristics of people at ITaccording to death (n=22) or survival (n=19) are reported in Table 1.

Two- and 5-year survival probabilities were 72% (55.1% – 83.4%) and 48% (31.7% – 62.7%) respectively. Differences between survived and dead pts were found in relation to the number of nodules p=0.01, AFP p= 0.036, AST p= 0.03, bilirubin p=0.005, PCHE p=0.001, CD4 p=0.035, CD8 cells count, p=0.0007, total lymphocytes p=0.005, creatinine p=0.005 and PTINR p=0.001, respectively.

Two and 5-year survival probabilities were higher in OLT [100% and 90.9%, respectively] in comparison to other therapies (LR, RFTA, CRE) [60.9% and 30.6%, respectively], log-rank p=0.0005.

RE was observed in 19/41 (42%) HIV-carriers. RE probability was 37% (23.1 – 55.0) and 52% (35.7 – 70.6) at 2 and 5 years from HCC diagnosis. RE was less frequent in males [RE 13 (68.4%) vs non-RE 21 (95.5%) =0.036]; all the other variables were similarly distributed. The 2- and 5-year survival probabilities among HIV-carriers with no-RE was 70.5% (45.7 – 85.6) and 54.6% (30.6 -73.4), respectively and 73.7% (47.9 – 88.1) and 42.1% (20.4 – 62.5) among HIV-carriers with RE, respectively, log-rank p=0.7772.

Conclusions: Fifty percent of HIV-carries survived at 5 years, with 91% among people treated with OLT. Five-year recurrence of HCC was observed in 52% of HIV-carries and OS did not seem to be affected by RE.

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Comorbidities

Cancers in HIV

P 29 AIDS-DEFINING CANCERS AND NON AIDS-DEFINING CANCERS IN A COHORT OF PLWH

F. Ginevri, S. Mazzanti, L. Brescini, V. Barocci, M. Di Pietrantonio, G. Cesaretti, B. Candelaresi, S. Olivieri, F. Pallotta, P. Mantini

Clinica Malattie Infettive Ospedali Riuniti Ancona

Nowadays, cancer in PLWH is one of the main causes of non-AIDS related death. We have two main categories of cancers: AIDS-defining (ADCs) and non-AIDS-defining (NADCs) cancers. With the advent of ART, ADCs have drastically decreased, while NADCs have increased. The aim of this retrospective study was to evaluate the risk factors related to the onset of NADCs in PLWH followed by our department.

Our population includes PLWH followed between January 1985 and April 2021: 409 patients, predominantly male (65%) and with a median age of 53 years. We considered demographic variables (age, sex), risk factors for the transmission of infection (heterosexuality, homosexuality or drug use), presence of co-infections (HBV, HCV), comorbidities, CDC stage, viro-immunological state in the last two years and at the time of cancer's diagnosis, days between the diagnosis of HIV and the onset of cART.

In our study, we recorded 90 cases of tumors, including 27 (30%) ADCs and 63 (70%) NADCs. In NADCs patients 25% had GI tract cancer, 8% developed urinary tract cancer, 3% had a pulmonary cancer, 14% had skin and soft tissue cancer, 11% liver and biliary tract cancer, 7% thyroid gland cancer, 9.5% breast cancer, 9.5% head and neck area cancer, 11% haematological disease and 2% gynecological cancer. Among the statistically significant risk factors we find the age of oncological patients (median of 55 years), which was greater than the age of patients without cancer (median 52 years); HIV-HCV coinfection was a particularly important factor in oncological patients (in cancer patients: 30%; in non-cancer patients: 21%); the most relevant comorbities were the metabolic ones (45% in non-oncologicals, 43% in NADCs), cardiovascular (21% in non-oncologicals, 30% in NADCs), gastrointestinal (12% in non-oncologicals, 28 % in NADCs), genitourinary (9% in non-oncologicals, 15% in NADCs), followed by psychiatric, neurological, osteoarticular and respiratory pathologies; statistical significance only emerged for GI comorbidities; days between HIV diagnosis and the onset of cART were relevant: actually, median of NADCs = 850 days, median of non-oncologicals = 132 days; we found CD4+ > 200 cells/μL in the last two years in the 84% of NADCs and in 93% of non-oncological PLWH.

The efficacy of ART has resulted in an increase of life span in PLWH: the average age of NADCs is greater than that of subjects without NADCs. In NADCs, HCC was the most frequent type of cancer, as well as the presence of HCV co-infection. Gastrointestinal comorbidities are considered the most significant for neoplastic onset. Many studies have shown that HIV infection has a negative impact on the intestinal microbiota, which can lead to an increase in potentially pathogenic bacterial populations resulting in a chronic inflammatory state of the gastrointestinal mucosa. Neither the nadir of the CD4+, nor their count at the time of the diagnosis of cancer represent an independent risk factor for NADCs.

Comorbidities
Cancers in HIV

P 30 **DON'T FORGET PREVENTION, SCREENING WITH CYTOLOGY, GENOTYPING AND HIGH RESOLUTION ANOSCOPY FOR ANAL HPV-RELATED PRECANCEROUS LESIONS IN PLWH CONTINUES DURING COVID19 PANDEMIC**

M. Digaetano[1], A. Catania[1], M.D. Di Trapani[1], M. Menozzi[1], R.P. Iachetta[2], R.D. Villani[2], A. Farinetti[3,5], G. Rolando[3], S. Tagliazucchi[4], M. Pecorari[4], R. Gelmini[3,5], C. Mussini[1,5]

[1]Infectious Diseases Unit, Azienda Ospedaliero-Universitaria Policlinico, Modena, Italy, [2]Pelvic Floor Center, Department of Proctology, Nuovo Ospedale Civile di Sassuolo,Modena, Italy, [3]Surgery Unit, Azienda Ospedaliero-Universitaria Policlinico, Modena, Italy, [4]Microbiology and Virology Unit, Azienda Ospedaliero-Universitaria Policlinico, Modena, Italy, [5]Department of Surgical, Medical, Dental and Morphological Sciences, University of Modena and Reggio Emilia, Modena, Italy

Background: HPV infection and the transformation of infected tissues into precancerous lesions underlie the development of cancers. Like all these neoplasms, squamous cell carcinoma of the anus (SCCA) occurs with greater prevalence in people living with HIV (PLWH), becoming one of the non-AIDS defining diseases most widespread in the population involved. Here we are presenting data from our SCCA screening program, we also are going to analyze the impact of COVID19 pandemic.

Methods: This screening program started in 2016 and involve PLWH of both sexes that are at risk for HPV infection (MSM, previous HPV neoplasms). They undergo an anal Pap test, HPV genotyping and, in case of positive cytology or high-risk HPV (HRHPV) genotype detection, high resolution anoscopy (HRA). High-grade lesions are treated with diathermocoagulation. From February 2020 the surgical outpatient clinics were closed, the activity was resumed in June 2020 with reduced hours and restricted accesses.

Results: 239 Pap tests were performed, 96,2% in males. 108 (45,2%) were positive for HPV related lesions, of these 94 (87%) were low grade squamous intra-epithelial lesions (LSIL) and 8 (7,4%) atypical squamous cells of undetermined significance (ASCUS), high grade lesions (HSIL) were found in 6 patients (5,6%). 154 of 239 screened (64,4%) also performed HPV genotyping and 123 carried HRHPV genotype. Only 49 HRHPV carriers had a positive Pap test. A total of 180 screened (75,3%) have the indication for HRA. Among 95 HRAs performed until today (76 in Pap test + and 18 in HRHPV carriers with Pap test negative), 21 resulted positive for HSIL (22,1%). 4 HSILs were found in HRHPV carriers with negative Pap test. 15 of 21 patients with HSIL underwent diathermocoagulation and follow up is still ongoing for the majority, in 3 patients HSIL relapsed, in one case the check resulted in carcinoma in situ which was then surgically removed. A second Pap test carried out one year later is available for 32 patients. The cytological examination did not change in 20 cases, in 5 it showed the presence of a higher grade lesion than in the previous test. Graph 1 shows that the reduction in outpatient activity due to COVID19 led to a sharp drop in the exams performed.

Conclusions: Palefsky et al. recently demonstrated that early treatment of HPV-related precancerous anal lesions reduces the risk of cancer development in PLWH. Our data show that the prevalence of HPV-related precancerous lesions in the population studied is high and in line with literature data. The association of genotyping and cytology appears to be the best first level screening method. HRA allows the surgical management of the patient who can also be treated and followed up. The one-year follow-up appears adequate for the patient with negative Pap test. COVID19 pandemic has resulted in an abrupt halt to all prevention activities and the effect on the long-term health of our patients will be evident in the coming decades.

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Comorbidities

HIV and nervous system

P 31 **A RARE CASE OF HIV-RELATED VACUOLAR MYELOPATHY IN A LIVING PATIENT**

A. Giacinta, A. Londero, P. Della Siega, C. De Carlo, C. Tascini

Unit of Infectious Diseases "Santa Maria della Misericordia (University Hospital)", Udine, Italy

Background: Among the causes of medullary impairment, HIV infection is associated with the development of vacuolar myelopathy. Clinical manifestations refer to spinal cord injury, such as paraparesis, and are related to the loss of positional and vibrational perception.

The onset of symptoms occurs in the advanced stages of infection, while most patients do not have any symptoms over the course of their life and the diagnosis is made in the post-mortem examination. Magnetic Resonance Imaging (MRI) very often does not show any alteration. Examination of the cerebrospinal fluid (CSF) may also be completely normal or non-specific. The study of evoked potentials could instead guide the diagnosis since sensory evoked potentials are frequently abnormal early.

It is believed that the onset of this pathology depends on deregulated mechanisms of transmethylation attributable to the infection itself or to the inflammatory response that would lead to the demyelination of the dorsal columns of the lateral columns with the formation of prominent vacuoles within the myelin sheaths.

Case report: We report the case of a 49-year-old man who came to our attention on June 2020 as a new diagnosis of HIV. In the medical history he reported acute leukemia at the age of 5 treated with chemotherapy and allogeneic transplant.

The clinical picture began in May 2020 with hypotension, dizziness, postural instability with falls. The patient reported since at least 6 months asthenia, pain in the thighs due to modest efforts, postural instability and arterial hypotension. In the previous 3 months, there were episodes of freezing of gait, followed by sudden anteropulsion with fast gait.

Once the patient resulted positive to the HIV screening test and to the Western Blot confirmation, he was admitted to the Infectious Disease Clinic.

Baseline tests showed HIV-RNA on blood equal to 4,440,000 copies/mL and CD4+ counts of 69/mmc (ratio of 0.04).

Rachicentesis was performed, which highlighted proteins elevation in the absence of other relevant findings.

CSF investigations excluded infection by neurotropic viruses (including CMV, JCV, EBV, HHV8), Toxoplasma or Cryptococcus. HIV-RNA was detected on CSF equal to 70310 copies/mL.

MRI of the spinal cord was also required, which did not show characteristic changes in the posterior and lateral cords of the spinal cord.

Finally, somato-sensory and motor evoked potentials were performed; the magnetic stimulation of the motor cortical area was normal, while the somatosensory evoked potentials showed signs of suffering of the afferent pathways, from probable medullary involvement.

Highly Active AntiRetroviral Therapy (HAART) was started with darunavir/cobicistat/emtricitabine/tenofovir alafenamide and dolutegravir (resistance tests pending). At subsequent re-evaluations, HAART was correctly taken and well tolerated, and the neurological symptoms regressed.

Comorbidities

Non infectious comorbidities in HIV

P 32 **POSITIVE CORRELATION BETWEEN BONE AND ENDOTHELIAL DAMAGE IN PATIENTS WITH HIV**

A. Masiello, V. Zollo, F. Simeone, A. Iodice, P. Maggi

AORN "S. Anna e San Sebastiano", Caserta, University of Campania "L. Vanvitelli"

Background: Persons Living With HIV (PLWH) are at high risk of non-AIDS comorbidities such as osteoporosis and atherosclerosis. These two comorbidities are considered associated to aging but few data exist regarding their correlations. Recent studies in general population have shown that, patients affected by osteoporosis, show higher risk of developing cardiovascular disease than those with normal bone mass. Several factors could contribute to bone disease and endothelial dysfunction. The aim of our study is to evaluate the eventual relationship between bone and endothelial damage in HIV infected patients effectively treated by antiretroviral therapy.

Materials and methods: We enrolled 49 patients, 13 females and 36males. Patients were submitted to measurement of carotid intima-media thickness (cIMT) with high resolution B mode Doppler USG and evaluation of mineral bone density with bioelectrical impedence analysis.We divided the patients in 2 groups based on cIMT: A) (#28) with normal cIMT(=/<1.3 mm) and B) (#21) with pathologic cIMT(>1.3 mm). For both groups we evaluated T and Z score values. For patients >50 years and for menopausal women we have considered the T score (normal >-1, osteopenia between -1 and -2,5, osteoporosis <-2,5) , for patients<50 years we have considered the Z score(<-2 pathologic, >-2 normal). For each group we also considered CD4, CD4 nadir, CD4/CD8 ratio, years of HAART, type of ART, total, HDL and LDL cholesterol and triglycerides levels. For statistical analysis we used t-student and X-square tests.

Results: Data are reported in Table 1. No significant differences emerged between the two groups regarding type of ART, CD4, nadir CD4,CD4/CD8 ratio, triglycerides, total cholesterol, HDL and LDL. A significant difference emerged for T and Z scores between the two groups, with pathological bone values in group B (p<0,005).

Conclusions: These data evidence a positive relationship between bone and endothelial damage in PLWH treated with ARV: persons with increased cIMT (>1,3 mm) show more frequently bone density alterations with osteopenia or osteoporosis.The major limitation of our study is the small number of patients enrolled. However, this positive correlation suggests the importance of a comprehensive diagnostic evaluation in PLWH.

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Comorbidities

Non infectious comorbidities in HIV

P 33 **LIMB-GIRDLE MUSCULAR DYSTROPHY IN A PATIENT WITH RECENT DIAGNOSIS OF HIV INFECTION**

D. Checchi[1], A Lodi[1], P.G. Pace[1], S. Tedde[1], F. Barreca[1], F. Caldara[1], A. Crea[1], T. Mulas[1], L. Ferrari[1], G. De Simone[1], M. Compagno[1], G. Merlonghi[2], M. Garibaldi[2], L. Sarmati[1], M. Andreoni[1], M. Iannetta[1]

[1]Fondazione PTV and University of Rome Tor Vergata, Rome, [2]SAPIENZA University of Rome, Sant'Andrea Hospital, Rome

Introduction: Limb-girdle muscular dystrophy type 2B is an autosomal recessive disease caused by mutations in the DYSF gene on chromosome 2p13, encoding for dysferlin, a protein located in the sarcolemma. Onset typically occurs during the second decade of life with a deficit of either the cingular musculature (limb-girdle phenotype), or the posterior compartment of the lower limbs (Miyoshi myopathy); the disease is progressive, and associated with a marked increase in serum creatine kinase (CK). No specific therapies are currently available

Case Report: A 26-years-old man from Guinea, a professional boxer with no significant past medical history, was admitted in august 2021 to our hospital, for thoracoabdominal pain, myalgia, asthenia and persisting fever for over a month. On admission, laboratory tests showed an increase in transaminases and muscle necrosis enzymes (AST/ALT 425/357 U/L, CK 10193 U/L, CK-MB> 600 ng/mL, Myoglobin 3020 ng/mL), without evidence of kidney injury and systemic inflammation. Autoimmunity screening tests were negative; traumatic, toxic or systemic inflammatory causes of rhabdomyolysis were excluded.

HIV serological test was positive, with HIV-RNA 664000 cp/mL, CD4+ 139/mL and CD4+/CD8+ ratio = 0.13 at baseline. The Western blot assay detected the presence of p31 band, ruling out the possibility of a recent infection. A month after HIV diagnosis, after other coinfections were excluded, and with persistently elevated muscle necrosis indices, HAART was started with DRV/c/FTC/TAF, with good immuno-virological response (Figure 1A)

Muscle MRI revealed edema in the posterior compartment of the thighs and in the rectus femoris muscle (Figure 1B), without marked fibrous-adipose replacement. Muscle biopsy showed a dystrophic pattern, with muscle necrosis and regeneration, connective tissue increase, in association with a marked inflammatory component (a predominantly macrophagic infiltrate with some NK lymphocytes, very rare CD8+ T cells, no CD4+ T cells); immunohistochemistry revealed a deficit of dysferlin expression. Molecular testing for mutations in the DYSF gene is ongoing

Conclusions: Rhabdomyolysis in HIV patients is frequently drug induced (e.g. raltegravir). T-mediated myositis (such as Inclusion Body Myositis) are associated with HIV infection. However, no cases of patients with dysferlinopathy and HIV infection have been reported so far, and it is not clear the influence of HIV infection on clinical manifestations and progression of dysferlinopathy. Even in our case, it remains unclear if HIV may have triggered the dystrophy onset.

HIV-associated myositis may respond to HAART and steroid therapy. In our case, no improvement in rhabdomyolysis was observed six months after the start of HAART; the use of either steroid therapy (generally not recommended in the treatment of dysferlinopathy) or immunosuppressive drugs is under consideration to reduce the inflammatory component, as a part of clinical trials for rare diseases

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Comorbidities

Sexually Transmitted Infections (STIs)

P 34 **SENSE AND HYPERSENSITIVITY - A CASE SERIES OF JARISCH-HERXHEIMER REACTION FOLLOWING GONORRHEA TREATMENT**

D. Moschese[1], M.V. Cossu[1], S. Merli[1], R. Giorgi[1], L. Caron[2], A. Capetti[1], G. Rizzardini[1]

[1]I Division of Infectious Diseases - Department of Infectious Diseases - Luigi Sacco University Hospital - Milan, Italy, [2]Allergology Unit - Department of Infectious Diseases - Luigi Sacco University Hospital - Milan, Italy

Background: People experiencing a sexually transmitted infection are at greater risk for other concomitant STDs. The JHR is a self-limiting, acute febrile reaction that occurs within hours after a patient receives any spirochetal infection treatment. Only rarely threatening, it usually pass unnoticed.
We present three cases of misdiagnosed hypersensitivity reaction to ceftriaxone in patients undergoing treatment for gonococcal infection with a concomitant unknown early syphilis.
Case series: The I case is a 38 yo MSM who accessed our STD Clinic complaining the onset of dysuria and urethral mucopurulent discharge. Med history was collected and a visit was conducted that identified GU. During the same visit, the pt was contextually treated with ceftriaxone and azithromycin (C+A). Within 6 hrs, the patient returned to our clinic reporting fever (38.5° C) and a macular rash; as the GP was consulted, a diagnosis of hypersensitivity reaction to ceftriaxone was suggested. An ID and allergologic evaluation were conducted but as laboratory exams tested positive for TP antibodies along with TPHA, a JHR was diagnosed and treatment was scheduled.
The II case is a 27 yo MSM on PrEP who accessed our clinic for a preemptive therapy of gonorrhea after a sexual contact with GU affected partner. The pt thus received C+A and within 8 hrs the patient returned to our STD clinic complaining of a possible allergic reaction because of the worsening of the previously evidenced rash. After allergologic consultation, the lab tests confirmed primary syphilis and the diagnosis of JHR was postulated.
The III case is the one of a 25 yo MSM who accessed the clinic complaining the onset of urethral mucopurulent discharge and dysuria. On the very same day, as a GU was diagnosed, a one shot C+A therapy was performed. After 7 hrs the pt accessed the ER at our hospital as suggested by his GP for the onset of fever (39° C), fatigue and a mild reddish skin rash. As the pt was evaluated by both the allergology and ID consultants and blood tests evidenced syphilis, a JHR was diagnosed. The symptoms resolved the same night and the following morning the pt was discharged.
Conclusions: Once again, an accurate medical history is the key for a fast and accurate diagnosis. Although JHR may not be well known among non-infectivologists, features of clinical signs and symptoms can orient to the non-allergic etiology of the manifestation. Although this reaction is rarely life-threatening, the misidentification of the condition can lead, as in the presented cases, to time- and money-wasting medical subsequent evaluation along with possible exposure to further unnecessary medications and labelling as beta-lactam allergic.
Of note is that prophylaxis of JHR with either oral antibiotics, NSAID, acetaminophen and steroids have been proposed but did not assure the avoidance of such reaction.
Appeal to sense and a careful medical history before lab tests and drugs is still essential in modern medicine.

Comorbidities

Sexually Transmitted Infections (STIs)

P 35 **ON THE IMPORTANCE OF THE SEXUAL HEALTH SCREENING: THE IMPACT OF A NEWBORN SERVICE IN THE POST COVID-19 ERA IN SOUTHERN ITALY**

E. Milano[1], L. Ronga[2], D. Fiordelisi[1], A. Ricciardi[1], E. Pallara[1], M. Camporeale[1], E. De Vita[1], R. Novara[1], G. Patti[1], V. Totaro[1], E. M. Ranieri[2], R. Del Prete[2], M.T. Montagna[2], A. Saracino[1]

[1]Clinic of Infectious Diseases, University of Bari, Bari, [2]Section of Microbiology and Virology, University of Bari

Background: COVID pandemic produced conflicting effects on the epidemiology of sexually transmitted infections (STI), as lockdown probably reduced their spread, but diagnosis was impaired due to interruption of many outpatient services, especially in centres without dedicated programs. Since January 2022, a new service was developed in the Infectious Diseases Clinic of University of Bari to uniform diagnosis and follow up procedures for STI and to offer pre-exposure prophylaxis (PrEP). Aim of the study was to evaluate the results of the first three months of activity of this service.

Methods: This monocentric retrospective analysis included all subjects attending our STI and PrEP out-patient service from January, 8th to March 2022, 31st. Demographic, clinical, laboratory data and behavioural risk were collected. All people were offered HIV, viral hepatitis and syphilis screening, if previously unknown. A multiplex Real Time PCR for common STI agents (AnyplexTM II, STI-7 Detection Kit, Seegene, Inc. Seoul, Korea) was performed on pharyngeal/anal swabs and urine. Anoscopy and HPV DNA testing (AnyplexTM II HPV 28 Detection System, Seegene, Inc. Seoul, Korea) from anal swab were offered to those who reported receptive anal intercourses.

Results: The analysis included 54 patients (Table 1), all Italians, median age 36 (IQR: 29.0-41.7) years, mainly males (53, 98.1%) and men who have sex with men (44, 81.5%) with high educational level and employed; 44.4% (24) were HIV-infected, all on antiretroviral therapy. The 27.8% (15) failed to report the use of condoms during sexual intercourses and 7.4% (4) engaged chemsex.

The 94.4% were at their first general screening for STI; however, patients with HIV infection and in follow-up were all previously tested for syphilis. Overall, in 28/54 at least one STI was diagnosed and treated, including condyloma; in 14 cases they were also HIV infected. In 38 cases, patients had accessed the service without reporting any symptom and asking for screening or for PrEP; ten of whom (26.3%), however, were diagnosed with STI, 9 of whom also presenting disease signs at the physical examination. Based on risk assessment, six new PrEP were offered. Among 33 anoscopies, 10 were positive for condyloma-like lesions. Moreover, 28 anal HPV-tests were performed with a positivity rate of 85.7%, of which 22 (78.6%) samples with at least one high risk HPV-type. Overall, syphilis was the most widespread infection (18.5%), followed by T. vaginalis, C. trachomatis, N. gonorrhoeae and M. genitalium; moreover, a colonization by U. urealyticum was found in 11 patients.

Conclusions: Our preliminary results on STI screening during the first three months of activity of a new outpatient service demonstrates that a large majority are underdiagnosed, even in people routinary followed for HIV-infection, and that a dedicated service is suitable.

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Comorbidities

Sexually Transmitted Infections (STIs)

P 36 **MALIGNANT SYPHILIS AND A NEWLY HIV INFECTION DIAGNOSIS**

G. Quartini[1], A. Lavagna[1], L. Ricci[2], M.E. Laurenti[2], M. Papini[3], M.B. Pasticci[1]

[1]Clinica di Malattie Infettive, Università degli Studi di Perugia, Ospedale Santa Maria di Terni, Terni, [2]Struttura Complessa di Anatomia Patologica, Università degli Studi di Perugia, Ospedale Santa Maria di Terni, Terni, [3]Clinica Dermatologica, Università degli Studi di Perugia, Ospedale Santa Maria di Terni, Terni

Background and aim: HIV and syphilis co-infection is a common condition associated also with atypical manifestation and/or treatment failure. Malignant syphilis (MS) is rare, atypical form of secondary syphilis, more frequently diagnosed in persons with HIV co-infection. We report a case of MS in a male immunocompromised patient with a new HIV infection diagnosis.

Case report: A 25-years old Caucasian male was seen at the emergency room of our Hospital for fever and eritamato-papular lesion over the body since one week. On physical examination we evidenced numerous macular-papular lesions, some ulcerated and covered with necrotic well defined edges crusts. These lesions extended over the body surface, including the scalp. However, palms and soles were not interested. Spleen and lever were also appreciable 1 cm below the costal margins, lymphadenopathy and neurologic deficit were not detected. Erythrocytes sedimentation rate (ESR) resulted 100 mm/1°h, C-reactive protein 4.4 mg/dL, GB 5.73X103/mmc, liver function tests were normal, HIV serology positive. HIV-RNA had a value of 1500000 copies/mL, CD4+ lymphocytes were 97/mmc. Bictegravir was prescribed. The patient refused to be admitted. Acute necrotic varioliform pitiriasis (PLEVA) in HIV infection was the suspected diagnosed. A week later, rapid reaginic test (RPR) 1:32, fluorescence treponemal antibodies (FTA) reactive (++++). Treponema pallidum agglutination (TPPA) 1:5120 allowed the diagnose of syphilis. A skin biopsy was performed and evidenced dermal chronic inflammatory infiltrates extending to the blood vessels. Immunostaining was positive for Treponema pallidum leading to diagnose malignant syphilis. Hearth sonogram and magnetic brain resonance with angiographic study were normal. Benzathine penicillin G 2.400.000 units intramuscular were administered two weeks later. Before this treatment the patient was prescribed clarithromycin 500 mg twice a day, either to avoid the Jarisch-Erxheimer reaction, either because the patient developed Covid-19 infection and was unable to leave his house. Benzathine penicillin was administered for three consecutive weeks. A week after the third dose, skin lesions were improved showing flat post inflammatory scars with hyperpigmentation. The patient was on the same anti-retroviral treatment and six weeks after it was started HIV-RNA resulted 642 copies/mL and CD4+ 258/mmc.

Conclusion: Given the increasing reported cases of malignant syphilis, especially in immunodeficiency due to HIV co-infection, this disease should always be included in differential diagnoses of a varied clinical manifestations and several dermatoses in HIV co-infected persons.

COVID-19

COVID-19 therapies

P 37 **MONLUPIRAVIR FOR THE EARLY TREATMENT OF COVID-19**

D. Altobelli, G.V. De Socio, G. Gamboni, S. Benedetti, M. Albagini, E. Baranello, D. Veramonti, E. Schiaroli, D. Francisci

Department of Medicine and Surgery, Clinic of Infectious Diseases, "Santa Maria della Misericordia" Hospital, University of Perugia, Perugia, Italy

Background: Molnupiravir is the first oral antiviral drug available for treatment of adults with mild to moderate COVID-19, who are within 5 days of symptom onset and at high risk of progressing to severe disease. In registrative MOVe-OUT Study the percentage of participants who were hospitalized for any reason or died through 1 month was in the Molnupiravir group 6.8% vs 9.7% in placebo group showing that treatment reduces the risk of hospitalization or death by approximately 31%. In an observational retrospective study, we report in clinical practice experience the results of efficacy and tolerability of Monlupiravir.

Materials and methods: Patients were enrolled at Infectious Diseases Clinic of Perugia according to AIFA prescription criteria from January to February 2022. Demographic, medical history, comorbidities and vaccination data were collected. We evaluated patients' symptoms presented at enrollment and at thirty days after Molnupiravir therapy. A standardized questionnaire to assess for potential adverse effects, need for hospitalization and death was administered. We evaluated: timelines of the treatment from the onset of symptoms, hospitalization for any cause, specific COVID-19 hospitalization or death through day 30.

Results: We enrolled 86 patients (45 females and 41 males), from 21 to 93 years of age; everyone presented at least one symptom related to COVID-19 and had at least one risk factor for progression to severe disease. Among them, 71 were vaccinated (54 with booster dose, 15 with 2 doses, 1 with a single dose). Evaluable patients were 64, lost at follow-up were 22.

The interval between symptoms onset and administering of Monlupiravir was a median of 3 days [IQR 2-4]. The median times to resolution of symptoms from treatment onset was 3 days [IQR 2-5]. At 30 days time, no deaths COVID-19 related were registered, 6/64 patients needed hospitalization for any reason (9.3%), of which 3 for COVID-19 pneumonia (4.6%). Adverse reaction was reported in 13 cases (gastrointestinal symptoms, headache, and itching), but not severe ones.

Conclusions: In our cohort, a relative low sample size, we observed the hospitalization rate for any reason (9.3%) slightly higher than expected from MOVe-OUT Study. 4.6% was hospitalized for progression of COVID-19; COVID -19 related deaths didn't occur. However, among 64 patients at 30 days follow-up, it emerged that 3 refused to take therapy and 3 interrupted drug assumption before full treatment time. After excluding the aforementioned patients and the ones who did not begin therapy within five days after symptoms onset, we are left with 50 patients. In this sub-cohort, no one died, 3/50 (6%) were hospitalized at 30 days, of which 2/50 (4%) for COVID-19 progression, results about efficacy comparable to the MOVe-OUT RCT.

COVID-19

COVID-19 therapies

P 38 **BARICITINIB ALONE AND IN COMBINATION WITH REMDESIVIR FOR THE LATE TREATMENT OF ADULTS HOSPITALIZED WITH COVID-19**

M. Niglio[1], M. Poliseno[1], D. Lacedonia[2], F. De Gregorio[1], G. Minafra[1], T. Campanino[2], I. Cassitti[2], T.A. Santantonio[1], M.P. Foschino Barbaro[2], S. Lo Caputo[1]

[1]Unit of Infectious Diseases, Foggia University Hospital - Foggia, Italy, [2]Unit of Respiratory Diseases, Foggia University Hospital - Foggia, Italy

Introduction: Despite the availability of treatments capable to prevent severe COVID-19, still a remarkable proportion of patients is hospitalized with advanced disease and oxygen needs. Immunomodulators, alone or in combination with antivirals, are recommended in similar settings. The present study aims to identify predictors of Intensive Care Unit (ICU) admission and/or death among patients with moderate to severe COVID-19 and to outline how the prescription of Baricitinib with or without Remdesivir could affect this outcome.

Materials and Methods: Clinical, therapeutical, and laboratory features of all patients with Sars-CoV2 pneumonia and oxygen requirement who were consecutively hospitalized in the Respiratory Diseases and Infectious Diseases Unit of Foggia University Hospital from October 1, 2021, to April 1, 2022, were retrospectively collected. Treatment with Remdesivir (5 days), Baricitinib (10 days), or both, associated with heparin and steroids, were prescribed according to guidelines. Descriptive statistic was performed for each treatment group. Chi-square test/Fisher exact test and non-parametric ANOVA were used, as appropriate, to outline differences between groups and with untreated patients. Kaplan-Meier curves were built to estimate the 30-days ICU admission/death rate among study participants. The Cox univariate and multivariate regression were performed to identify factors associated with the above-mentioned outcomes.

Results: 162 patients were enrolled. At admission, Baricitinib was prescribed in 28 subjects (17%) with advanced disease, while 72 (44%) started Remdesivir. Baricitinib was subsequently added in 22 (30%) of them. Because of underlying conditions, 62 subjects (38%) did not receive any treatment. Older age and a higher proportion of subjects with chronic kidney disease (CKD) were observed among untreated patients. Delayed hospitalization from symptom onset and a higher prevalence of Non-Invasive Ventilation (NIV) requirements were noticed among patients treated with Baricitinib (Table 1). An HR 0.37 (95% C.I. 0.17-0.81, p=.01) of ICU admission/death was reported in treated vs untreated patients, although no differences were observed based on the type of treatment received (Figure 1, a) and b)). At multivariable analysis, presence of CKD (aHR 7.67, 95% C.I. 2.67-23.4, p<.001), type II Diabetes (aHR 2.03, 95% C.I. 0.97-4.23, p=.05), older age (aHR 0.95, 95% C.I. 0.93-0.98 , p<.001), NIV requirement (aHR 0.21, 95% C.I. 0.11-0.42, p<.001) and longer time interval from symptom onset (aHR 1.08 C.I. 1.01-1.15, p=.02) were predictors of worse outcome (Table 2).

Conclusions: Baricitinib, Remdesivir and their association showed good efficacy in the treatment of patients with moderate/severe COVID-19. The applicability of these treatments was limited by older age, presence of renal disease, and delayed hospital admission from symptom onset, all factors that negatively influenced patients' outcomes.

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COVID-19
COVID-19 therapies

P 39 **TYPE OF PATIENTS TRAITED WITH MAB IN COVID-19: THE REALITY OF AMEDEO DI SAVOIA**

C. Marchiaro[1], E. Catellani[1], D. Piccioni[1], S. Bertini[1], F. Donato[1], M. Ferrara[2], G. Cinnirella[1]

[1]ASL Città di Torino, SSD Infectious Deseases Pharmacy - HCV, Hospital Amedeo di Savoia, [2]Unity of Infectious Deseases, Department of Medical Sciences, University of Torino, Torino

Background: COVID-19 pandemic, caused by SARS-CoV-2, has provocked so far 485 million cases and 6 million deaths. Due to its high spread, morbidity and mortality, along with the consequent socioeconomical impact, the development of new therapies, together with vaccines, has become a priority for health care systems. In Italy, monoclonal antibodies (mAbs) were approved for the treatment of COVID-19 disease through the Ministerial Decrees published in the Gazzetta Ufficiale in February and December 2021. The aim of this study is to analyse patients' status (comorbidity criteria and COVID-19 vaccination) and the relative safety profile of mABs used at the Amedeo di Savoia Hospital (OAS) in Turin. These are casirivimab/imdevimab (C/I), bamlanivimab/etesevimab (B/E) and sotrovimab (S).

Material and methods: Data related to treatements were obtained through the monitoring logs of the Italian Medicines Agency (AIFA) and subsequently analysed using Microsoft Excel. The study population was divided based on the mAbs administrated, sex, COVID-19 symptomatology, comorbidity and, where possible, COVID-19 vaccine received. Finally, the safety profile of mAbs was evaluated by defining the percentage of side effects and their severity.

Results: Since march 2021 to march 2022, 668 patients (347 men and 311 women) were treated with mAbs. Among them, 409 (61.2%) were treated with the combination C/I, 38 (5.7%) with B/E and 211 (33.1%) with S. The majority of the patients were aged over 65 (50%), while 40% of the study population were aged between 35 and 65, and only 10% were aged under 35. The most frequent symptoms were fever and cough (registered respectively in 57% and 64% of cases), while the most frequent comorbidities encountered were obesity and cardiovasular diseases in patients treated with C/I (32%) and primary or secondary immunodeficiency in patients treated with S (66%). Analysing patients' COVID-19 vaccine status, 43% of patients treated with C/I were found to be not vaccinated, while only 13.5% of the patients treated with S did not receive the vaccine. During and after the infusion 8 patients showed ADRs, 3 treated with C/I, 1 treated with B/E and 4 treated with S.

Conclusions: The lower utilization rate of sotrovimab compared to casirivamb/imdevimab reflects the subsequent favorable opinion of use of the former over the latter. In addition, studies have shown the C/I reduced ability to neutralize the omicron 1 variant. This explains the large consumption of S, active on this variant, since the end of the year 2021. Finally, the lower percentage of unvaccinated persons found for patients treated with S compared with C/I is justified by the advancement of the vaccination campaign.

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COVID-19

COVID-19 therapies

P 40 **EFFICACY OF SOTROVIMAB AS EARLY COVID TREATMENT OF BA.1 SUBLINEAGE OF OMICRON VARIANT**

E. Drappero[1], M. Ferrara[1], A. Gaviraghi[1], F. Alladio[1], F. Venuti[1], G, Stroffolini[1], G. Accardo[1], S. Fantino[1], F. Traverso[1], G. Trevisan[1], D. Vita[1], L. Di Girolamo[1], L. Ponzetta[1], M. Quaranta[1], F. Ranzani[1], A. Serra[1], L. Trentini[1], E. Burdino[2], G. Gregori[2], F. Cerutti[2], V. Ghisetti[2], C. Marchiaro[3], E. Catellani[3], G. Cinnirella[3], G. Di Perri[1], S. Bonora[1]

[1]Unit of Infectious Diseases, Department of Medical Sciences, University of Torino, Torino, [2]Laboratory of Microbiology and Virology, Amedeo di Savoia Hospital, ASL Città di Torino, Torino, [3]SDD Infectious Diseases Pharmacy – HCV. Amedeo di Savoia Hospital, ASL Città di Torino, Torino

Background: Sotrovimab has received emergency use authorization to treat patients (pts) with mildto-moderate SARS-CoV-2 infection in order to prevent disease progression. Sotrovimab has been shown to retain “in vitro” activity against the recent omicron BA.1 variant, however clinical data are lacking. Aim of our study was to evaluate Sotrovimab efficacy in the clinical setting.

Methods: Pts with mild-to-moderate COVID-19 symptoms, at high-risk for disease progression according to major FDA/AIFA criteria and treated with Sotrovimab infusion between January and February 2022 were considered. Pts with RT-PCR nasopharyngeal swab presumptively positive for Omicron BA.1 variant by S gene target failure (SGTF) were selected. Routine blood tests including inflammatory markers, SARS-CoV-2 serology and peripheral room-air blood oxygen saturation (SpO2) were collected on infusion day. Hospitalisation/death at 28 days was recorded as primary end-point; worsening of symptoms within 24-hours from infusion was collected. Study population
characteristics were descripted as mean (CI95%). Binary Logistic Regression analysis was performed as appropriate.

Results: 158 pts were evaluated: 54% male, mean age 62 years (59-65), 84% were vaccinated, the majority with 3 doses (75%), while 69% had a positive IgG serology. Ten percent resulted to have a 24-hours worsening after treatment. At 28 days, 15 (10%) pts were admitted to hospital due to disease progression and 3 died. On multivariate regression analysis, worsening within 24-hours from Sotrovimab infusion (p=0.003), and elevated values of troponin I (p=0.022) were independently associated with a higher risk of hospitalisation/death. Longer SARS-CoV-2 PCR length of negativization time (p=0.056) and lymphocyte count (p=0.057) were borderline associated with disease progression. Presence of IgG anti-SARS-CoV-2 at baseline resulted to be protective from hospitalisation/death (p=0.044).

Conclusions: In our population of patients affected by Omicron BA.1 variant infection and at high-risk for disease progression, Sotrovimab showed to be effective by preventing hospitalisation and/or death in 90% of subjects. Efficacy was somewhat lower to values reported in previous clinical trial (99%), but a more heterogeneous population could have been enrolled in our clinical setting. Efficacy seemed to be reduced in pts presenting with biochemical signs of active inflammatory phase, instead was more favourable in subjects with detectable IgG antibody titer against SARS-CoV-2 at baseline.

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COVID-19

COVID-19 therapies

P 41 **CYSTEAMINE EXERTS IN VITRO ANTIVIRAL ACTIVITY AGAINST THE SARS-COV-2 DELTA AND OMICRON VARIANTS**

T. Alonzi[1], A. Aiello[1], F. Repele[1], L. Falasca[1], M. Francalancia[1], A.R. Garbuglia[1], G. Delogu[3,4], M. Piacentini[1,2], D. Goletti[1]

[1]National Institute for Infectious Diseases "L. Spallanzani" IRCCS, [2]Department of Biology, University of Rome "Tor Vergata", [3]Institute of Microbiology, Università Cattolica del Sacro Cuore - Fondazione Policlinico Gemelli, [4]Mater Olbia Hospital

Background: The novel SARS-CoV-2 variants of concern (VOC) represent a considerable global alarm because their mutations are known to affect transmissibility and cause immune escape. The available vaccines do not avoid infection although they prevent severe disease and deaths, therefore COVID-19 still needs effective therapies.
We have recently reported that the aminothiol cysteamine, an already human applied drug, exerts direct anti-viral properties against SARS-CoV-2 and has in vitro immunomodulatory effect.
Material and Methods: To determine whether these compounds exert antiviral effects against SARS-CoV-2, we used the kidney epithelial african green monkey-derived Vero E6 cells and the human epithelial lung adenocarcinoma Calu-3 cells to perform different in vitro viral infected cell-based assays. Cysteamine antiviral effects against the wild type, Delta or Omicron VOC were evaluated through cytopathic effect (CPE) inhibition assay on Vero E6 cells; SARS-CoV-2 virus yield assay on supernatants from either Vero E6 or Calu-3 cells and transmission electron microscopy analysis on Vero E6 cells.
Results: We found that cysteamine significantly reduces the cytopathic effect induced by SARS-CoV-2 Wild type and Delta variant in Vero E6 cells.
On the other hand, cysteamine had no effects on the survival of cells infected with the Omicron variant, due to the lack of cytotoxicity exerted by the Omicron variant on Vero E6 cells, when infected at a MOI=0.001 for 72 hours. Interestingly, Delta variant induced an intermediate degree of cell death between the Wild type and Omicron variant viruses.
We also found that cysteamine significantly reduces the production of Wild type, Delta and Omicron variants in Vero E6 and Calu-3 cells as observed by the decreased virus yield measured in the culture media and by transmission electron microscopy analysis. Notably, cysteamine is more effective in inhibiting the Omicron rather than Delta or the Wild type viruses, with an 80% inhibition of Omicron production compared to 40% of Wild type and Delta variant.
Conclusions: Overall, our findings demonstrated that cysteamine exerts direct anti-viral actions against SARS-CoV-2 Delta and Omicron variants, in addition to the Wild type virus.
Since we previously reported that cysteamine exerts its antiviral effect independently on the time of treatment respect to the SARS-CoV-2 infection, the blockage of host factors required for viral production and/spreading further sustains that cysteamine is a good candidate as a repurposing drug for the treatment of SARS-CoV-2 infection and has to be necessarily investigated in randomized clinical trials.

COVID-19

COVID-19 therapies

P 42 **A POSSIBLE TREATMENT ALGORITHM FOR THE USE OF ANTIVIRAL THERAPIES AND MONOCLONAL ANTIBODIES AGAINST COVID-19**

L. Diella[1], D.F. Bavaro[1], D. Fiordelisi[1], G. Guido[1], A. Belati[1], G. Brindicci[1], G. Loseto[2], C. Minoia[2], A. Guarini[2], I. Attolico[3], T. Perrone[3], P. Musto[4], S. Simone[5], L. Gesualdo[5], M. Rendina[6], A. Di Leo[6], M. Santoro[7], M. Dell'Aera[7], F. Di Gennaro[1], A. Saracino[1]

[1]Clinic of Infectious Diseases, Department of Biomedical Sciences and Human Oncology, University of Bari "Aldo Moro", Bari, Italy, [2]Hematology Unit, IRCCS Istituto Tumori "Giovanni Paolo II", Bari, Italy, [3]Unit of Hematology and Stem Cell Transplantation, AOUC Policlinico, Bari, Italy, [4]Department of Emergency and Organ Transplantation, "Aldo Moro" University School of Medicine and Unit of Hematology and Stem Cell Transplantation, AOUC Policlinico, Bari, Italy, [5]Nephrology, Dialysis and Transplantation Unit, Department of Emergency and Organ Transplantation (DETO), University of Bari Aldo Moro, Bari, Italy, [6]Section of Gastroenterology, Department of Emergency and Organ Transplantation, University "Aldo Moro" of Bari, Bari, Italy, [7]Farmacia Ospedaliera AOU Policlinico di Bari – Bari, Italy

Background: Two oral antivirals, nirmatrelvir/ritonavir (NIR/r) and molnupiravir (MOL), and one wide spectrum monoclonal antibody, sotrovimab (SOT), have been recently approved to reduce the risk of severe COVID-19 in high-risk population. However, clinical guidelines leading to the appropriate drug choice in real life are still lacking. Aim of this study was to evaluate the efficacy and safety of outpatient COVID-19 treatments in a real-life context according to our internal treatment protocol.

Methods: This is a prospective cohort study including all consecutive patients with COVID-19 evaluated from February 10th, 2022, to April 1st, 2022, in a COVID-19 outpatient service at our Unit. Medical data of COVID-19 patients was sent to a dedicated mail address by general practitioners; then, clinical status of the patients was evaluated by telephone interview. Based on an internal arbitrary score, considering comorbidities and immunological status (Figure 1), risk of progression to severe COVID-19 was attributed to each patient. Finally, treatment with antiviral and/or monoclonal antibodies was prescribed according to a pre-established algorithm (Figure 2). In case of inconclusive telephonic screening or complications during treatment, medical evaluation was also offered. Patients were followed up for 28 days from treatment administration. Endpoints of the study were hospitalization due to respiratory failure, adverse events to treatments and death.

Results: A total of 205 patients were enrolled. Median (q1-q3) age was 62 (45–71) years old, 52% were males. According to our risk score 98 (48%) were considered at low risk, 94 (46%) at moderate risk and 5 (2%) at high risk of severe COVID-19; 9/205 (4%) resulted not eligible for absence of risk factors, and 2 initially eligible patients were excluded because affected by severe COVID-19 at time of treatment prescription. Moreover, among the 196 remaining patients, 16 (8%) were treated in other centers or refused therapy. Therefore, the analysis included 178 patients. Median time from diagnosis of COVID-19 to treatment was of 1 (1 – 3) days. A total of 77 (43%) were treated with NIR/r, 48 (27%) with MOL, 46 (26%) with SOT and 7 (4%) with combination therapy (5 NIR/r + SOT and 2 MOL + SOT): only 4 (2,2%) patients developed a lung failure requiring hospitalization (3 in medium-risk group and 1 in low-risk group), but no deaths were recorded. Finally, adverse events were reported only in NIR/r group; indeed, 10% of them reported dysgeusia and one early discontinued the therapy for this reason.

Conclusion: In our cohort, the adoption of a treatment algorithm based on a risk stratification score for leading the choice of the most appropriate antiviral/monoclonal drug against SARS-CoV-2 for eligible subjects was associated with a low rate of hospitalization and adverse events.

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COVID-19

COVID-19 therapies

P 43 **THERAPIES CONSUMPTION TO TREAT COVID-19 PATIENTS HOSPITALIZED IN A LARGE TERTIARY HOSPITAL IN NORTHERN ITALY DURING THE FIRST THREE PANDEMIC WAVES**

E. Focà[1], S. Calza[2], S. Piva[3], I. Ettori[1], C. De Ciuceis[4], F. Rasulo[3], A. Paini[5], S. Gipponi[6], G. Levi[7], M. Metra[8], M. Castellano[9], M. Nardin[10], C. Ricci[11], R. Badolato[12], F. Odicino[13], R. Orabonai[13], F. Scolari[14], E. Quiros Roldan[1], F. Marinoni[15], A.M. Roccaro[16], C. Rossi[17], F. Castelli[1]

[1]Unit of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili, Brescia, Italy, [2]Unit of Biostatistics and Bioinformatics, University of Brescia, Brescia, Italy, [3]Unit of Anesthesiology and Critical Care Medicine, ASST Spedali Civili, Italy, [4]Second Unit of Internal Medicine, University of Brescia and ASST Spedali Civili, Italy, [5]Unit of Emergency Internal Medicine, University of Brescia and ASST Spedali Civili, Italy, [6]Unit of Neurology, University of Brescia and ASST Spedali Civili, Brescia, Italy, [7]Unit of Pneumology, ASST Spedali Civili, Brescia, Italy, [8]Unit of Cardiology, University of Brescia and ASST Spedali Civili, Brescia, Italy, [9]Unit of Internal Medicine and Endocrinology, University of Brescia and ASST Spedali Civili, Brescia, Italy, [10]Third Unit of Internal Medicine, ASST Spedali Civili, Italy, [11]Unit of Gastroenterology University of Brescia and ASST Spedali Civili, Brescia, Italy, [12]Unit of Pediatrics, Children's Hospital University of Brescia and ASST Spedali Civili, Brescia, Italy, [13]Unit of Gynecology and Obstetrics, University of Brescia and ASST Spedali Civili, Brescia, Italy, [14]Unit of Nephrology and Dialysis, University of Brescia and ASST Spedali Civili, Brescia, Italy, [15]Unit of Planning and Management Control Service, ASST Spedali Civili, Brescia, Italy, [16]Unit of Clinical Research and Phase I Studies, ASST Spedali Civili, Brescia, Italy, [17]Chief Medical Officer Institution, ASST Spedali Civili, Brescia, Italy

Background: Several classes of molecules have been used to tackle the spread of Covid-19 and treat infected patients. In this study we evaluated the consumption of different agents used against Covid-19 in a large tertiary Hospital in Northern Italy.

Methods: we retrospectively identified a subset of hospitalized patients with COVID-19. The admissions were divided into three periods: the first wave from 21 February 2020 to 30 June 2020, the second wave from 1 July 2020 to 31 December 2020 and the third wave from 1 January 2021 to 30 April 2021. We evaluated the consumption of several molecules involved in the treatment of SARS-CoV-2 infected patients categorized as antivirals, steroids, heparin and biologic agents. We observed their evolution during the first three pandemic waves.

Results: Among 7054 patients hospitalized in the first three waves, a subset of 2550 patients was analyzed here. 1138 in the first wave, 931 in the second wave and 481 in the third wave. The mortality rate and in-hospital length of stay were described and analyzed elsewhere. We observed a reduction in antibiotic use across the three waves (78% vs. 68% vs. 58%, p<0.001); in particular azithromycin use decreased 559 (93%) 312 (84%)and 89 (76%) in the three waves respectively (p <0.001). Antivirals were predominantly administered in the first wave with a significant reduction in the last two waves (80% vs. 26% vs. 28%, p<0.001). Among them Chloroquine/hydroxychloroquine decreased significantly 769 (68%), 11 (1.2%) and 12 (2.5%)in the three waves respectively (<0.001) as it happened for Lopinavir /ritonavir and other antiretrovirals 552 (49%), 9 (1.0%) and 7 (1.5%) in the three waves respectively. Heparin administration goes from 61% in the first wave, to 81% in the second, to 74% in the third wave (p<0.001) while biological agents (including hyperimmune plasma) were primarily used during the first pandemic wave (19% vs. 1,6% vs. 2,7%) and decreased in the second and third one (p<0.001). Interestingly, the consumption of corticosteroids has instead increased 454 (41%), 593 (64%), 300 (63%) in the three waves respectively (p<0.001) with a predominance of dexamethasone 323 (74%), 473 (80%) and 212 (72%) (p=0.007) compared to methylprednisolone 29 (6.7%) 44 (7.5%) and 31 (11%) (P=0.15)

Conclusions: The initial therapeutical choice to treat COVID-19 was empirical, ”emotional” and suffered by a lack of evidence, this is particular true in the first wave. In the second and third waves we observed a decrease in the use of azithromycin as “antiviral” and other supposed antiviral molecules. The only remaining antiviral was remdesivir. Regarding steroid, the use of this treatment increased according to the evidences available and guidelines recommendations. In the second and third waves we seem to have offered to patients more reasoned and evidence-based treatment choice and compliant with guidelines recommendations.

COVID-19

COVID-19 therapies

P 44 **REMDESIVIR IN COMBINATION WITH CASIRIVIMAB/IMDEVIMAB MONOCLONAL ANTIBODIES FOR THE TREATMENT OF SEVERE COVID-19**

I. Gentile, I. Di Filippo, N. Esposito, M. Sarno, L. Fusco, F. Licciardi, A. Truono, N. Schiano Moriello, R. Scotto, B. Pinchera, G. Viceconte, A. Iuliano, E. Zappulo, M. Foggia, A.R. Buonomo

Department of Clinical Medicine and Surgery, Infectious Diseases Unit, University "Federico II", Naples, Italy

Introduction: Since the outbreak of the SARS-CoV2 pandemic in March 2020, numerous advances have been made both in the prevention and management of COVID-19. Despite the availability of effective vaccines, fragile patients (e.g.; those with comorbidities or immunodeficiency) remain at risk of progression to severe disease. Monoclonal antibodies may play an important role, in patients with mild or moderate disease at risk of progression and, in case of casirivimab/imdevimab combination, also in patients with severe COVID-19 and negative for anti-spike antibodies. Moreover, few data are available about the combination of monoclonal antibodies with remdesivir (the only antiviral approved for the treatment of severe COVID-19). Aim of our study was to analyze efficacy of the combination of the antiviral Remdesivir with anti-SARS-CoV-2 monoclonal antibodies casirivimab/imdevimab in patients hospitalized for severe COVID-19.
Material and Methods: All patients hospitalized for severe COVID-19 between July 2021 and March 2022 at Federico II University in Naples with negative anti-spike IgG serology and treated with casirivimab/imdevimab and remdesivir were enrolled. We assessed the rate of clinical worsening and mortality.
Results: We enrolled 20 patients. Main clinical and personal data are given in the table. Hematological diseases, primary or acquired immunodeficiencies, and cardiovascular diseases were the most frequently observed comorbidities. More than half of the patients did not receive any dose of vaccine or completed the primary course. Five patients (25%) experienced a worsening in respiratory conditions. One patient (5%) died.
Conclusions: In our real-life study, the combination of remdesivir and casirivimab/imdevimab in the treatment with severe COVID-19 was associated with a very low mortality rate, despite the presence of several risk factors for fatal outcome and the absence of protective anti-spike antibodies. We acknowledge that our study has several limitations, mainly the lack of a control group and the small sample size but it provides the first real-life data of such a combination. Larger studies are needed to confirm these results.

Attach: https://www.icar2022.it/public/abstract/Attach_ABS_309.PNG

COVID-19

COVID-19 therapies

P 45 **MONOCLONAL ANTIBODIES ADMINISTRATION AGAINST SARS-COV-2. THE EXPERIENCE OF THE TOR VERGATA HOSPITAL**

R.A. Cavasio[1], N. Braccialarghe[1], D. Zaçe[1], I. Spalliera[1], L. Coppola[1], L. Campogiani[1], L. Piermatteo[2], M.C. Bellocchi[2], F. Ceccherini Silberstein[2], M. Iannetta[1], L. Sarmati[1], M. Andreoni[1] and the Tor Vergata Hospital group

[1]Infectious Diseases Department, University of Rome Tor Vergata, Rome, Italy, [2]Virology Department, University of Rome Tor Vergata

Background: To cope with the SARS-CoV-2 pandemic several treatments were studied and out of these, monoclonal antibodies (MAbs) have shown efficacy to prevent the development of pneumonia after the infection.
Material and Methods: We conducted a retrospective, single-center study including data from patients with SARS-CoV-2 infection, treated according to AIFA criteria with MAbs (bamlanivimab/etesevimab (B/E), casirivimab/imdevimab (C/I) or sotrovimab (S)) from March 2021 to February 2022.
Results: Our cohort included 504 patients with a median age of 62 years (IQR 49-72), 51% males, 30% with a BMI≥30 and 42% with age>65. Before MAbs infusion, 33% of patients received antibiotic therapy, 13% corticosteroids and 9% both; at the moment of infusion 66% had completed the vaccination schedule according to the current Italian regulations. The most frequent risk factors for pneumonia development were cardiovascular disease (49%), primary or acquired immunodeficiency (26%), COPD (18%) and diabetes (13%). As for MAbs combination, patients were treated more often with B/E (54%), followed by C/I (30%) and S (16%). The outcome was positive (no pneumonia nor hospitalization) in 81% of cases, 3% needed hospitalization and 1% died. 15% of patients were lost at follow-up.
Nasopharyngeal swab (NPS) negativization time had a positive correlation with patients' age (r=0.16; p=0.001), C-reactive protein (CRP) (r=0.26; p<0.001) and creatinine values (r=0.22; p<0.001) at baseline (MAbs infusion day). Time of NPS negativization was 6.9 (95% C.I. [4.5-9.2]) days shorter for vaccinated compared to non-vaccinated patients (p<0.001). At the multivariate analysis the significancy of these values was confirmed.
Patients treated with C/I had a negative NPS on average 4.5 (95% C.I.= [1.8-7.3] days earlier than patients treated with B/E; patients who received S reached negativization 6.0 (95% C.I.= [2.2, 9.9]) days earlier than those treated with B/E (p=0.004). Patients with positive outcome had a negative NPS on average 14.3 (95% C.I.= [6.8, 23.1)], 25.5 (95% C.I.= [18.9, 33.4] and 68.3 (95% C.I.= [47.7, 90.2]) days earlier than patients who needed oxygen support or ventilation and patients who died, respectively (p=0.007, p<0.001, p<0.001, respectively).
Non-vaccinated patients had a higher rate of oxygen support need compared to vaccinated ones (p=0.006). Patients with worse outcomes were significantly older and had higher values of CRP and creatinine at baseline (p=0.04, p<0.001, p<0.001, respectively).
Conclusions: MAbs reduce the risk of hospitalization in fragile patients. Vaccination should not be a reason of exclusion for MAbs treatment, as vaccinated patients had shorter time of NPS negativization and lower probability of hospitalization. Older age, higher CRP and creatinine values assessed at baseline, correlated with worse outcomes. As for the time of NPS negativization, S was the most effective treatment amongst the MAbs used in our study.

COVID-19
COVID-19 therapies

P 46 **ORAL ANTIVIRALS AGAINST SARS-COV-2: THE EXPERIENCE OF THE TOR VERGATA HOSPITAL**

N. Braccialarghe, R.A. Cavasio, D. Zaçe, I. Spalliera, L. Coppola, M. Iannetta, L. Sarmati, M. Andreoni and the Tor Vergata Hospital group
Infectious Diseases Department, University of Rome Tor Vergata, Rome, Italy

Since the outbreak of COVID-19 pandemic the scientific community efforts have been focused on finding a vaccine to prevent the contagion and a treatment for infected people. Several antivirals with activity against SARS-CoV-2 were investigated and Remdesivir was the first to receive the approval from FDA. Since the end of 2021 orally administered antivirals have been used in SARS-CoV-2 positive patients.

Materials and Methods: We conducted a retrospective, single-center study including data from 135 outpatients who resulted positive for SARS-CoV-2 and were selected according to AIFA criteria to receive Molnupiravir (M) or Nirmaltrelvir/Ritonavir (N/R) in the Infectious Disease Clinic of the Tor Vergata Hospital from January 2022 to February 2022.

Results: Our cohort included 135 patients with a median age of 71 years (IQR 56,5 – 80,5), 51% were male, 91% received M and 9% received N/R. The median time of antiviral administration from symptoms onset was of 3,4 days. 75% of patients were vaccinated with booster dose at the time of the infection, 19% were vaccinated with two doses and 7% were unvaccinated; 10% started antibiotic therapy before the antiviral treatment, 4% started corticosteroids and 4% both therapies. The most frequent criteria of eligibility were cardiovascular disease (40%), primary or acquired immunodeficiency (28%), COPD (23%), BMI>30 (21%), diabetes (16%) and active tumor (16%). The majority of patients (84%) did not need hospitalization, only 2 were hospitalized receiving oxygen support and they were still positive at the nasopharyngeal swab (NPS) at the moment of this data analysis, 1 patient died and 14% of the enrolled subjects were lost at follow up. 13% of patients treated with M developed adverse events such as nausea and diarrhea. Time of negativization at the NPS had a negative correlation to the value of anti-Spike (r=-0.29; p=0.01).

The difference between cycle threshold (Ct) value of NPS at T7 and Ct value at the first positive NPS (T0) was higher among not hospitalized (NH) vs hospitalized (H) patients, for Gene E [12.1 (SD 5.8) vs -1.7 (SD 10.8); p=0.02], Gene N [12.3 (SD 10.8) vs -0.9 (SD 11.6); p=0.01] and Gene RDRP [11.8 (SD 5.3) vs -1.5 (SD 11.1); p=0.01]. Anti-Spike were higher among NH vs H patients [1714 (SD 1044.7) vs [43 (SD 60.3); p=0.028]. The patient who died had an RCP value 50.04 higher (p=0.04) compared to NH patients.

Delta Ct E, delta Ct N and delta Ct RdRp were significantly higher in patients without neoplastic disease (p=0.04, p=0.02, p=0.01, respectively) and had a negative correlation with creatinine levels (r=-0.36, p<0.001; r=-0.3, p=0.03; r=-0.32, p=0.02).

Conclusions: Oral antivirals represent a new effective treatment against COVID-19 in selected patients, reducing the time of negativization and the risk of hospitalization and of death. Solid tumor or oncohematologic diseases are associated to a slower negativization of NPS compared to other risk factors.

Further studies are necessary to compare M to N/R in real life setting.

COVID-19

COVID-19 therapies

P 47 **SARS COV 2 VIRAL VARIANTS AND MABS: THE RESULTS OF A COHORT STUDY IN SOUTHERN ITALY**

S. De Pascalis[1], L. Alessio[1], M. Pisaturo[1], A. Russo[1], R. Palladino[1], A.R. Buonomo[2], B. Pinchera[2], I. Gentile[2], C. Tiberio[3], L. Atripaldi[3], N. Coppola[1]

[1]AOU L.Vanvitelli, Naples, [2]AOU FedericoII, Naples, [3]AORN dei Colli, PO D.Cotugno, Naples

Introduction: The COVID-19 pandemic counts more than 160 million cases and over 3 million deaths worldwide and an unprecedentedly large number of mAbs have been developed to fight coronavirus disease 2019 (COVID -19).

Neutralizing mAbs are recombinant proteins that can be derived from the B cells of convalescent patients or humanized mice, decrease viral load when given early on in the course of SARS-CoV-2 infection and favourably impact clinical outcomes for patients with mild-to-moderate COVID-19.

Aims: we describe epidemiological and clinical characteristics and outcome of our population treated with mabs.

Metods: an observational retrospective multicentric study, we enrolled every patient treated with Mabs in 2 hospital center of Naples. In hospital the patients were undergone TNF and if it were positive they were analyzed for check Covid variants.

Results: we enrolled 133 subjects by December 2021 at January 2022. They were males for the 51.1% and 56.5 years of median, the subjects presented the Age the major recommendation for this treatment. The 21% of patients were treated with Bamlanivimab/Etesevimab, 37% with Casirivimab/Imdevimab and 56% with Sotrovimab.

We compared the subjects in 3 groups according to the 3 Mabs. The patients underwent to treat with Mabs were infected mostly with the omicron variant (p 0.0001) (TAB 1). In the table 2 we compared the clinical and epidemiological characteristic of 3 mabs groups of the 21 Delta variant subjects. There are no statistically significant differences except for the negative days where the 2 patients treated with casirivimab/imdevimab became negative in 11 days (fig 1: p 0.003).

Instead in table 3 we compared the clinical and epidemiological characteristic of 3 mabs groups of the 106 Omicron variant subjects. The population represented is the one most treated with Sotrovimab and especially those affected by malignant pathologies (p 0.023), while the obese more treated with casirivimab/imdevimab (p 0.001). There are no statistically significant differences between 3 omicron variant groups.

Conclusions: the higher prevalence of Omicron variant virus in this population reflectes the national epidemiology of this period and that Sotrovimab does not appear to have any effect on time to negative.

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COVID-19

HIV and COVID-19

P 48 **LACK OF ANTI-N IGG AFTER SYMPTOMATIC COVID-19 IN AN IMMUNOCOMPETENT PLWH: A CASE REPORT**

Y. Russotto[1], C. Micali[1], G. Nunnari[1], E. Venanzi Rullo[1], G.F. Pellicanò[2]

[1]Unit of Infectious Diseases, Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy, [2]Unit of Infectious Diseases, Department of Adult and Childhood Human Pathology "Gaetano Barresi", University of Messina, Messina, Italy

Background: It is proved that SARS-CoV-2 infection induces the production of specific antibodies (Ab) targeted against the nucleocapsid (N), differently from the vaccine which only induces anti-Spike (S) Ab. It has been observed that anti-N Ab wane within months since the infection, faster in asymptomatic people. Lack of antibodies has been observed in immunosuppressed people, even after severe SARS-CoV-2 infection.
Case presentation: We present a case of a man, caucasian, 42 years old, diagnosed with infection by Human Immunodeficiency Virus (HIV) in december 2021. At diagnosis, he presented HIV plasma viral load (VL) of 169,000 cps/ml, CD4+ 38,7% (942/mmc) CD8+ 46,2% (1125/mmc) CD4+/CD8+ 0,82. He started antiretroviral therapy (ART) with Dolutegravir (DTG) + Emtricitabine (FTC)/Tenofovir AF (TAF). After a month of ART, he presented HIV plasma VL Target-Not-Detected (TND), CD4+ 50,7% (1502/mmc) CD8+ 33,4% (989/mmc) CD4 +/CD8+ 1,51. He underwent vaccinations for SARS-CoV-2 in 2021, and the 3rd dose in 2022 on January 19th. From February 18th he started to show fatigue and then fever, headache and malaise appeared. In the same day, he underwent antigenic nasopharyngeal swab for SARS-CoV-2 by Special Units of Care Continuity (USCA) instituted in Italy for coronavirus emergency, which resulted positive. He tested positive to a second antigenic swab a week later too, on February 25th. He had the first negative swab on March 04th. He performed a serological test for N-Protein and S-Protein IgG Ab tests, which resulted positive at high titer for Spike Protein IgG (> 12.500 B.A. U./ml, limit of our Laboratory 12.500 B.A.U./ml) and notably negative for Nucleocapsid Protein (0.40 COI, positive value > 1 COI).
Discussion: It has already been observed the lack of immunity response to SARS-CoV-2 infection in immunocompromised people. Although it seems there are no differences between PLWH with no immunocompromisation and people without HIV [1]. The case of our patient is peculiar since his blood tests showed a normal CD4+ and CD8+ count, which increased after starting ART. He tested positive for SARS-CoV-2 after the third shot of the vaccine. Significantly, the serological test showed a high titer of anti-Spike Ab and no anti-N Ab. We could assume that the anti-Spike Ab were induced by the vaccination.
Conclusions: In agreement to literature regarding PLWH and vaccinations, our immunocompetent patient elicited satisfactory anti-S Ab titers after SARS-CoV-2 vaccine. Notably, he did not develop anti-NC Ab after symptomatic COVID19. The possible interactions between the two viruses are yet to be explored.

[1]Alcaide ML, Nogueira NF, Salazar AS, Montgomerie EK, Rodriguez VJ, Raccamarich PD, Barreto IT, McGaugh A, Sharkey ME, Mantero AM, Rodriguez AE, Beauchamps L, Jones DL. A Longitudinal Analysis of SARS-CoV-2 Antibody Responses Among People With HIV. Front Med (Lausanne). 2022 Mar 7;9:768138. doi: 10.3389/fmed.2022.768138. PMID: 35330585; PMCID: PMC8940197.

COVID-19

HIV and COVID-19

P 49 **COVID-19 OUTCOMES AMONG PEOPLE LIVING WITH HIV IN COMPARISON TO THE GENERAL POPULATION OF THE LOMBARDY REGION**

L. Galli[1], D. Ceccarelli[1], O. Leoni[3], D. Cereda[4], A. D'Arminio-Monforte[5], G. Rizzardini[6], R. Rossotti[7], M. Rizzi[8], F. Castelli[9], F. Franzetti[10], L. Pusterla[11], S. Dal Zoppo[12], P. Bonfanti[13], S. Rusconi[14], A. Regazzetti[15], L. Palvarini[16], S. Antinori[17], A. Gori[18], S. Piconi[19], R. Bruno[20], P.A. Grossi[21], A. Lazzarin[2], A. Castagna[1,2]

[1]Infectious Diseases Unit, IRCSS San Raffaele Hospital, Milan, Italy, [2]Vita-Salute San Raffaele University, Milan, Italy, [3]Struttura Epidemiologia e Valutazione delle performance, U.O. Osservatorio Epidemiologico Regionale, Milan, Italy, [4]UO Prevenzione Direzione Generale Welfare di Regione Lombardia, Milan, Italy, [5]ASST Santi Paolo e Carlo Ospedale San Paolo, Milan, Italy, [6]ASST FBF-Sacco Ospedale Luigi Sacco, UOC Malattie Infettive 1-2, Milan, Italy, [7]ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy, [8]ASST Papa Giovanni XXIII, Bergamo, Italy, [9]ASST Spedali Civili, UOC Malattie Infettive, Brescia, Italy, [10]ASST Valle Olona Ospedale di Busto Arsizio, Busto Arsizio, Italy, [11]ASST Lariana Ospedale Sant'Anna, Como, Italy, [12]ASST Cremona Ospedale di Cremona, Cremona, Italy, [13]ASST Monza Ospedale San Gerardo, Monza, Italy, [14]ASST Ovest Milanese Ospedale Nuovo di Legnano, Legnano, Italy, [15]ASST Lodi Ospedale Delmati, Sant'Angelo Lodigiano, Italy, [16]ASST Mantova Ospedale Carlo Poma, Mantova, Italy, [17]ASST FBF-Sacco Ospedale Luigi Sacco, UOC Malattie Infettive 3, Milan, Italy, [18]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, [19]ASST Lecco Ospedale A. Manzoni, Lecco, Italy, [20]Fondazione IRCCS Policlinico San Matteo, UOC Malattie Infettive, Pavia, Italy, [21]ASST Sette Laghi Ospedale di Circolo, Varese, Italy

Background: The outbreak of COVID-19 infection was characterized by an increase in virus spread and hospitalization rate, as well as in overall mortality. To date, COVID-19 infection has caused 145334 deaths in Italy, 53.5% and 40.7% in 2020 and in 2021, respectively; almost 25% of them occurred in Lombardy.
The primary aim of this study was to assess the mortality rate among people living with HIV (PLWHIV) compared to the General Population (GP) living in the Lombardy Region. The secondary aims included the estimate of the infection rate among PLWHIV and the comparison of the lethality rate and positivity rate between the two populations.
Material and methods: This is an observational population study using data collected by the Healthcare System of the Lombardy Region (ARIA S.p.A.) during February 2020 – August 2021 on PLWHIV resident in Lombardy and followed in the Infectious Diseases Units of the region. Data of the general population were retrieved from the Istituto Superiore di Sanità (ISS) and the Istituto Nazionale di Statistica (ISTAT).
The mortality rate was calculated as the number of deaths during the considered time frame divided by the population at risk.
The lethality rate was calculated as the number of deaths divided by the number of people with a COVID-19 infection.
The positivity rate was calculated as the number of positive tests divided the number of COVID-19 tests.
The mortality, lethality and positivity rates were estimated overall, by study month and according to age and sex.
In PLWHIV the considered rates were also evaluated in relation to the type of the ART regimen used in the considered study period.
Results: In February 2020, GP of the Lombardy Region consisted of 10027602 individuals and there were 29458 PLWHIV.
During the study period, 67 (0.23%) and 33219 (0.33%) deaths occurred among PLWHIV and GP respectively (p=0.002); as age (37% and 21% people with age≥60 years in GP and PLWHIV, respectively) and sex (49% and 74% males in GP and PLWHIV, respectively) were differently distributed in the two populations, the mortality rate comparison was then performed considering these two factors showing similar findings (Figure 1 and Figure 2).
Among PLWHIV, 2029 (6.9%) had a COVID-19 infection for a lethality rate of 3.3% and a positivity rate of 9.4%; similar lethality and positivity rates were found in both populations, as shown in Figure 3 and Figure 4, respectively.
Data on ART drugs were available for 22723 PLWHIV: at February 2020, 23.5%, 12.3%, 51.0%, 13.2% treated with NNRTI-, PI-, INSTI-based regimens or other ART regimens; the estimated rates were substantially similar during the study period when considering the type of ART.
Conclusions: Similar results were found between PLWHIV and General Population living in Lombardy in terms of mortality, lethality and positivity rates. The use of any type of ART regimen was not associated with a protective effect on COVID-19 outcomes.

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COVID-19

HIV and COVID-19

P 50 **WHO'S NO-VAX? SARS-COV2 VACCINATION ADHERENCE IN PLWHA: A SINGLE CENTER EXPERIENCE. CHECK TO HELP**

G. Orofino[1], M. Guastavigna[1]. L. Carani[2], M. Farenga[1], F, Bert[3], A. Pivi[3], B. Mollero[3], A. Russotto[3], GD Greco[4], G. Calleri[1]

[1]Divisione A di Malattie Infettive e Tropicali, Ospedale Amedeo di Savoia, Torino, [2]Dipartimento di Scienze Mediche, Università di Torino, Torino, [3]Dipartimento di Salute Pubblica, Università di Torino, Torino, [4]SSD SISP Emergenze infettive e Prevenzione, ASL Città di Torino, Torino

Introduction: In the last six years in our center many efforts have been made to implement vaccinations in PLWHA, as recommended by guidelines, especially after COVID19 outbreak. For this purpose, all of our patients are generally sent to their hometown vaccination hub. At the same time, however, we achieved to recognize and to propose those with difficulties or problems a direct inner administration (COVID excluded). This study intends to check characteristics of no-vax population in our HIV care unit and to estimate adherence rate to COVID vaccines. This work springs out as an active project aimed, through physician-patient relationship, to improve awareness about importance of immunization in PLWHA.

Methods: Our center takes part to SIRVA, the Piemonte Regional Informative System of Vaccination. Also before SARS-CoV2, we used to verify, thanks to this system, vaccinal state and compliance of our patients. We included 943 individuals living with HIV/AIDS on HAART: 739 male and 204 female subjects. Median age (years) in the two groups was respectively 50,93 and 50,43. We also characterized study population according to nationality: 784 individuals were Italian while 159 foreigners.

Results: Data analysis show that in the study population (943 individuals): 93,1 % (878) had the first and second anti SARS-CoV2 dose of vaccine. Only 6,9% (65) didn't get any vaccine. In order to understand which factors could play a role in determinizing no-vax choice we concentrate our attention mainly on sex and nationality. We found a significant association between no adherence and female sex (p 0.013) with an OR 0.51 (IC 95% 0.29 -0.87). On the other hand, no association with nationality were seen from our data.

Conclusions: Our study rises from the necessity to cope with no-vax population and from the importance of vaccines in PLWHA. It demonstrates that women are more likely to be not vaccinated against SARS-CoV2 compared with men. To be Italian or foreigner seems not to be related to vaccine hesitancy. New and bigger studies must be conducted on this important topic. They may support our results focusing, in depth, on potential factors related to this phenomenon, especially between PLWHA. Future step will be exploring no vax population and try to remove, if possible, the reasons of hesitancy. More effective medical actions can arise from knowledge of these aspects promoting the idea of vaccines as a key tool in infectious disease prevention.

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COVID-19

HIV and COVID-19

P 51 **THE "UNKNOWN"- LOST TO FOLLOW-UP AND VIROLOGICAL FAILURE IN THE COVID-19 ERA: COMPARISON BETWEEN THE THREE WAVES, DETERMINANTS OF VF AND FAILURE FOR ALL CAUSES IN PLWH IN CART**

L. Montemurro[1], G. Di Teodoro[2,3], A. Borghetti[4], F. Conti[5], F. Lombardi[6], L. Pezzati[5], M. Poliseno[1],A. Shallvari[3,7], A. Bezenchek[3,7], S. Rusconi[5,8], V. Borghi[9]

[1]U.O. Malattie Infettive Universitaria, University of Foggia, Foggia, Italy, [2]Dipartimento di Ingegneria informatica automatica e gestionale A. Ruberti, Sapienza Università di Roma, Roma, Italy, [3]EuResist Network GEIE, Roma, Italy, [4]Policlinico Gemelli, Roma, Italy, [5]Department of Biomedical and Clinical Sciences "L. Sacco", University of Milan, Milano, Italy, [6]Fondazione Policlinico Universitario A. Gemelli IRCCS, UOC Malattie Infettive, Roma, Italy, [7]InformaPRO SRL, Roma, Italy, [8]UOC Malattie Infettive, ASST Ovest Milanese, Ospedale di Legnano, Milano, Italy, [9]Clinica Malattie Infettive, Azienda Ospedaliero Universitaria di Modena, Modena, Italy

Background: Antiviral treatment is pivotal in maintaining an adequate immunovirological balance and avoid clinical progression. A major concern during COVID-19 pandemic is the lack of follow-up of patients living with HIV (PLWH) in our centers. With this aim, we analized PLWH lost to follow-up and virologically failed while on cART with at least one viral load (VL) detection from Jan 1, 2017 to Dec 31, 2019.

Methods: PLWH, on cART, with at least one HIV-RNA determination in the period 01/01/2017 to 31/12/2019 were selected from the ARCA database. All consecutive HIV-RNA determinations up to 31/12/2021 were included in the follow-up analysis. Centres with an update of ARCA dataset earlier than 01/01/2022 were excluded. PLWH were defined "lost to follow-up" if a distance between two consecutives HIV-RNA determination was >365 days. Two consecutive determinations of HIV-RNA >50 or one over 1000 copies/mL were considered as Virological Failure (VF) in PLWH on cART. Continuous variables were described by the median and interquartile range (IQR), categorical variables by frequencies. Non- parametric tests were used: Chi-squared test was used to determine whether there is a statistically significant difference between the expected proportions and the observed ones and Mann-Whitney and Kruskal-Wallis tests were used for differences, to test the hypothesis that two or more samples coming from the two periods, were drawn from the same distribution.

Results: 5,908 PLWH were included in the analysis, 3,409 were males (57.7%), median age was 54 yo (IQR 46 -60) and 10.8% of them were born abroad. At 01/01/2017, 86.7% were cART experienced and 13.3% were naïve. PLWH were mainly on triple treatment (81.6%) and 16.0% on dual therapy. During the follow-up 30.13 % of PLWH experienced a lack of follow-up; 12.66 % in the first period (2018-2019) and 17.58% in the second period (2020 -2021) (p-value <0.001). During COVID-19 era (2020-2021) an increase in time which occurred between two HIV-RNA determinations was observed: median 5.53 months (IQR 3.77-7.93) in the first period vs 5.97 months (IQR 4.13-7.97) in these last (p-value <0.001). Occurrence of VF did not show statistically significant differences between the two periods: 4.44 vs 4.0 VF/100 PY respectively (p=0.051). Of note, a low number of events (VF) was observed in the last period in PLWH who experienced a VF >1000, 2.49 vs 2.11 event/100 PY (p=0.049) as shown in Table 1.

Conclusions: During COVID-19 pandemic, despite an increase of PLWH lost to follow-up and an increase in the period between visits, virological suppression and cART adherence were not affected by the pandemic.

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COVID-19

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P 52 **ACUTE MESENTERIC ISCHEMIA IN A PATIENT WITH COVID-19 INFECTION: A CASE REPORT**

G. D'Aguanno[1], F. Savalli[1], G. Consuelo[1], P. Miraglia[1], M.C. Morsellino[1], S. Cianchino[1], G. Ribaudo[2], P. Colletti[1]

[1]Department of Infection Diseases, Paolo Borsellino Hospital, Marsala TP, [2]Department of Surgery, Paolo Borsellino Hospital, Marsala TP

Background: 62-year-old unvaccinated, obese hypertensive woman, arrived in ED for cough, dyspnea, dyspepsia and epigastralgia, with hemodynamic compensation and good saturation. She had nose-pharyngeal swab positive for SARS COV 2; blood sampling in range, with PCR 137,55 mg/l; CHEST CT: "Some areas of increased density, ground glass appearance, submantellar distribution". She had good general conditions, eupnoic, SO294%, 38.3°C, treatable abdomen. SARS COV2 IgG RBD 25 AU/ml, PCT 0.05 ng/ml. On the 1th day she started O2 2 l/ m, dexamethasone 6 mg iv, remdesevir 200 mg iv, omeprazole iv, enoxaparin 4000 fl sc, ramipril 5 mg. On the 2th day: she complained intense epigastralgia, sweating and dyspnea. Objective examination: BP 180/90, treatable abdomen, painful in epigastrium, normal ECG. Blood gas analysis at 6 lit/min: PH 7.44, PCO2 38.4, PO2 75.7, La 2.1, SO2 95.7%, normal blood chemistry routine, D-dimer and enzymatic curve. Therapy: Omeprazole, paracetamol, furosemide iv, without clinical benefit. She performed abdominal and thoracic TC: "complete thrombosis of the superior mesenteric artery for approximately 28 mm; poor appreciation of the wall enhancement with associated fluid distension and some antideclive hydro-aereal levels affecting some loops of the mid-distal segment of the ileum, findings suggested of ischemia of the intestinal loop". The patient was subjected to massive bowel resection and right hemicolectomy ". Regular post-operative course. She discharged at home.
Discussion: The COVID-19 pandemic is a fast-evolving situation, so reports of unique aspects of this infection are essential to aid clinicians in managing these patients. Thrombotic complications associated with COVID-19 have been described; these have mainly included venous thromboembolic events. Arterial thrombosis has been reported, but the prevalence is not known. The artery mesenteric ischemia (AMI) is a rare abdominal emergency that usually requires a wide intestinal resection. Potential mechanisms of COVID-19-induced thrombosis are: high affinity RS-CoV2 to ACE2 receptor; the binding between the spike protein of the virus and ACE2 is associated with downregulation of ACE2 activity, this will lead to augmentation of Ang II signaling and pro-thrombotic pathways; oxidative stress damage: angiotensin II has been shown to be a potent mediator of oxidative stress damage through rapid generation of reactive oxygen species mediated by NADPH oxidases; activation of von Willebrand factor Endothelial: upon endothelial damage, subendothelial vWF is released, further multimerized by disulfide bonds and activated by exposing both platelet-binding and collagen-binding domains; dysregulated innate immune response in COVID-19: uncontrolled innate immune response elicited by overactivated neutrophils will initiate coagulopathic pathways.
Conclusions: The precise pathological mechanism leading to the complication of AMI in COVID-19 is still not known.

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P 53 **OBESITY AND COVID-19: THE RESULTS OF A MULTICENTRIC CHOORT STUDY IN CAMPANIA**

V. Zollo[1], M. Pisaturo[1], P. Maggi[2], F. G. Numis[3], I. Gentile[4], V. Sangiovanni[5], V. Esposito[6], R. Punzi[7], G. Calabria[8], C. Rescigno[9], A. Salomone Megna[10], A. Masullo[11], E. Manzillo[12], G. Russo[13], R. Parrella[14], G. Dell'Aquila[15], M. Gambardella[16], A. Ponticiello[17], N. Coppola[1] on behalf of CoviCam group

[1]Infectious Diseases, Department of Mental Health and Public Medicine, University of Campania "L. Vanvitelli", Napoli, Italy, [2]Infectious Diseases Unit, A.O. S Anna e S Sebastiano Caserta, Italy, [3]Emergency unit, PO Santa Maria delle Grazie, Pozzuoli, Italy, [4]Infectious disease unit; University Federico II, Naples, Italy, [5]Third Infectious Diseases Unit, AORN dei Colli, P.O. Cotugno, Naples, Italy, [6]IV Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [7]Hepatic Infectious Disease Unit, AORN dei Colli, PO Cotugno, Naples, Italy, [8]IX Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [9]First Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [10]Infectious Diseease Unit, A.O. San Pio, PO Rummo, Benevento, Italy, [11]Infectious disease unit, A.O. San Giovanni di Dio e Ruggi D'Aragona Salerno, Italy, [12]VIII Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, Italy, [13]Infectious Disease Unit, Ospedale Maria S.S. Addolorata di Eboli, ASL Salerno, Italy, [14]Respiratory Infectious Diseases Unit, AORN dei Colli, PO Cotugno, Naples, Italy, [15]Infectious Diseases Unit, AO Avellino, Italy, [16]Infectious Diseease Unit, PO S. Luca, Vallo della Lucania, ASL Salerno, Italy, [17]Pneumology Unit, AORN Caserta, Italy

Background: The aim of this study was to investigate the outcome Covid-19 in patients with a BMI >30.
Materials and methods: We enrolled in a multicenter, observational, retrospective study, coordinated by Simit Campania and involving nine COVID-19 Units in seven cities of the Campania region in southern Italy, patients that have been hospitalized from March 2020 to July 2021 for SARS CoV-2 infection. At the admission the demographic, clinical, biochemical, virological and therapeutic data of the subjects hospitalized for covid 19 were collected in an electronic database. Charlson index was considered an index of severity. Obesity was defined as a body mass index (BMI)>30. Clinical presentation was categorized according to Centers for Disease Control and Prevention (CDC) recommendations.
Results: 1271 patients were enrolled. Table 1 shows the epidemiological, clinical and the outcome of 1128 patients with Covid-19 with BMI<30 versus 143 patients with BMI>30. In the group of obese 673 (59,66%) were male, in the group of non obese 97 (67,83%). Subjects with a BMI>30 were younger than subjects with BMI<30 (mean age 58,8+SD15,1 vs 61,96+SD16,2; p=0,029). In the age group 40-59 the prevalence was higher in the group of obese, while in the age group 70-80 the prevalence was higher in the group of non obese, which was statistically significant (Table 1). Data about days of hospitalization were not statistically significant. Healthcare workers were observed only in the group of non obese. In the group of BMI>30 110 (83,22%) were affected by underlying chronic diseases compared to 728 (64,54%) in the group of BMI<30 (p=0,0032). The Charlson comorbidity index was higher in the group of non obese patients (mean 3,03+SD2,47; 2,66+SD2,42 respectively), thus it was not statistically significant. Hypertension, diabetes and COPD (Chronic obstructive pulmonary disease) were more prevalent in the group of obese patients, which were statistically significant (p=0,001; p=0,045; p=0,007 respectively). Asthenia was more prevalent in the group of BMI<30 (28,55% vs 16,78% p=0,004). More frequently obese patients were presenting pneumonia, compared to patients without obesity (97,9% vs 92,02%; p=0,018). Clinical presentation of Covid-19 was more severe in obese patients compared to non obese patients (40,56% vs 30,32% respectively; p=0,014). In the multivariate analysis it has been highlighted that age, hypertension, diabetes, COPD, asthenia, pneumonia and clinical presentation are risk factors independently related to obesity (Table 1).
Conclusions: This multicenter observational study highlighted how obesity is a risk factor for having a severe clinical presentation of Covid-19.

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COVID-19

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P 54 **EPIDEMIOLOGICAL AND CLINICAL FACTORS RELATED TO LATE NEGATIVIZATION OF SARS-COV 2 NASOPHARYNGEAL SWAB**

P. Grimaldi[1], M. Pisaturo[1], P. Maggi[2], F. G. Numis[3], I. Gentile[4], V. Sangiovanni[5], V. Esposito[6], R. Punzi[7], G.Calabria[8], C. Rescigno[9], A. Salomone Megna[10], A.Masullo[11], E. Manzillo[12], G. Russo[13], R. Parrella[14], G. Dell'Aquila[15], M.Gambardella[16], A. Ponticiello[17], N. Coppola[1] on behalf of CoviCam group

[1]Infectious Diseases, Department of Mental Health and Public Medicine, University of Campania "L. Vanvitelli", Napoli, [2]Infectious Diseases Unit, A.O. S Anna e S Sebastiano Caserta, [3]Emergency unit, PO Santa Maria delle Grazie, Pozzuoli, [4]Infectious disease unit; University Federico II, Naples, [5]Third Infectious Diseases Unit, AORN dei Colli, P.O. Cotugno, Naples, [6]IV Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, [7]Hepatic Infectious Disease Unit, AORN dei Colli, PO Cotugno, Naples, [8]IX Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, [9]First Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, [10]Infectious Diseease Unit, A.O. San Pio, PO Rummo, Benevento, [11]Infectious disease unit, A.O. San Giovanni di Dio e Ruggi D'Aragona Salerno, [12]VIII Infectious Disease Unit, AORN dei Coli, PO Cotugno, Naples, [13]Infectious Disease Unit, Ospedale Maria S.S. Addolorata di Eboli, ASL Salerno, [14]Respiratory Infectious Diseases Unit, AORN dei Colli, PO Cotugno, Naples, [15]Infectious Diseases Unit, AO Avellino, [16]Infectious Diseease Unit, PO S. Luca, Vallo della Lucania, ASL Salerno, [17]Pneumology Unit, AORN Caserta

Background: RT-PCR for SARS-CoV 2 on nasopharyngeal swab is considered a standard for COVID-19 etiological diagnosis. Furthermore, due to public health measures meant to reduce the viral transmission, the swab-positive time span determines how much a patient observes isolation, regardless of their clinical status. Our aim is to determine which elements influence the swab-negativization time.

Materials and methods: We enrolled, in a multicenter, observational, retrospective study, coordinated by Simit Campania and involving nine COVID-19 Units in seven cities of the Campania, all patients admitted from March 2020 to July 2021 with the diagnosis of SARS CoV-2 infection, of which we knew the first positive and first negative swab date. At the admission we collected in an electronic shared database the demographic, clinical, hematochemical, virological data of this subjects. Clinical severity was defined according to the CDC criteria.

Results: 2005 patients were enrolled; of those, 801 were selected according to the availability of the necessary data. We divided them according to whether their SARS-CoV 2 first negative swab was performed in ≤10 days (group A) or >10 days (group B) from the first positive one. Table 1 shows epidemiological and clinical carachteristics of the enrolled patients. The group A counted 168 patients and the group B 633 patients. In the group A males were the 64.88% and in the >10 days group males were the 63.5% while the median age resulted 62 in both groups, with an IQR respectively of 20.2 and 18.2. The age stratification did not produce any statistically significant difference between group A and B. Charlson index resulted to be 3 with IQR 3 in both group A and B. 67% of group A presented a chronic disease, while 84% of the group B, $p < 0{,}00001$. Among the chronic diseases, Hypertension was present in 42% of patients of the group A while in 51.5% of the group B, $p = 0.03$, while other comorbidities (CKD, DM, COPD, Cirrhosis, CV disease and cancer) did not show correlation. Dyspnea was the only symptom linked with a longer positivity time span, (52%, vs 71%, $p < 0.00001$). Non-severe patients represented the majority 70% vs 30% in group A, while severe and non-severe patients were almost equally distributed in group B, 49.6% vs 49.9%; this difference was statistically significant ($p < 0.00001$).

Conclusions: Neither gender nor age influenced the positivity time span, while comorbidities and disease severity appeared to be highly influencing factors. Among comorbidities, hypertension was the only factor showing a strong influence on the negativization time. It is possible to speculate that there could be a relation with the different expression of ACE2R in these patients, an element representing the receptor for the SARS-CoV 2 Spike protein and that plays a key-role in hypertension physiopathology.

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P 55 **MAJOR BLEEDING EVENTS IN COVID-19 PATIENTS ADMITTED TO HOSPITAL: A CASE SERIES**

G. Casalini[1,2], A. Giacomelli[2], G. Pozza[1,2], A. Poloni[1,2], V. Colombo[1], F. Petri[1], M. Gerbi[1], C. Fusetti[1], G. Carrozzo[1,2], G. Rizzardini[1], S. Antinori[1,2]

[1]Luigi Sacco Department of Biomedical and Clinical Sciences, University of Milan, Italy, [2]III Division of Infectious Diseases, ASST Fatebenefratelli Sacco, Milan, Italy

Background: COVID-19 has been associated with an increased risk of thrombotic events due to a systemic prothrombotic and inflammatory state. Because of this concern, different anticoagulation strategies were employed. Nevertheless, the risk benefit ratio of therapeutic or prophylactic anticoagulation remains unclear. Bleeding is not as frequent as clotting in patients with COVID-19, but it may occur especially in high-risk individuals who receive therapeutic anticoagulation. We aimed to characterize the patients experiencing major bleeding event included in the Luigi Sacco Hospital registry.

Material and methods: This is a case series of COVID-19 patients admitted to Luigi Sacco Hospital in Milan, Italy, from February 2020 to January 2022, who experienced at least one major bleeding event according to the International Society on Thrombosis and Haemostasis (Table 2) while hospitalized. We describe the characteristics of the study population, the type of bleeding event, the anticoagulation intensity status before and the day of bleeding, the treatment required and the outcome.

Results: Twenty patients had a major bleeding event during hospitalization for COVID-19: in 4 cases it was fatal, in other 4 cases it involved a critical organ/area and in 12 cases it led to a fall in haemoglobin level of ≥ 2 g/dL or to transfusion ≥ 2 units of red blood cells. The median age was 81 years (IQR 74-84), 65% of patients were male, the most common comorbidities were coronary heart disease (8, 40%) and diabetes (7, 35%); median Charlson Comorbidity Index was 5 (IQR 3-8) (Table 1). The most common bleeding type was intramuscular (12, 60%), followed by lower gastrointestinal bleeding (3, 15%). Bleeding occurred at a median of 12.5 days since hospital admission (IQR 7-23.5). Nineteen patients were receiving therapeutic anticoagulation the day of bleeding; 6 (31.6%) were already on anticoagulation prior to hospitalization while in 13 patients (68.4%) anticoagulation intensity was increased during hospitalization, because of pulmonary thromboembolisms (5), clinical deterioration along with D-dimer elevation (4), atrial fibrillation (3) and deep venous thrombosis (1). The median time from anticoagulation intensity increase and bleeding was 10 days (IQR 3.5-20.5). Bleeding events required percutaneous arterial or venous embolization in 9 cases (45%). Six patients died (30%) and in 4 cases death was attributable to the bleeding event. Two bleeding events (10%), of whom one fatal, occurred in Intensive Care Unit, the others in medical wards.

Conclusions: In our study, four out of six patients died for a direct consequence of the bleeding event. In case of an anticoagulation treatment start clinicians should be aware of the risk of major bleeding event especially in elderly patients with multimorbidity.

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P 56 **SECONDARY ORGANIZING PNEUMONIA (SOP) IN TWO LATE COVID-19 HAEMATOLOGICAL PATIENTS**

A. Tommasi[1], A. Tosti[1], N. Murgia[2], E. Stolaj[1], G. Genga[1], L. Malincarne[1], S. Morosi[1], D. Francisci[1]

[1]Infectious Disease Clinic, Department of Medicine and Surgery, Santa Maria della Misericordia Hospital, University of Perugia - Perugia (Italy), [2]Occupational and Respiratory Medicine, Department of Medicine and Surgery, Santa Maria della Misericordia Hospital, University of Perugia - Perugia (Italy)

Background: Organizing pneumonia is a sub-acute process of pulmonary tissue repair secondary to lung injury, defined histopathologically by intra-alveolar buds of granulation tissue within the lumen of distal pulmonary airspaces. Diagnosis is made by imaging and clinical criteria, in particular evidence of multiple bilateral and peripheral alveolar opacities after initial improvement of fever and dyspnea. Most patients respond to corticosteroids.

Methods: A case-report study describing two cases of OP associated to SARS-CoV-2 pneumonia, admitted at Infectious Disease Clinic in Perugia Hospital.

Results: Case 1: A 54-year-old man positive for SARS-CoV-2 with clinical history of B-cell non-Hodgkin lymphoma treated with rituximab maintenance therapy. At first paucisintomatic, on 25th day of illness he was hospitalized due to fever and respiratory failure: offlabel therapy with remdesivir was set up for 10 days with benefit. After discharge fever reappeared in a few days requiring a new hospitalization while SARS-CoV2 infection resolved on 61st day of positivity. Due to fever empirical antibiotic therapy was set up and new HRCT showed multiple ground glass bilateral thickened areas with a "crazy-paving" framework, multiple consolidations to RUL and other peribronchial lesions in RLL. High doses intravenous steroid therapy was started (methylprednisolone 30mg q12h) in the suspicion of SOP and a BAL was carried out. All microbiologic tests were negative, while cytommunological examination showed lymphocytosis with a sharp reduction in the CD4/CD8 ratio confirming the clinical suspicion.

Case 2: A 56-year-old man positive for SARS-CoV-2 with a history of B-cell lymphoma treated with rituximab. Initially paucisintomatic, after an admission to ER for dyspnea, steroid, antibiotic and LMWH were set. On 38th day of illness he was admitted to hospital for persistent fever, starting isavuconazole for very low positivity of plasma Aspergillus DNA and antibiotical empiric therapy. A first BAL was carried out but was negative for infections. On 53rd day of illness, he had worsening of respiratory function with CT evidence of multiple bilateral interstitial opacities, ground glass and aerial bronchogram on apex of the lung. Intravenous steroid therapy was set (methylprednisolone 30mg q12h) in the suspicion of SOP and a new BAL showed lymphocytosis with a sharp reduction in the CD4/CD8 ratio confirming the clinical suspicion.

Conclusions: In both cases we suspected OP secondary to viral infection following clinical deterioration (fever and/or respiratory failure) occurred after an initial improvment. The clinical hypothesis of OP can be supported by the negativity of microbiological tests, a characteristic CT radiological chest pattern and by cyto-immunology on BAL. Both patients presented sudden improvement after the introduction of steroid therapy and were discharged without oxygen support, with oral steroid therapy and indication to pneumological follow up.

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P 57 **CAMPYLOBACTER COLI BACTEREMIA IN PATIENT WITH COMMON VARIABLE IMMUNODEFICIENCY (CVID) AND SARS-COV-2 INFECTION**

N. Esposito[1], S. Di Bari[2,3], F. Taglietti[3], M. Sarno[1], F. Gavaruzzi[2,3], S. Al Moghazi[3], D.R. Donno[3], E. Caraffa[3], G. Granata[3], P. Chinello[3]

[1]Department of Clinical Medicine and Surgery, Infectious Diseases Unit, University "Federico II", Naples, Italy, [2]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Italy, [3]Clinical and Research Department for Infectious Diseases, National Institute for Infectious Diseases L. Spallanzani, IRCCS Rome, Italy

Background: Campylobacter species are gram negative flagellated bacteria, representing one of the most frequent causes of enteritis and gastro-intestinal tract infections in humans. However, some species can sometimes cross the intestine-blood barrier and cause bacteremia. The recognized risk factors for Campylobacter bacteremia are HIV infection, liver diseases, and malignancies, but also immunodeficiency conditions in young people and elderly patients seem to be particularly predisposed to this event.
Case presentation: We present a case of a 36-year-old male with CVID on monthly therapy with human immunoglobulins and smoldering IgA multiple myeloma ,who presented to the emergency room in Rome, Italy, due to the onset of fever, pharyngitis and diarrhea. He performed a naso-pharyngeal swab, which resulted positive for SARS-CoV-2 Omicron BA.2 variant. On check-in, vital signs were stable and chest CT scan showed: alveolar involvement at the level of the left posterior basal segment suggestive of bacterial pneumonia. He was moved to the Infectious Diseases Unit of the National Institute for Infectious Diseases L. Spallanzani where he performed blood cultures and started antibiotic therapy with piperacillin plus tazobactam 4.5 g every 8 hours. Over the next few days, as the fever persisted (37.9°C), he performed new blood cultures, which were positive for meropenem-susceptible Campylobacter coli. Therefore he started therapy with meropenem 1g every 8 hours for 14 days. Surveillance blood cultures tested negative. He performed echocardiography which showed no "plus" images that may suggest endocarditis.The patient was discharged after 19 days of hospitalization in good health status.
Discussion: The presented case allows us to evaluate the nuances of symptoms related to SARS-CoV-2 infection. As well known, diarrhea and other gastro-intestinal symptoms are associated with SARS-CoV-2 disease, especially in the Omicron Variant of Concern. Campylobacter spp. infections are usually self-limited and complications are rare. The incidence of Campylobacter spp. bacteremias are <1%, but in young people with primary or acquired immunodeficiency and in the elderly, they are more common and can also recur over time and be associated with both systemic and intestinal complications, as suggested by several studies. Moreover in our case, the isolated strain showed resistance to ciprofloxacin, which is not frequent in Europe and Campylobacter spp. ciprofloxacin-resistant bacteraemias may have a more severe course. The authors aim to add to this case report a systematic review about Campylobacter coli bacteremias.
Conclusion: This is the first case described of co-infection with SARS-CoV-2 and Campylobacter coli. It could be speculated that SARS-CoV-2 itself might play a role in disrupting the intestinal barrier and promoting translocation of such pathogens, but observations on a larger scale of patients would be needed.

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COVID-19

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P 58 **HAEMATOLOGICAL MALIGNANCIES AND COVID-19: DO WE HAVE EFFECTIVE TREATMENTS? A CASE REPORT**

E. Binetti, A. Pupo, R. Donà, D. Giangiulio, S. Lobello, F. Romano, V. Vola, F. Cogliati Dezza, G. Russo, G. Siccardi, C. M. Mastroianni

Università La Sapienza, Roma

Background: During the SARS-CoV-2 pandemic it has been rapidly clear that patients suffering from haematological malignancies seem to present a more severe infection, higher mortality, prolonged viral shedding and worst outcome compared to general population.

Case Description: We described two cases of COVID-19 related pneumonia in hematological patients hospitalized at the end of January at Policlinico Umberto I, Rome. The two patients had both an active haematologiacal disease and a recent chemotherapeutic treatment. Both had received two doses of anti-SARS-CoV-2 vaccine. However, they underwent an initial improvement followed by a rapid deterioration of general condition, laboratory parameters and respiratory exchanges despite the prompt and numerous therapies administered. None of them survived. Figure 1 and 2 show treatments, need of oxygen and inflammation parameters trends during hospitalization.

Results: COVID-19 patients with haematologiacal malignancies have a mortality rate threefold–fourfold higher than general population. In both cases we observed a progressive cycle threshold reduction in the nasopharyngeal swabs performed as the day went by, indicating an increase in viral load. Both patients had received only two doses of anti-SARS-CoV-2 vaccine and had negative serology. In haematologiacal patients, it has been reported a heterogenous antibody responses to vaccination with an overall low seroconversion rate. They received the monoclonal antibodies (mAbs) combination casirivimab/ imdevimab at early stage of infection, although the Omicron variant, which wasthe most prevalence VOC in Italy in that time, is resistant to neutralization by this mAbs. At first, Remdesivir was administrated, then when respiratory condition worsened, one dose of Tocilizumab was given but the treatment was interrupted due to the lack of the drug at the hospital pharmacy. We wondered whether other strategies could have changed the outcome of these patients. The booster dose could have been an option, but they might not have responded due to their hematologic disease and the recent chemotherapy. Another possibility could have been Sotrovimab, which seems to overcome Omicron-mediated immune evasion, but it still is not approved for hospitalized patients. The last chance could have be the convalescent plasma (CP), that wasn't available at that time. CP is not recommended by international guidelines, in spit of it has shown some clinical improve in haematological patients with humoral deficiency.

Conclusions: Despite the therapeutic advances to fight the COVID-19 pandemic, patients with haematologiacal malignancies remain a population with high mortality risk. Non-pharmacological interventions while SARS-CoV-2 is circulating in the community are still important, but prospective studies to develop optimal vaccination strategies as well as novel pharmacological toolsfor these patients are warranted.

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COVID-19

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P 59 **PRE-EXISTING CHRONIC KIDNEY DISEASE (CKD) IS ASSOCIATED WITH AN INCREASE IN THE DURATION OF HOSPITALIZATION IN COVID-19 PATIENTS BUT NOT WITH INCREASED MORTALITY: RESULTS OF A CASE-CONTROL STUDY**

M.G. Palamone[1], F. Calò[10], A. Russo[1], P. Maggi[1,2], V. Sangiovanni[3], F.G. Numis[4], I. Gentile[5], A. Masullo[6], C. Rescigno[3], G. Calabria[3], A. Salomone Megna[7], M. Gambardella[8], E. Manzillo[3], G. Russo[9], V. Esposito[3], N. Coppola[1,10], Simit Campania Group

[1]Infectious Diseases, Departement of Mental Health and Public Medicine, University of Campania "Luigi Vanvitelli" Naples, Italy, [2]Infectious Diseases Unit, A.O. S. Anna e S. Sebastiano Caserta, Italy, [3]Infectious Diseases Unit, AORN dei Colli, P.O. Cotugno, Naples, Italy, [4]Emergency Unit, PO Santa Maria delle Grazie, Pozzuoli, Italy, [5]Infectious Diseases Unit; University Federico II, Naples, Italy, [6]Infectious Diseases Unit, A.O. San Giovanni di Dio e Ruggi D'Aragona, Salerno, Italy, [7]Infectious Diseases Unit, A.O. San Pio, PO Rummo, Benevento, Italy, [8]Infectious Diseases Unit, PO S. Luca, Vallo della Lucania, ASL Salerno, Italy, [9]Infectious Diseases Unit, Ospedale Maria S.S. Addolorata di Eboli, ASL Salerno, Italy, [10]AOU L. Vanvitelli, Naples, Italy

Introduction: The presence of comorbidities is associated with an unfavorable outcome in COVID-19 patients. The aim of the present study was to observe the outcomes of patients with SARS-CoV-2 infection and chronic kidney disease (CKD) in order to evaluate their impact on mortality and disease severity.
Methods: We conducted a multicenter, observational case-control study, with a 1: 2 allocation, which involved nine operating units active in the health emergency from COVID-19 in southern Italy. All adults admitted with SARS-CoV-2 infection and with pre-existing CKD (Cases) were included. For each case, two patients without CKD were enrolled, matched by sex, age (±5 years), number of comorbidities (±1) (excluding CKD) (Controls).
Results: Of the 2054 SARS-CoV-2 infected patients followed during the study period, 115 patients with CKD and 230 patients without CKD were enrolled in the Case and Control groups, respectively. Between the Case and Control groups, no statistical differences were observed in the prevalence of moderate (33.9% vs 42.1%) or severe (33.9% vs 37.8%) clinical presentation of COVID-19 or death. (25.2% versus 16.5%) in hospital. Considering the comorbidities there were no statistical differences except for the Charlson Comorbidity Index which was statistically higher in the case group (5 (IQR 3-7) versus 4 (IQR 3-6); p = 0.015). Patients with cancer were more frequent in the Control group (13% vs 6%; p = 0.049), as well as patients with hypertension were more frequent in the Case group (69% vs 57%; p = 0.034).
Statistical differences were observed between the Case and Control groups regarding the duration of hospitalization (excluding patients who died during hospitalization). In patients with CKD there is a median of days of hospitalization equal to 14 days (IQR 9-28), in patients without CKD there is a median days of hospitalization equal to 14 days (IQR 10-21) (p = 0.031) (OR 1.026 95% CI: 1.002-1.051). Regarding mortality, there were no significant differences between the two groups (25% vs 16%; p = 0.054) (OR 0.975 95% CI: 0.925-1.028).
Discussion: Chronic kidney disease (CKD) is not associated with an increased risk of severe clinical presentation from COVID-19 and death in hospital, however, significantly affects the duration of hospitalization.

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COVID-19

Management of COVID-19

P 60 **EVOLUTION OF MORTALITY AMONG THE FIRST THREE WAVES IN THE LARGEST ITALIAN HOSPITAL RECEIVING SARS-COV-2 INFECTED PATIENTS. RESULTS FROM THE BRESCIA HUB PROJECT**

E. Focà[1], S. Calza[2], S. Piva[3], I. Ettori[1], M.L. Muiesan[4], M. Salvetti[5], F. Rasulo[3], A. Padovani[6], M. Bezzi[7], M. Metra[8], M. Castellano[9], F. Legati[10], C. Ricci[11], R. Badolato[12], F. Odicino[13], R. Orabona[13], F. Scolari[14], F. Marinoni[15], A.M. Roccaro[16], C. Rossi[17], F. Castelli[1]

[1]Unit of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili, Brescia, Italy, [2]Unit of Biostatistics and Bioinformatics, University of Brescia, Brescia, Italy, [3]Unit of Anesthesiology and Critical Care Medicine, ASST Spedali Civili, Italy, [4]Second Unit of Internal Medicine, University of Brescia and ASST Spedali Civili, Italy, [5]Unit of Emergency Internal Medicine, University of Brescia and ASST Spedali Civili, Italy, [6]Unit of Neurology, University of Brescia and ASST Spedali Civili, Brescia, Italy, [7]Unit of Pneumology, ASST Spedali Civili, Brescia, Italy, [8]Unit of Cardiology, University of Brescia and ASST Spedali Civili, Brescia, Italy, [9]Unit of Internal Medicine and Endocrinology, University of Brescia and ASST Spedali Civili, Brescia, Italy, [10]Third Unit of Internal Medicine, ASST Spedali Civili, Italy, [11]Unit of Gastroenterology University of Brescia and ASST Spedali Civili, Brescia, Italy, [12]Unit of Pediatrics, Children's Hospital University of Brescia and ASST Spedali Civili, Brescia, Italy, [13]Unit of Gynecology and Obstetrics, University of Brescia and ASST Spedali Civili, Brescia, Italy, [14]Unit of Nephrology and Dialysis, University of Brescia and ASST Spedali Civili, Brescia, Italy, [15]Unit of Planning and Management Control Service, ASST Spedali Civili, Brescia, Italy, [16]Unit of Clinical Research and Phase I Studies, ASST Spedali Civili, Brescia, Italy, [17]Chief Medical Officer Institution, ASST Spedali Civili, Brescia, Italy

Background: Italy was the first western Country to be hit by SARS-CoV-2 and suffered an initial wave of COVID -19 cases from February to June 2020. Cases surged again between June and December 2020 following the easing of restrictions. Then, a third significant increase in cases was recorded between December and April 2021. Here we aimed to describe the evolution of mortality among the first three pandemic waves among patients hospitalized because of COVID-19.

Methods: Observational retrospective study. We identified hospitalized patients with COVID-19 in the largest Italian hospital receiving SARS-CoV-2 infected patients. The accesses were divided into three periods: the first wave from 21 February 2020 to 30 June 2020, the second wave from 1 July 2020 to 31 December 2020 and the third wave from 1 January 2021 to 30 April 2021. We compared crude in-hospital mortality and ICU admission rate of the patients among the first three pandemic waves.

Results: We identified a total of 7054 patients admitted to our hospital with a diagnosis of Covid-19. Of this number of patients, 2630 were admitted during the first pandemic wave, 1724 during the second wave and 2700 during the third wave. Studying the mortality trend among the three pandemic waves we observed that in the first wave mortality is significantly higher than in second and third waves (21% vs. 10% vs. 12%, respectively $p < 0.001$). Overall, 439 (6.2%)patients were admitted in ICU during the study period. In the first wave ICU admissions were 127 (4.8%), lower than in the second and third wave 132 (7.7%) and 180 (6.7%) respectively ($p < 0.001$).

Conclusions: Mortality in the first pandemic wave was higher than in following waves according to improvements of knowledge about clinical and therapeutical aspects of disease and in particular due to hospital organization. ICU admissions are lower in the first wave compared to the successive ones also in light to the progressive increase of the availability of ICU beds.

COVID-19

Management of COVID-19

P 61 **A CASE REPORT OF ADENOVIRUS INFECTION AND HSV-1 HEPATITIS IN A NON-TRANSPLANTED HEMATOLOGICAL PATIENT WITH COVID-19 PNEUMONIA**

N. Corti[1,2], G. Lapadula[1,2], M. Rossi[1], E. Colella[1], A. Rugova[1], P. Columpsi[1], A. Soria[1], E. Pollastri[1], L. Bisi[1], S. Limonta[1], F. Sabbatini[1], A. Cappelletti[1], A. Ranzani[1], N. Squillace[1], G.M. Migliorino[1], S. Foresti[1], P. Bonfanti[1,2]

[1]Infectious Disease Unit, San Gerardo Hospital, ASST Monza-Brianza, [2]Department of Medicine and Surgery, University of Milano-Bicocca, Monza

Background: Herpesviridae reactivation in COVID-19 has been rarely described: reports illustrate reactivations predominantly in critically ill and intubated patients. The extent to which these events contribute to mortality is unknown. Furthermore, adenovirus infection may be clinically relevant for hematopoietic stem cell transplant and solid organ transplant recipients; significant cases in non-transplanted COVID-19 patients have not been described so far.

Materials: Single case report.

Case report: A 73-year-old male patient with a history of marginal zone non-Hodgkin lymphoma previously treated with a 6-cycle regimen of rituximab-bendamustine (concluded 10 months before current hospitalization) presented to our institution for COVID-19 pneumonia requiring non-invasive ventilation. The patient was fully vaccinated for COVID-19, yet serology for SARS-CoV-2 was negative. Methylprednisolone (1 mg/kg) was started and the patient's clinical conditions gradually improved. Steroid tapering and respiratory weaning were slowly initiated. On day 13 of hospitalization, fever and respiratory failure relapsed; broad-spectrum antibiotics were started suspecting nosocomial pneumonia. Due to symptom persistence, negative blood and bronchoalveolar lavage (BAL) cultures and suggestive chest computed tomography (CT) findings, methylprednisolone (1mg/kg) was reinitiated in the suspect of organizing pneumonia. Initial response to treatment with defervescence for 24 hours was observed. Nonetheless, the patient subsequently developed sub-continuous fever and respiratory worsening. Viral PCR on BAL tested positive for adenovirus (267994 copies/mL), CMV-DNA (1128 copies/mL) and HSV-1-DNA (2552 copies/mL). Adenovirus tested negative on blood and urine. Cidofovir, probenecid and intravenous immunoglobulins were initiated. Profound lymphopenia and progressive rise in transaminases and ferritin (as shown in table 1) were investigated with a total-body CT with contrast. Multiple areas of hepatic necrosis were detected suggesting an uncommon type of hepatitis. Blood levels of HBV-DNA and HCV-RNA were negative, while a high HSV-1 viral load was detected on plasma (>25000000 copies/mL). Therapy with acyclovir was started. The patient's clinical conditions deteriorated shortly after initiation of antiviral therapy, with lower gastrointestinal bleeding conditioning hemorrhagic shock due to ischemic colitis. Multi-organ failure followed, determining a fatal outcome.

Discussion: We report a case of adenovirus pneumonia and disseminated HSV-1 infection in a non-transplanted patient, in the context of severe iatrogenic, hematological and COVID-19-associated immunodepression. Previous chemotherapy, despite the absence of active hematological disease, may compromise the effect of COVID-19 vaccination and predispose to rare viral reactivations. The role of SARS-CoV-2 infection and its treatment in precipitating immunosuppression warrant further investigation.

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COVID-19

Management of COVID-19

P 62 **OVERLOOKED CLINICAL SIGNS IN EARLY SARS-COV-2 INFECTION AMONG ELDERLY PEOPLE: ACUTE KIDNEY INJURY AND ALTERED STATE OF CONSCIOUSNESS**

C. Fanelli, A. Puggioni, L. Firino, I. Maida, G. Madeddu, S. Rubino, S. Babudieri

University of Sassari, Italy

Background: Since the outbreak of the SARS-CoV-2 pandemic, millions of people have died. Many early symptoms have been identified as suggestive for SARS-CoV-2 infections, mainly belonging to respiratory or gastrointestinal tract. Rare symptoms are considered to be those belonging to other systems, such as urinary tract and the central nervous system (CNS). The aim of our study was to compare the frequency of peripheral oxygen desaturation with the frequency acute kidney injury, cerebrovascular accidents, and altered state of consciousness as admission clinical signs of COVID-19 patients hospitalized in our COVID Unit.

Material and Methods: We conducted a retrospective study to evaluate the frequency of overlooked symptoms among hospitalized patients aged more than 65 years old. We included all SARS-CoV-2 infected patients followed by our Unit between 15/01/2022 and 01/03/2022. We excluded patients with missing data. Qualitative and quantitative variables were summarized with frequencies and means. Genotyping was performed to assess the variant of SARS-CoV-2 virus.

Results: A total of 58 SARS-CoV-2 hospitalized elderly patients were evaluated, with 34 (58.6%) males and a mean age of 75.8 (± 14) years. Overall, eight patients (13.8%) died. SARS-CoV-2 omicron variant (B.1.1.529) and delta variant (B.1.617.2) were identified respectively in 36 (55.8%) and 2 (3.5%) patients. In 20 (34.5%) cases genotyping was not diriment or not performed for any reason. In total, 28 patients (48.3%) presented acute kidney injury (AKI) at admission. Of them, only seven suffered from chronic kidney injury and 19 were omicron variant carrier; no delta variant carrier was identified among AKI patients. Moreover, 37 patients were treated with antibiotics during hospitalization, including 26 patients (44.8%) who developed a urinary tract infection during hospitalization. Altered state of consciousness was observed in 26 patients (44.8%), namely syncope, state of drowsiness and delirium. Among them, 16 were identified with omicron variant and one with delta variant. Three of them were eventually diagnosed with cerebrovascular accident. Peripheral oxygen desaturation was the reason for admission in 24 patients (41.4%); 19 omicron variant and one delta were detected. The main characteristics are displayed in Table 1.

Conclusions: We highlighted how overlooked clinical signs in patients with early COVID-19, such as kidney failure and altered state of consciousness, seem to be more frequent than reported in current literature. Thus, further studies are needed to establish the recurrence of these clinical signs at hospital admission as to be taken in consideration as suggestive for COVID-19, especially in elderly people.

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COVID-19

Management of COVID-19

P 63 **COMPARATIVE ANALYSIS BETWEEN THE DIFFERENT EPIDEMIC WAVES OF SARS - COV-2 INFECTION: THE EXPERIENCE OF THE PONTINE HOSPITAL**

P. Zuccalà[1], R. Marocco[1], S. Gismondi[1], V. Belvisi[1], B. Kertusha[1], T. Tieghi[1], M. Del Borgo[1], A. Gasperin[1,2], S. Cacace[1,2], A. Carraro[1,2], A. Parente[1,2], A.R. Cacciotti[3], S. Parrocchia[3], M. Lichtner[1,2]

[1]UOC Infectious Diseases, "S.Maria Goretti Hospital", Latina, [2]Department of Public Healt, Microbiology and Infectious Diseases, Sapienza University of Rome, Polo Pontino [3]Health Management, "S.Maria Goretti Hospital", Latina

Background: On 11 March 2020 WHO declared COVID-19 a pandemic infection. Many regions have experienced epidemic waves of COVID-19 since the emergence of SARS-CoV-2 with differences in mortality.
The aim of the study is to describe the clinical-epidemiological and temporal changes of a cohort of patients infected with SARS-CoV-2. Also, we investigated whether mortality differed by epidemic wave and whether individual-level demographic (e.g., age and sex) affected mortality among COVID-19 patients admitted to our hospital. Elucidating factors differentially associated with mortality between epidemic waves may inform clinical and public health strategies.
Material and Methods: This longitudinal observational study examines all patients (pts) admitted to the S.M. Goretti Hospital of Latina from 3 March of 2020 to 01 April of 2022. We have analyzed demographic data among patients admitted with COVID-19 during the first (March 1, 2020, to May 30, 2020), second (October 1, 2020, to May 1, 2021) and third (December 1, 2021, to March 31, 2022) epidemic waves. All patients were treated with the same protocol. Values were expressed as median, range, absolute numbers and percentages. The results were analyzed using Graph Prism 8.0.
Results: 3805 patients were enrolled, they was predominantly male (60% men, 2048 pts), with an age of 68 years (min 1, max 100). About 83% (2676 pts) of the pts were discharged, while 17,9% (574 pts) were died. The median of the days of hospitalization was 13 days.
Patients were grouped by date of admission into the first wave (372 pts), second wave (2239 pts), and the third wave (729 pts). We found a significant difference in age between groups (p=0,0124 with Kruskal-Wallis test), in particular pts admitted during the third wave were found to be significantly older than those in the second wave (p=0,0097 with Dunn's multiple comparisons test). No difference was found about sex of pts. The median length of hospitalization decreased significantly (p<0,0001 with Kruskal-Wallis test) from the first wave to the third (respectively 17, 12 and 10 days), it was shorter in second and third waves than in the first (p<0,0001 with Dunn's multiple comparisons test).
Hospitalized patients had lower mortality during the first wave (14%) than the second (19%) and the third (16,6%). Finally, we found that dead pts were significant older than total of enrolled pts (p<0,0001 with Mann-Whitney test, median of age 80,55) without difference between waves.
Conclusions: The difference in mortality that occurred in parallel with the increase in the volume of Sars-CoV-2 infection is probably a measure of the strain in the health system. Several demographic and clinical patient factors were associated with an increased risk of mortality independent of waves. It will be interesting to evaluate how the different viral variants and the entry of vaccination have influenced the outcome of hospitalization in patients with COVID-19 disease.

COVID-19

Management of COVID-19

P 64 **INVASIVE CRYPTOCOCCAL DISEASE IN COVID-19: A CASE REPORT, SYSTEMATIC REVIEW OF THE LITERATURE AND ANALYSIS**

G. Pipitone[1], G. Ciusa[1], D. Spicola[1], F. Di Lorenzo[1], A. Sanfilippo[1], F. Onorato[1], A. Ficalora[1], C. Buscemi[1], T. Prestileo[1], C. Imburgia[1], I. Alongi[1], F. Guida Marascia[2], A. Gizzi[2], M. Abbott2, M.S. Verde[3], F. Di Bernardo[3], A. Scafidi[4], V. Mazzarese[4], A. Cascio[2], N. Petrosillo[5], C. Iaria[1]

[1]Infectious Disease Unit - ARNAS Civico-Di Cristina Hospital, Palermo, [2]Infectious Disease Unit - University Hospital "P. Giaccone", Palermo, [3]Microbiology Unit - ARNAS Civico-Di Cristina Hospital, Palermo, [4]Intensive Care Unit - ARNAS Civico-Di Cristina Hospital, Palermo, [5]Infectious Disease Unit - University Hospital "Campus Bio-Medico", Rome

Background: Coronavirus disease 2019 (COVID-19) pandemic represents the major health problem in several countries. With the increase of severe COVID-19 cases, several opportunist infection complications have emerged, including bacterial and fungal infections. Indeed, fungal infections have been reported among patients with Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection. Patients with COVID-19, particularly in severe forms, can develop lymphopenia and this can lead to an increased susceptibility to fungal infections, including cryptococcosis. We describe a case of cryptococcosis and concomitant SARS-CoV-2 infection, and a systematic review of the literature on this topic.

Materials and Methods: Two independent researchers performed a Systematic Review of the literature of SARS-CoV-2 and Cryptococcal co- infections via the databases PubMed and Embase, according to PRISMA statement. Patients were divided in two groups, to evaluate the mortality risk: dead and alive patients after treatment. To compare categorical data (qualitative variables) a Fisher-exact test was used ($a < 0.05$). To compare quantitative variables (Age, Time from SARS-CoV-2 infection to Cryptococcal infection, Lymphocyte nadir, CD4+ nadir) a U Mann-Whitney test to compare ($a < 0.05$).

Results: A total of 32 case reports were analyzed. Overall, 17/32 (53.1%) of patients died.

Most of patients were males 25/32 (78.1%), median age was 60 years (IQR 53.25-70) with non-statistically significant difference between two groups ($p = 0.911$); median lymphocytes count was 400 cells/μL (IQR 400-700), and median CD4+ values was 252 cells/μL (IQR 70-438), with no statistically significant difference between the two groups ($p= 1$ and $p= 0.190$, respectively).

Overall, 21 out of 24 (87.5%) were in ARDS; among alive patients ARDS were less frequent ($p= 0.028$).

ICU admission for COVID-19 was observed in 18/26 (69.2%) of patients and was more frequent in dead patients ($p= 0.034$).

Overall, patients who undergone an adequate treatment (Amphotericin B + Flucytosine) were 15/32 (46.9%), alive patients more frequently were treated correctly with a significant difference ($p= 0.039$).

Conclusions: Analysis of data shown that cryptococcosis is a rare but life-threatening complication during severe COVID-19. In literature, around 80% of patients with cryptococcosis had almost one comorbidity, this is in line with our review: 87.5% of patients carries almost one comorbidity. A question could be posed: do the severe SARS-CoV-2 infection and its immunity alteration could be considered the pathophysiological basis for cryptococcosis?

Invasive cryptococcosis could be a life-threating disease, an early diagnosis and appropriate treatment help clinicians to reduce mortality.

COVID-19

Post-acute COVID-19 syndrome (PASC)

P 65 **THE USE OF LUNG ULTRASOUND TO MONITORING THE LUNG DAMAGE AFTER COVID19 PNEUMONIA**

S. Mazzanti, L. Brescini, V. Barocci, P. Mantini, M. Di Pietrantonio, B. Candelaresi, F. Pallotta, S. Olivieri, G. Cesaretti, F. Ginevri

Clinica Malattie Infettive, Ospedali Riuniti di Ancona, Università Politecnica delle Marche

Background: Sars-Cov-2 infection frequently determine COVID-19 related pneumonia that require hospitalization. During the hospital stay, tomography is the main exam to study the severity of lung disease, the presence of trombo-embolic complications and to monitoring the evolution of lung damage. Usually, patients discharged from a Covid-department, need a multidisciplinary follow up for the persistence of symptoms during the post-acute period but also sometimes the “long-Covid”.

Obviously, is not cost-effective to practice a CT scan every month to study the evolution of pulmonary thickenings but at the same time is important to early select patients who are developing some fibrosis or permanent damage.

Material and methods: In our department, post-Covid outpatients visits are scheduled for the first, third and sixth month from the discharging. In every appointment, patients receive a medical examination, blood test and lung ultrasound.

In pauci-sintomatic patients, CT was scheduled

- at the 3th month appointment only if there was no improvement from the previous lung ultrasound;
- After the 6th month follow up only if (despite an improvement), there was a persistence of a pathological pattern at the end of the follow up.

Results: In the 1st month visit, the majority (101 out of 163, 62%) of patients had still some findings related to Covid pneumonia (diffuse B−lines or bilateral patchy sub pleural or peripheral consolidations).

The 3th month appointment shows that (74 out of 142, 52%) of patient still have these patterns; in 17% (27 out of 74) there was no improvement so patients received a CT. The results demonstrate that 33% (9 out of 27) of patients who underwent CT showed sign of lung fibrosis.

At the 6th month, 20% (15 out of 85) of patients tested had still pathological aspects so received a CT. 47% (7 out of 15) of these show at the exams signs of lung fibrosis.

All of these patients, who developed a long-term long damage, were addressed to a pneumological management.

Conclusions: Lung ultrasound is a valid instrument not only to early detect pneumonia in acute phase of Covid-19 but also to individuate long-term lung damage and lung fibrosis. It lead to direct the use on tomography only in selected patients. In consequence, it can reduce the amount of not necessary radiation especially in young patients, the health costs and the waiting lists.

COVID-19

SARS-CoV-2 vaccines

P 66 **SAFETY AND IMMUNOGENICITY OF A THIRD-DOSE COVID-19 BNT162B2 BOOSTING VACCINATION IN PEOPLE LIVING WITH HIV**

L. Gianserra[1], M.G. Donà[1], E. Giuliani[2], C. Stingone[1], M. Pontone[3], A.R. Buonomini[1], M. Giuliani[1], F. Pimpinelli[3], A. Morrone[2], A. Latini[1]

[1]STI/HIV Unit, San Gallicano Dermatological Institute IRCCS, Rome, Italy, [2]Scientific Direction, San Gallicano Dermatological Institute IRCCS, Rome, Italy, [3]Microbiology and Clinical Pathology, San Gallicano Dermatological Institute IRCCS, Rome, Italy

Background: Due to the reduced protection of previous vaccination, a COVID-19 booster dose has been recommended. Yet, data on the safety and immunogenicity of boosting vaccination in People Living With HIV (PLWH) are scant. We have previously shown immunogenicity and safety of primary vaccination (two doses) with SARS-CoV-2 mRNA BNT162b2 vaccine. Here, we report updated data about immunogenicity and safety of the booster dose.

Material and methods: Anti-SARS-CoV-2 spike antibodies (AU/ml measured with LIAISON® SARS-CoV-2 S1/S2 IgG test, DiaSorin®), CD4+, CD8+, viraemia, and adverse events were monitored at the following time points: T0 (pre-vaccination), T1 (post-primary vaccination, i.e., 4 weeks after the second dose), T2 (pre-booster) and T3 (post-booster, i.e., 4 weeks after the booster dose). Humoral immune responses were evaluated according to sex, age, Body Mass Index (BMI), nadir and baseline CD4+ counts, cART regimen.

Results: Of the 63 subjects originally enrolled, 42 (66.7%) entered the booster group (median age: 53 years, IQR: 48-61; 37 males, 88.1%; median time since HIV diagnosis: 12.4 years, IQR: 6.5-18.3). Median counts of nadir and T0 CD4+ were 165 (IQR: 104-291) and 687 cells/mm3 (IQR: 488-929), respectively. The booster dose was administered a median of 5.5 months after the second dose. Seroconversion had been observed in 100% of the patients at T1, and 41 subjects were still reactive at T2 (97.6%). All the patients were reactive at T3. The median concentration of anti-SARS-CoV-2 IgG significantly increased from T0 to T1 (3.8 vs. 377.0, p<0.0001), but a significant decrease was observed at T2 compared to T1 (107 vs. 377, p<0.0001). The highest antibody level was reached after the booster dose (median: 1580), with a significant increase compared with both T0 (p<0.0001) and T2 (p<0.0001). The antibody response after the booster dose did not significantly differ by sex, age (≤53 and >53 years), BMI, nadir CD4+ (≤200 and >200 cells/mm3) and baseline CD4+ (≤500 and >500 cells/mm3). The antibody levels were higher in those treated vs. those not treated with dual therapy (median: 1960 vs. 1270, p=0.09), and in those treated vs. those not treated with an INSTI-based regimen (median: 1820 vs. 967, p=0.07), but these differences were not significant.

No severe adverse events were observed. Only one patient developed hearing loss 24 hours after the booster dose, but no tinnitus, vertigo or dizziness were reported. The patient referred a previous episode of sensorineural hearing loss (SNHL), with a mild function loss at the right ear. The audiometric curve after boosting indicated a condition of bilateral SNHL. The patient was treated with endothympanic administration of corticosteroid and recovered auditory function and audiometric characteristics as prior to vaccination in about 1 month.

Conclusions: Boosting vaccination with BNT162b2 in PLWH is safe and greatly increased the immune response with respect to the primary vaccination.

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COVID-19

SARS-CoV-2 vaccines

P 67 **FATAL OUTCOME OF COVID-19 RELAPSE IN A FULLY VACCINATED PATIENT WITH NON-HODGKIN'S LYMPHOMA IN MAINTENANCE THERAPY WITH ANTI-B CELLS MONOCLONAL ANTIBODIES: A CASE REPORT**

F. Calò[1], L. Onorato[1], C. Monari[1], M. Pisaturo[1], L. Alessio[1], A. Di Fraia[1], C. Minichini[1], L. Atripaldi[2], A. Pinto[3], N. Coppola[1]

[1]Department of Mental Health and Public Medicine – Infectious Diseases Unit. University of Campania Luigi Vanvitelli, Naples, Italy, [2]Unit of Microbiology and Virology, AORN Ospedali dei Colli, Cotugno-Monaldi Hospital, Naples, Italy, [3]Hematology-Oncology & Stem Cell Transplantation Unit. National Cancer Institute, Fondazione 'G. Pascale', IRCCS, Naples, Italy

Background: Few data are available in the literature regarding the effectiveness of anti-SARSCoV2 vaccine in patients with immunodepression.
Material and methods: We report the virological and clinical characteristics of a 53-years-old male patient with follicular Non-Hodgkin's lymphoma on therapy with obinutuzumab who had received 3 doses of BNT162b2 vaccine.
Results: On January 3 2022,a week after the vaccine,he developed mild symptoms characterized by low-grade fever and cough for which he underwent a nasal/oropharyngeal swab test for SARS-CoV-2 which resulted positive. In order to prevent the progression of COVID-19,on 10 January he received infusion of Sotrovimab with a rapid remission of symptoms.On 21 January,he tested negative for SARS-CoV-2.However, from the same day the patient experienced high-grade fever (39°C) with chill and dyspnoea.On 31 January, he tested again negative for SARS-CoV-2 on the molecular swab.On 4 February he was admitted to the hospital due to persisting fever; SpO2 was 96% on ambient air.Blood tests revealed a marked inflammatory state (CRP 175 mg/L, procalcitonin 0.60 µg/mL, fibrinogen 771 mg/dL, ferritin 544 µg/mL, and D-dimer 533 µg/mL).Blood cultures, HIV Ab, CMV and EBV-DNA, b-d-glucan, galactomannan, sputum examination for common bacteria and M.tuberculosis, filmArray respiratory panel for virus and atypical bacterial, legionella antigen resulted negative.Only quantiferon was found positive.The CT scan showed bilaterally multiple areas of ground glass with crazy paving.The prophylaxis in place with co-trimoxazole and acyclovir was continued and antibiotic therapy with piperacillin/tazobactam was started. From February 8th, the patient began to complain worsening dyspnea with desaturation.On 10 February,he tested again negative for SARS-CoV-2 PCR.On 13 February he was put on HFNC,50% FiO2 with a PA02/FIO2 ratio of 163.For the worsening of the respiratory picture a chest CT was performed and showed a worsening of the radiological picture. A further swab for SARS-CoV-2 PCR was analyzed and this time resulted positive (TC 27 for ORF1ab and 28 for N and E genes). Fibrobronchoscopy resulted negative for tuberculosis and common bacterial culture, but positive for SARS-CoV-2-RNA.On 16 February he was referred to ICU where he underwent orotracheal intubation and received broad-spectrum antibiotics, corticosteroid and tocilizumab treatment. On March 4, the COVID-19 surveillance swab was still positive. After a few days of ICU stays he developed various infectious complications which led him to death on March 6.The analysis of the SARS-CoV-2 RNA isolated on January 10, 2022 (first course of SARS-CoV-2 infection) and on February 15 showed the same viral clade, Omicron variant (VOC-21NOV-01 (B.1.1.529) variant).Figure 1 shows COVID-19 timeline .
Conclusions: SARS-CoV-2 infection can cause prolonged and severe diseases in cancer patients and vaccination show a suboptimal efficacy in this immunocompromised population.

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COVID-19

SARS-CoV-2 vaccines

P 68 **A RECENT SARS-COV-2 OMICRON VARIANT RE-INFECTION SHORTLY AFTER SARS-COV-2 DELTA VARIANT RELATED SEVERE PNEUMONIA IN AN IMMUNOCOMPROMISED PATIENT WITH THREE-DOSE VACCINATION (BNT162B2 MRNA VACCINE): IMMUNOLOGICAL CHARACTERIZATION AND THERAPEUTIC APPROACH**

A. Di Lorenzo[1], M. Iannetta[1], B. Rossi[1], V. Malagnino[1], M. Zordan[1], L. Ansaldo[1], N. Braccialarghe[1], M. L. Minardi[1], C. Sorace[1], C. Cerini[1], D. Zace[1], L. Alborghetti[1], S. Tedde[1], L. Piermatteo[2], E. Andreassi[2], M.C. Bellocchi[2], F. Ceccherini Silberstein[2], L. Sarmati[1], M. Andreoni[1]

[1]Department of System Medicine, Tor Vergata University, Rome, Italy, [2]Virology department, University of Rome Tor Vergata, Rome, Italy

Since the vaccination campaign started, the scientific community questioned about the necessity of a vaccine booster dose and the target population.
Immunocompromised subjects mount inadequate response to COVID-19 vaccination, and are more susceptible to develop severe disease, or re-infection.
A 70-year-old woman with follicular lymphoma, was hospitalized in the Infectious Diseases (ID) Unit of Policlinico Tor Vergata (PTV) in Rome, because of SARS-CoV-2 related pneumonia. She was vaccinated with three doses of BNT162b2 mRNA vaccine (last dose 27 days before hospitalization)
She tested positive for SARS-CoV-2 RNA on a surveillance nasopharyngeal swab (NPhS) 11 days before hospitalization. Symptoms started 3 days later, with hyperpyrexia, cough and coryza.
Although chest radiography was negative for interstitial pneumonia, steroid treatment and ceftriaxone were started at home. Because of the persistence of the symptoms, the patient came to PTV Emergency Room, where a Chest Computed Tomography Scan (Chest-CTscan) showed bilateral ground glass areas and an arterial blood gas (ABG) test indicated the need of oxygen supply with Venturi Mask. Considering the worsening of ABG parameters and the appearance of new lung infiltrates, High Flow Nasal Cannula Oxygen therapy was started.
The patient was also treated with intravenous (iv) casirivimab/imdevimab. After 13 days from hospitalization, clinical conditions improved, Oxygen therapy was discontinued and patient was discharged.
SARS-CoV-2 genome was sequenced and characterized as a Delta Variant (Clade 21J, Nextrain; AY46.6 PANGO lineage). Anti-SARS-CoV-2 Spike antibody titer was 232,9 U/ml (positive>0,8 U/mL).
Specific T-lymphocyte stimulation with SARS-CoV-2 peptides was performed on whole blood at 7 days after hospitalization, showing detectable production of interferon-gamma upon spike and nucleoprotein stimulation.
After 40 days from discharge, fever and cough reappeared. A NPhS for SARS-CoV-2-RNA detection tested positive, therfore the patient was administered iv sotrovimab as an outpatient. Anti-SARS-CoV-2 nucleocapside antibodies were undetectable.
The sequencing of SARS-CoV-2 genome revealed an Omicron Variant (Clade 21k, Nextrain BA.1).
Specific T-lymphocyte stimulation with SARS-CoV-2 peptides showed an increase of interferon-gamma production for both spike and nucleocapside stimulation, with an increase in the lymphocyte absolute count (fig.1). After 7 days SARS-CoV-2-RNA was undetectable and symptoms disappeard.
This case report underlines the risk of developing SARS-CoV-2 related pneumonia and severe COVID-19 in immunocompromised patients, despite the presence of humoral and cell-mediated immune responses. Furthermore, SARS-CoV-2 omicron variant can infect immunocompromised patients, even shortly after a natural infection due to Delta variant and a full vaccine schedule.
New treatment and prevention strategies are advisable.

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COVID-19

SARS-CoV-2 vaccines

P 69 **EVALUATION OF HUMORAL AND T-SPECIFIC RESPONSES AFTER THE BOOSTER DOSE OF BNT162B2 COVID-19 VACCINE IN RESIDENTS OF A LONG TERM CARE FACILITY**

A. Lai[1], B. Caimi[2], A. Bergna[1], A. Gatti[2], M. Franzetti[3], A. Gabrieli[1], M. Tarkowski[1], P.L. Rossi[2], M. D'Orso[4], F. Pregliasco[5], C. Balotta[1,2], A. Riva[1], G. Calicchio[2]

[1]Department of Biomedical and Clinical Sciences L. Sacco, University of Milan, Milan, Italy, [2]Azienda Servizi alla Persona, Istituti Milanesi Martinitt e Stelline e Pio Albergo Trivulzio, Milan, Italy, [3]Infectious Diseases Unit, Legnano General Hospital, ASST Ovest Milanese, Legnano, Italy, [4]Department of Medicine and Surgery, University of Milan-Bicocca, Monza, Italy, [5]Department of Biomedical Sciences, University of Milan and IRCCS Istituto Ortopedico Galeazzi, Milan, Italy

Background: Residents of long-term care facilities (LTCFs) have been dramatically affected by the COVID-19 pandemic at global scale as older age and comorbidities pose at high risk of severe disease and death. Aim of the study was to monitor levels and durability of specific antibody response to SARS-CoV-2 after the third dose of BNT162b2 vaccine.

Methods: We studied 92 residents and 25 Health Care Workers (HCWs) of Pio Albergo Trivulzio, the largest Italian LTCF. SARS-CoV-2 S-IgG antibodies were evaluated at month 2 and 6 after first cycle and before and 2 months after the booster dose. Before vaccination all subjects were screened for SARS-CoV-2 N-IgG. Response to vaccination was defined as high, medium, low and null response by stratifying anti-S IgG values in 4 levels: >1,000, 101-1,000, 1-100 and <1 BAU/mL. T cell responses were evaluated thought QuantiFERON SARS-CoV-2 IFN-γ 2 months before and after booster dose.

Results: Among LTCF residents 85.9% (n=79) were female and the median age was 88.6 years (IQR: 83.1-93.1). Median levels of anti-S IgG significantly decreased from 7,385 BAU/mL (IQR: 32.8-7,005) to 1,482 (IQR: 33.3 -5,970) at 2 and 6 months after first cycle, respectively. Titers were 3,675 (IQR: 2,003-6,213) and 9,823 (IQR: 3,742-12,005) at baseline and 2 months after the booster dose, respectively. HCWs titers significantly decreased from 1,042 (IQR:348-4,412) to 371 (IQR:165-854) overtime while increased at 12,447 (IQR: 5,503-12,500) after the booster dose.

A significant association was observed between null and suboptimal anti-S IgG response and age >80 years at first, second and third time point. Experience of COVID-19 was positive in 40.2% of cases with a significant different distribution among residents and HCWs (45.6% vs. 20%, p=0.03). Residents with positive nucleocapsid serology showed a significantly highest response considering all levels of serologic responses at all time points (p<0.001).

Residents with ischemic heart diseases showed a reduced degree of response to vaccination considering all the levels of specific antibodies at first, second and third time point (p=0.005; p=0.009; p=0.05), but not at fourth one. Chronic lung disease, diabetes, cancer, corticosteroid and anticoagulant therapies not influenced humoral response.

Residents as well as HCWs with IFN-γ positive response significantly increased after booster dose from 22.8% (n=21) to 57.6% (n=53) and from 24%, (n=6) to 72% (n=18), respectively. No differences were observed in IFN-γ response among subjects with or without previous exposure to COVID-19 at both time points.

Conclusions: Our data provide additional insights into the longitudinal dynamics of the immune response to vaccination in elderly after the administration of first cycle and booster dose. Future studies evaluating both humoral and cellular responses to SARS-CoV-2 will help to determine the longer-term effectiveness of the booster dose against current and emerging variants in elderly.

COVID-19

SARS-CoV-2 vaccines

P 70 **DETECTION OF MATERNAL ANTIBODIES ELICITED BY COVID-19 VACCINATION IN AMNIOTIC FLUID**

F. Colavita, A. Oliva, A. Bettini, E. Girardi, A. Antinori, C. Castilletti, F. Vaia, G. Liuzzi

National Institute for Infectious Diseases "L. Spallanzani" IRCCS, Rome, Italy

Background: SARS-CoV-2 infection may pose pregnant women at high risk for severe disease and adverse perinatal outcome. COVID-19 vaccination campaign represents the key strategy to struggle the pandemic; however, public acceptance of maternal immunization has to be improved, highlighting the mechanism of passive immunity for protecting newborns against SARS-CoV-2 infection. Here, we report the evidence of maternal anti-SARS-CoV-2 IgG in amniotic fluid (AF) samples collected from two pregnant women following COVID-19 vaccination at the National Institute for Infectious Diseases "L. Spallanzani" (INMI, Rome, Italy).

Materials and Methods: Blood samples and AF were collected from two pregnant women, receiving mRNA COVID-19 vaccine (BNT162b2, Pfizer-Biontech) second dose at the 10th week of gestation (patient A) and on the day of last menstrual period (patient B). Both women were prescribed amniocentesis at the 18th week of pregnancy for evaluating the risk of Toxoplasmosis vertical transmission. Anti-SARS-CoV-2 IgG levels in AF residual samples were evaluated by home-made Indirect immunofluorescence assay (IFA) using slides prepared with Vero E6 cells infected with SARS-CoV-2 isolate (2019-nCoV/Italy-INMI1, GISAID accession number EPI_ISL_410546), and by 2-fold titration starting from 1:2 dilution. Levels of anti-Spike/Receptor Binding Domain (RBD) IgG were determined in serum samples by an automated chemiluminescent immunoassay (ARCHITECT SARS-CoV-2 IgG II Quantitative, Abbott Laboratories, Wiesbaden, Germany) and expressed as Binding Antibody Units (BAU)/mL (positive≥7.1). Both women signed informed consent for the examination of the residual clinical samples.

Results: Both women had detectable anti-S/RBD IgG (Table 1): patient A, 144.4 BAU/ml after 92 days from second dose (15th week of gestation); patient B, 92.5 BAU/ml after 131 days from second dose (18th week of gestation). Anti-SARS-CoV-2 IgG were found in AF collected from both women at the 18th week of gestation (131 days in patient A and 113 days in patient B, after second vaccine dose). Titers were correlated to the levels detected in serum (patient A, 1:8; patient B, 1:2) and inversely associated to the time from vaccination. Notably, both patients had no adverse effect to the vaccination.

Conclusions: Our findings confirm that antibodies elicited by COVID-19 vaccination are able to cross placenta. It is critical to fully understand the kinetics of maternal response to vaccination, the efficiency of IgG transfer, and the persistence of antibodies in infants in order to optimize maternal immunization regimens.

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COVID-19

SARS-CoV-2 vaccines

P 71 **HUMORAL AND T-CELL MEDIATED RESPONSE AFTER ADMINISTRATION OF MRNA VACCINE BNT162B2 IN FRAIL PATIENTS**

R. Campagna[1], L. Mazzuti[1], G. Guerrizio[1], C. Nonne[1], G. Migliara[2], C. De Vito[2], I. Mezzaroma[3], V. Pistolesi[4], S. Morabito[4], O. Turriziani[1]

[1]Department of Molecular Medicine Sapienza University, Rome, [2]Department of Public Health and Infectious Diseases Sapienza University, Rome, [3]Department of Translational and Precision Medicine Sapienza University, Rome, [4]Department of Internal Medicine and Medical Specialties Sapienza University, Rome

Background: To contrast the viral spread and prevent the most severe consequences led by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, one of the most effective strategies is vaccination. The first authorized vaccine has been the mRNA vaccine BNT162b2 produced by Pfizer-BioNTech. In this unprecedented condition, patients with frailty are considered to be at greater risk to get severe infection which can require hospitalization and lead to poor outcome.
The aim of our study was to both evaluate the humoral immune response elicited by the vaccination at different time points, and analyze the T-cell response in terms of interferon (IFN)-γ production both in frail patients and healthy donors.
Material and methods: Fifty-seven patients (31 patients undergoing hemodialysis and 26 HIV positive subjects; median age=69) and 39 healthcare workers (median age=46) were enrolled. All participants received two doses of the mRNA vaccine BNT162b2. Hemodialysis and HIV patients were considered as a whole group. For each subject we collected a serum sample 21 days after the first dose and 7 (t7), 14 (t14), 21 (t21), 90 (t90) and 270 (t270) days after the second dose. Samples were centrifuged for serum separation and later analyzed. IgG antibodies were detected by LIAISON® SARS-CoV-2 TrimericS IgG kit. For a subset of our population (29 hemodialysis patients and 22 healthcare workers) we collected a plasma sample at t270; the samples were analyzed to evaluate IFN-γ production by T-cells after stimulation with different peptides using the IFN-γ release assay (IGRA) Covi-FERON test by SD biosensor.
Results: Twenty-one days after the first dose, healthcare workers showed a significantly higher antibody titer than patients ($p<0.001$). The difference persisted at all time points except 270 days after second dose ($p=0.052$). By establishing as reference time 7 days after the second dose, we observed a decline of the antibody levels at t21, t90 and t270 for both groups, but with a steeper slope of decline in the patients group. Regarding T-cell response, analyzing the 51 subjects as a single group, 47.1% of the population resulted reactive to the test. The only significant difference between non-reactive and reactive subjects was found in median antibody levels, higher in the responders group than in non-responders (177.5, IQR 81.7 – 1160, vs. 61.4, IQR 23.4 – 189 BAU/ml, respectively).
Conclusions: Despite some limitations our study shows that the healthcare workers seemed to better respond to the vaccination in terms of antibodies production, but a decrease of IgG levels was observed in both groups. In addition, the lack of T-cell response in about 50% of the participants seems to suggest that both humoral and cell-mediated response decline over time. Given these considerations it seems undeniable the importance of vaccination to maintain a protection against SARS-CoV-2 infection especially in patients with frailty.

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COVID-19

SARS-CoV-2 vaccines

P 72 **EARLY EVIDENCE ON VACCINE EFFECTIVENESS OF COVID VACCINES IN PLWHA**

M. Sane Schepisi[1], A. Meggiolaro[1], A. Mammone[1], S. Farina[2], C. Castagna[2], A. Siddu[1], A. Caraglia[1], F. Maraglino[1], S. Boccia[2], G. Rezza[1]

[1]Italian Ministry of Health, General Directorate for Health Prevention, Rome, Italy, [2]Department of Life Sciences and Public Health, Section of Hygiene, Università Cattolica del Sacro Cuore, Rome, Italy

Background: COVID-19 vaccination is recommended for people living with HIV/AIDS and they are a priority group in vaccination programmes. Available information suggests current WHO recommended COVID-19 vaccines are safe for people living with HIV. The uptake of COVID-19 vaccination follows patterns seen in the wider population, with significant disparities within and between countries. Studies conducted in people living with HIV found low non-response rates or comparable antibody titres compared to an HIV-negative population. Despite full vaccination, persons with immune dysfunction had substantially higher risk for COVID-19 breakthrough infection than those without such a condition. [1, 2] Several studies have shown that antibody responses in people with HIV depend on CD4 count and people with HIV with CD4 counts below 500 may have a weaker response to vaccination.

This systematic review aims at evaluating vaccine effectiveness reported by real world studies on HIV patients.

Materials and Methods: PubMed, medRxiv/bioRxiv, WHO covid-19 databases, the VIEW-hub platform and the 2022 CROI (Conference on Retroviruses and Opportunistic Infections) site were searched using the terms “COVID -19″, “SARS-CoV-2″, “vaccine efficacy”, “people living with HIV” to identify published/preprint studies or abstract presented in the period 01/01/2021- 11/04/2022 on real world studies reporting vaccine effectiveness results among people living with HIV

Results: 4 of the 3284 screened records met the inclusion criteria. Of them, 2 studies were presented at the 2022 “Annual Conference on Retroviruses and Opportunistic Infections” (CROI). Real world studies were conducted during years 2021-2 in Zambia [3], Taiwan [4], South Africa [5], and the Russian Federation [6]. Vaccines considered included both mRNA and viral vector vaccines (Table 1)

Main reason for exclusion was inclusion of immune dysfunctions or immunosuppressive conditions.

Vaccine effectiveness estimates ranges varied widely across included studies according to the outome considered (Table 2):

- infection: 65,8 [6]- 100% [4]
- severe disease/hospitalization/ICU admission: 73,2 - 79,3% [5]
- death/in-hospital mortality: 67,2 [5] - 76,0 % [3]

Only one study [6] reported results stratified by CD4 cell count and found a trend, although not statistically significant, of declining vaccine efficiency in immune-compromised individuals (CD4+ < 350 cells/µl).

Conclusions: Data extracted were limited and heterogeneous, so we were unable to produce a pooled estimate of vaccine effectiveness through meta-analysis. Taken together, the available evidence shows that PLWHA are protected by current WHO recommended COVID-19 vaccines. Further studies are needed to confirm this preliminar findings. In the near future, responses to universal pancoranavirus vaccines as well as novel vaccine strategies should be tested among people living with HIV.

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Pathogenesis and Immunology

COVID-19 pathogenesis

P 73 **LONGITUDINAL EVALUATION OF QUANTIFERON-TB GOLD PLUS RESPONSES IN COVID-19 PATIENTS**

G. Alessio, A. Imeneo, A. Di Lorenzo, B. Rossi, M. Compagno, L. Coppola, L. Campogiani, M. Andreoni, L. Sarmati, M. Iannetta

Policlinico Tor Vergata, Roma

Several studies reported an increased rate of indeterminate QuantiFERON-TB Gold Plus (QFT-P) assay results in patients hospitalized for severe Coronavirus Disease (COVID)-19, due to peripheral blood T-lymphocyte depletion and dysfunction. To longitudinally evaluate QFT-P responses and the relationship with lymphocyte count and inflammation markers, the test was reassessed in patients who survived COVID-19, with a previous indeterminate result.

In the Infectious Disease Unit of Policlinico Tor Vergata, all patients hospitalized for COVID-19 underwent QFT-P assay on admission. In a subgroup of patients the test was reassessed after recovery. Demographics, clinical and laboratory data were collected. Statistical analysis was performed with Prism-GraphPad.

We observed 93 indeterminate QFT-P among 420 patients (22%) and 130 among 529 patients (25%) during 2020 and 2021, respectively. 30 patients among those with an indeterminate QFT-P test were enrolled for reassessing the test after recovery from COVID-19. Considering disease severity, 25 were classified as severe and 5 as non-severe; 1 patient was admitted in the Intensive Care Unit (ICU). Median age was 57 (interquartile range [IQR]: 51 -63), with a prevalence of male sex (M/F: 21/9); median Charlson Comorbidity Index was 2 (IQR: 1-3).

The second QFT-P assay was performed after at least 1 month from the first assay (median time 6 months, IQR: 4 -9 months). All QFT-P assays gave a determined result, with 2 positive (6,7%) and 28 negative (93,3%) tests. A statistically significant difference was observed after comparing the laboratory parameters at the time of the first and the second QFT-P assay. Specifically, lymphocyte absolute counts were increased ($p<0.0001$) while neutrophil absolute counts, neutrophil to lymphocyte (N/L) ratio, D-dimer, fibrinogen, ferritin, C-reactive protein (CRP) were significantly reduced ($p=0.0048$; $p=0.0001$; $P=0.0035$; $p<0.0001$; $p<0.0001$; $p<0.0001$, respectively). Concerning the QFT-P assay, interferon gamma production in the Mitogen-Nil, TB1-Nil and TB2-Nil condition was significantly increased ($p<0.0001$; $p=0.0034$; $p=0.0091$, respectively).

Once the acute phase of COVID-19 is resolved, inflammatory markers tend to normalize as well as peripheral blood leucocyte counts. The reduction of inflammation and the recovery of total peripheral blood lymphocyte counts is associated to an effective interferon-gamma production after specific mycobacterial peptide and nonspecific phytohemagglutinin stimulation. In our cohort, all the 30 QFT-P reassessed showed a determinate result. Moreover, we observed 2 positive QFT-P assay (6,7%), supporting the importance of retesting patients with indeterminate result, to identify latent tuberculosis infection (LTBI) and monitor patients for possible reactivation as a consequence of the immune-suppression associated with COVID-19.

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Pathogenesis and Immunology

COVID-19 pathogenesis

P 74 **HUMORAL AND CELLULAR RESPONSES TO SPIKE OF Δ SARS-COV-2 VARIANT IN VACCINATED PATIENTS WITH IMMUNE MEDIATED INFLAMMATORY DISEASES**

L. Petrone[1], A. Picchianti-Diamanti[2], G.D. Sebastiani[3], A. Aiello[1], B. Laganà[2], G. Cuzzi[1], V. Vanini[1,4], G. Gualano[5], A. Grifoni[6], M. Ferraioli[7], C. Castilletti[8], S. Meschi[8], F. Vaia[9], E. Nicastri[10], A. Sette[6], D. Goletti[1]

[1]Translational Research Unit, National Institute for Infectious Diseases Lazzaro Spallanzani-IRCCS, Rome, Italy, [2]Department of Clinical and Molecular Medicine, "Sapienza" University, S. Andrea University Hospital, Rome, Italy, [3]Department of Rheumatology, San Camillo Hospital, Rome, Italy, [4]Unità Operativa Semplice (UOS) Professioni Sanitarie Tecniche, National Institute for Infectious Diseases Lazzaro Spallanzani-IRCCS, Rome, Italy, [5]Respiratory Infectious Diseases Unit, National Institute for Infectious Diseases Lazzaro Spallanzani-IRCCS, Rome, Italy, [6]Center for Infectious Disease and Vaccine Research, La Jolla Institute for Immunology (LJI), La Jolla, CA, USA, [7]Rheumatology, Allergology and Clinical Immunology, Dipartimento di medicina dei sistemi, University of Rome Tor Vergata, Rome, Italy, [8]Virology Unit, National Institute for Infectious Diseases Lazzaro Spallanzani-IRCCS, Rome, Italy, [9]UOC Direzione Sanitaria, National Institute for Infectious Diseases Lazzaro Spallanzani-IRCCS, Rome, Italy, [10]UOC Malattie Infettive ad Alta Intensità di Cura, National Institute for Infectious Diseases Lazzaro Spallanzani-IRCCS, Rome, Italy

Background: Immune Mediated Inflammatory Diseases (IMID) are associated to increased risk of hospitalization and death from COVID-19. We recently demonstrated that mRNA vaccines induce an immune response, both humoral and T-cell response, in patients with rheumatoid arthritis. However, the magnitude of the response depends on the immunosuppressive therapy. In particular, the lowest T-cell viral specific response was observed in IMID patients under therapy with Cytotoxic T-Lymphocyte Antigen (CTLA) 4-IgG, Tumor Necrosis Factor (TNF)-α or Interleukin (IL)-6 inhibitors. Few evidences are available on the impact of variants of concern on the vaccine-induced T-cell response in vulnerable populations. Therefore, we assessed vaccination-induced cellular responses against spike from the ancestral strain and from the delta (δ) SARS-CoV-2 variant in patients with Immune Mediated Inflammatory Diseases (IMID) on immunosuppressive therapy in comparison with immunocompetent subjects. The antibody response was concomitantly evaluated

Materials and Methods. We enrolled IMID patients and immunocompetent subjects having completed the vaccination schedule within 4-6 months from the first dose. The Interferon (IFN)-γ-response to spike peptides derived from the ancestral and the δ SARS-CoV-2 and the anti-Receptor Binding Domain (RBD) IgG antibodies were measured by ELISA.

Results: We enrolled 43 IMID patients and 9 immunocompetent subjects. No significant differences were found comparing the specific immune response (IFN-γ) between IMID patients and immunocompetent subjects to the ancestral (p=0.36) or delta peptide pool (p=0.51). Nevertheless, IFN-γ-specific response to the ancestral or to the δ pools was reduced in subjects taking CTLA4-IgG or TNF-α inhibitors compared to subjects treated with IL-6 inhibitors or DMARDs. Regarding the antibody response, no significant differences were observed between IMID and immunocompetent individuals.

Conclusions. Cellular responses to δ SARS-CoV-2 variant remain largely intact in IMID patients. However, the magnitude of these responses are dependent on the specific IMID immune suppressive regimen. Serological response was also similar among the IMID and control groups.

Pathogenesis and Immunology

COVID-19 pathogenesis

P 75 **SERUM LEVELS OF SURFACTANT PROTEINS A AND D IN SARSCOV2 INFECTED PATIENTS**

L. Maddaloni[1], L. Santinelli[1], V. Zullino[2], C. De Panfilis[2], A. Lazzaro[1], C.M. Lofaro[1], S. Caiazzo[1], F. Ruberto[2], C. Scagnolari[3], C.M. Mastroianni[1], G. d'Ettorre[1], G. Ceccarelli[1]

[1]Department of Public Health and Infectious Diseases, Sapienza University of Rome, Italy, [2]Department of Anestesia, Sapienza University of Rome, Italy, [3]Virology Laboratory, Department of Molecular Medicine, Sapienza University of Rome, Italy

Background: Surfactant Proteins A (SP-A) and D (SP-D) are soluble molecules physiologically involved in the lung homeostasis playing an anti-viral and immunomodulatory role. High serum levels of these proteins have been related with severe pulmonary diseases, such as interstitial lung disease. Both SP-A and SP-D levels decrease in bronchoalveolar lavage (BAL), while their serum concentrations increase in pathological lung conditions. Thus, the aim of this study was to assess whether alteration in SP-A and SP-D serum concentrations can be correlated with a severe clinical outcome of COVID-19.

Material and Methods: Blood samples were collected from SARS-CoV-2 infected patients, hospitalized at Policlinico Umberto I Hospital in Rome, at admission (T0) and seven days later (T1). A group of healthy individuals was also enrolled. Detection of SP-A and SP-D proteins in patient's serum was performed using Human surfactant protein A (SP-A) ELISA Kit (MyBioSource) and RayBio® Human SP-D ELISA Kit. The data acquisition was performed using iMarkTM Microplate Absorbance Reader (Bio-Rad) and the analysis were conducted using "Four Parameter Logistic Curve" online data analysis tool (MyAssays Ltd.). Statistical analysis was performed using PRISM v. 9.3.1.

Results: 51 SARS-CoV-2 infected patients, with a mean age of 68 (± 15) years were enrolled. According to the clinical severity, 21 patients (41%) required non-invasive ventilation or were not treated with oxygen, considered as mild, while 30 patients (59%) were under Continuous Positive Airway Pressure (CPAP) ventilatory system, considered as severe. 22 healthy controls were also enrolled; their normal values were 64.0 ng/l for SP-A and 5.353 ng/ml for SP-D. Increased SP-A serum levels was observed at the time of hospitalization in SARS-CoV-2 infected patients compared to healthy control (107.8 ng/l; p=0.0224). In the mild group, but not in the severe group, SP-A serum levels decreased at T1 compared to T0 (T1:75,53 vs T0:110,7 ng/l; p=0.015) returning to values comparable to those of healthy controls. Indeed, SP-D serum levels were higher at T0 (19.62 ng/ml; p=0.0003) and T1 (11.24 ng/ml; p=0.0121) in SARSCoV2 infected patients compared to those measured in healthy controls. Moreover, SP-D serum levels observed at T1 in the severe group remain enhanced than those measured in the mild group (severe:14,31 vs mild:8,73 ng/ml; p=0.037).

Conclusions: Despite the high inter-individual variability in SP-A/D serum levels observed among COVID-19 patients, the decrease of SP-A serum levels recorded at T1 in patients with moderate disease might reflect the recovery of homeostasis in lung mucosal barrier, not yet reached in those with critical ill disease. Similarly, the persistence of increased serum SP-D levels in severe COVID-19 patients might underline the presence of interstitial lung damage. Further studies are needed to delineate SP-A and SP-D role as potential predictive severity biomarkers of COVID-19 outcome.

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Pathogenesis and Immunology

COVID-19 pathogenesis

P 76 **COORDINATED INNATE AND T-CELL IMMUNE RESPONSES IN MILD COVID-19 PATIENTS FROM HOUSEHOLD CONTACTS OF COVID-19 CASES DURING THE FIRST PANDEMIC WAVE**

A. Aiello[1], A. Grossi[2], S. Meschi[3], M. Meledandri[4], V. Vanini[1,5], L. Petrone[1], R. Casetti[6], G. Cuzzi[1], A. Salmi[1], A.M.G. Altera[1], L. Pierelli[7], G. Gualano[8], T. Ascoli Bartoli[9], C.Castilletti[3], C. Agrati[4], E. Girardi[10], F. Palmieri[8], E.Nicastri[9], E. di Rosa[2], D. Goletti[1]

[1]Translational Research Unit, National Institute for Infectious Diseases Lazzaro Spallanzani-IRCCS, Rome, Italy, [2]UOC Public Health Hygiene Service, ASL Roma 1, [3]Laboratory of Virology, National Institute for Infectious Diseases Lazzaro Spallanzani-IRCCS, Rome, Italy, [4]UOC Microbiology and Virology, ASL Roma 1-San Filippo Neri Hospital, Rome, Italy, [5]UOS Professioni Sanitarie Tecniche, National Institute for Infectious Diseases Lazzaro Spallanzani-IRCCS, [6]Laboratory of Cellular Immunology, National Institute for Infectious Diseases Lazzaro Spallanzani-IRCCS, Rome, Italy, [7]UOC Transfusion Medicine and Stem Cell Unit, San Camillo Forlanini Hospital, Rome, Italy, [8]Respiratory Infectious Diseases Unit, National Institute for Infectious Diseases Lazzaro Spallanzani-IRCCS, Rome, Italy, [9]Clinical Division of Infectious Diseases, National Institute for Infectious Diseases Lazzaro Spallanzani-IRCCS, Rome, Italy, [10]Clinical Epidemiology, National Institute for Infectious Diseases Lazzaro Spallanzani-IRCCS, Rome, Italy

Background: A coordinated innate and adaptive immune response is necessary to mount an appropriate immune protection that counteracts SARS-CoV-2 infection. It is of great importance to evaluate the combination, as well as the kinetics of the immune response against COVID-19 in the various stages of the disease, starting from the earliest. In this study, we characterized the innate and adaptive immune responses in individuals early exposed to SARS-CoV-2 in the household, who have presented an asymptomatic or mild COVID-19, correlating the results with the outcome of the nasopharyngeal swab.

Materials and Methods: Household contacts of COVID-19 cases that were screened for infection by nasopharyngeal swab for surveillance purposes were enrolled (T0, n=42). Of these, 28 subjects returned for a follow-up test (T1), at the end of the quarantine. The innate response was assessed by detecting a panel of soluble factors by multiplex-technology in plasma samples. Cell-mediated response was evaluated by measuring interferon (IFN)-γ levels by ELISA in plasma from whole-blood stimulated with SARS−CoV−2 peptide pools, including spike (S), nucleocapsid (N) and membrane (M). The serological response was assessed by quantifying anti-Receptor-Binding-Domain (RBD), anti-Nucleocapsid (N), whole virus indirect immunofluorescence, and neutralizing antibodies.

Results: At T0, higher levels of plasmatic IFN-α, IL-1ra, MCP-1 and IP-10, and lower levels of IL-1β, IL-9, MIP-1β and RANTES were observed in subjects with positive swab compared to individuals with a negative one ($p<0.05$). Plasmatic IFN-α was the only cytokine detectable in subjects with positive SARS-CoV-2 swabs with high accuracy for swab score positivity (0.93, $p<0.0001$). Among subjects with positive swabs, significant negative correlations were found among the RT-PCR cycle threshold values reported for genes S and N and IFN-α or IP-10 levels. At T0, the IFN-γ T-cell specific response was detected in 50% (5/10) of subjects with positive swab, while anti-RBD/anti-N antibodies showed a positivity rate of 10% (1/10).

At T1, the IFN-γ T-cell specific response was detected in most of the confirmed-infection subjects (77.8%, 7/9), whereas the serological response was still observed in a minority of them (44.4%, 4/9). Significant positive correlations were found among T-cell response, anti-RBD/anti-N and neutralizing antibodies. Overall, the swab test showed a moderate concordance with the T-cell response (78.6%, k=0.467), and a scarce concordance with the serological one (72.9%, k=0.194).

Conclusions: Plasmatic IFN-α and the IFN-γ T-cell specific response appear early and show a greater positivity rate than the serological response in household contacts with positive swab, suggesting their potential role as additional indicators of SARS-Co-V-2 exposure in respect to antibodies.

Social science, Epidemiology and Prevention

HIV epidemiology and retention in care

P 77 **CREATION OF A MODEL OF DATA COLLECTION AND SURVEY ON LONG-ACTING HIV MEDICATIONS IN THE TRANSGENDER POPULATION**

M. Formisano, M. Errico, A. Moznich, M. Cascio, A. Lascari, L. Brogonzoli

NPS ITALIA, Milano

Background: The rationale in identifying the transgender population as the target of our research: the fight against inequities within the healthcare system, the main barriers to effective healthcare planning for the transgender population and the consideration that for trans people living with HIV undergoing hormone therapy and at the same time on ART treatment there is the need of a regular and constant monitoring of health status; transgender people are considered one of the main unmet needs in HIV care at national and international level. Based on these considerations, what emerges is the urgency of providing guidance on the acceptability and use of new long-acting formulations in the treatment of HIV, that will soon be available for the first time and that based on current ongoing developments in research, will allow for different modalities and intervals of administration.
Materials and methods: The analysis is focused on examining the key elements to consider in "targeting" the cluster of transgender people for access to long-acting formulations. The analysis has been carried out through a questionnaire administered to transgender patients, via online, through emails and through the compilation of paper questionnaires. The administration of the questionnaire has been facilitated through infectious disease clinical centers and through community organizations of transgender people that have been invited to disseminate the questionnaire. Type of questionnaire: self-administered, target: 100 transgender persons living with HIV
Expected output: data and information on the knowledge, expectations and concerns related to new long-acting formulations.
Results: As of today, the results emerging from the survey are partial because the questionnaire is still online and open and the number of transgender persons having replied can be subject to change. The objective is that of investigating the issue of long-acting formulations among the transgender population through an analysis of their perceptions, expectations and possible concerns; Further, the project aims at raising awareness and informing healthcare professionals through the production of ad
hoc material and the publishing of an article.
Conclusions: Long-acting treatments have the undoubtful advantage of offering an alternative to a daily and "domestic" compliance to medications, through a once-every two months administration with potentially longer intervals foreseen in the near future, correlated only with complying to longer intervals of dosing. Through an effective counseling able to support the compliance of the patient, such innovative treatments can be considered an important option for those group of patients having difficulties with compliance, such as the transgender population.

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Social science, Epidemiology and Prevention

HIV epidemiology and retention in care

P 78 **ANTI-HIV ANTIBODIES AND AVIDITY INDEX: COMPARISON BETWEEN TWO FOURTH-GENERATION IMMUNOASSAYS**

A. Morellini[1], M. Tamburello[1], S. Vituliano[1], V. Ferraro[1], A. Primavera[2], A. Bertoldi[2], G. Gallinella[3], T. Lazzarotto[1,2], I. Bon[2]

[1]Section of Microbiology, Department of Experimental, Diagnostic and Specialty Medicine, University of Bologna, Bologna, [2]Microbiology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, [3]Department of Pharmacy and Biotechnology, University of Bologna, Bologna

Background: The possibility to discriminate against recent and long-lasting infections represents one of the most crucial problems in HIV diagnosis. This information could be essential for the incidence estimation, clinical and prevention purposes. Previous studies have explored the possibility of modifying the HIV screening assay into an avidity index (AI) test, able to date the viral infection.

The aim of this work was to evaluate and compare the previously automated Chemiluminescent ImmunoAssay (CMIA) modified to calculate AI, to the ElectroChemiLuminescent ImmunoAssay (ECLIA) routinely used to detect HIV infection at Sant'Orsola Hospital, Microbiology Unit, Bologna.

Material and Methods: 113 serum samples, collected from HIV naive patients between 2015 and 2017, were tested for Avidity Index (AI) using ECLIA test (Roche Diagnostic). All specimens were previously assayed for HIV serological reactivity and AI by CMIA (Abbott Diagnostic).

The serum of each sample was divided in two aliquots: one diluted 1:10 with guanidine 1 M (G), and the other diluted 1:10 with phosphate buffered saline (PBS). After an incubation of 10 minutes at room temperature, both aliquots were tested using ECLIA, which gives as result a sample/cut-off ratio. So, the AI was calculated as AI = Guanidine aliquot S/CO / PBS aliquot S/CO.

Correlation for the method comparison was based on parametric data distribution (Pearson correlation coefficient) and agreement was evaluated by Deming regression analysis, as well as Bland–Altman analysis.

Sensibility, specificity, positive and negative predictive value, and FRR (False Recent Rate) were calculated by contingency tables, using an increasing range of cut-off values (from 0.60 to 0.90).

Results: Deming regression analysis of data showed good correlation (r=0.79), demonstrating the absence of constant and proportional systematic errors (y=1.095+0.1580x). According to the Bland-Altman plot, no statistically significant bias (mean difference −0.072 [95% confidence interval: −0.247 to 0.391]) was observed between avidity index obtained by ECLIA and CMIA.

The highest sensibility (97%) is associated with 0.80, 0.85 and 0.90 cut-offs, while the highest specificity (100%) with 0.60, 0.65, 0.70 cut-offs. The FRR is around 0% using 0.60, 0.65 and 0.70 cut-offs. The best cut-off for discriminating between recent and chronic infections was 0.80, with a PPV of 85%, NPV of 99% and FRR around 4% (misclassified samples).

Conclusions: Statistical analysis demonstrates an acceptable variability and a good linear agreement between the two methods. The best combination of sensitivity and specificity was obtained using a cut-off of 0.80, confirming data previously published.

Although these results argue in favor of a good reproducibility and robustness of the new test, it should be investigated more in detail the relationship between the AI and the viro-immunological data of the patients, in order to perform a complete evaluation of each sample.

Social science, Epidemiology and Prevention

HIV prevention (PrEP and PEP)

P 79 **THE ANLAIDS FORUM BETWEEN OLD AND NEW TOOLS FOR HIV PREVENTION**

A. Venturelli, C. Balotta, R. Galipò, G.V. Calvino, B. Marchini

Anlaids Onlus, Rome, Italy

Background: The ANLAIDS forum is an online platform where people can post questions about their HIV concerns in terms of prevention and risks in sexual behaviors.
We aimed to investigate the degree of awareness of PrEP (Pre-Exposure Prophylaxis), that has been authorized in Italy since 2017. Furthermore, we assessed the knowledge of TASP (Treatment as Prevention) and U=U (Undetectable equals Untransmittable). We also considered queries about the third-generation HIV Self-Test, on the market since 2016; finally, we assessed questions about PEP (Post-Exposure Prophylaxis), to understand if people were familiar with this protocol.
Material and methods: We reread and categorized all discussions requesting information on HIV prevention topics under consideration, dividing them by year (2018 to 2021).
Next, the data were analyzed to evaluate variations in number of questions about PrEP, TASP/U=U, Self-Test and PEP. We applied a linear regression model to study correlations and trends between time and number of posts.
Results: Overall, of the 4,838 posts in the analyzed period, 423 were related to prevention strategies, giving an average of 9.0% per year (2018: 8.7%; 2019: 7.9%; 2020: 9.5%; 2021: 10.1%). By considering the PrEP only, we found 29 discussions (2018: 0.4%; 2019: 0.5%; 2020: 0.7; 2021: 1.1%; average 0.7%); looking at TASP/U=U, users have asked 45 times on this topic (2018: 1.3%; 2019: 0.5%; 2020: 0.7; 2021: 1.3%; avg. 1.0%). Self-test information was asked 185 times (2018: 4.0%; 2019: 3.3%; 2020: 4.2; 2021: 4.3%; avg. 3.9%); questions on PEP were 164 (2018: 3.1%; 2019: 3.4%; 2020: 3.8; 2021: 3.3%; avg. 3.4%).
Globally, considering all discussions, we did not find a positive correlation between time and increase in above mentioned queries. Therefore, we checked the trend over time of the individual investigated topics.
Of note, data on PrEP showed a linear increase with excellent goodness of fit ($p=0.02$; $R2 =0.95$), indicating that this tool is gaining knowledge in the general population.
It was not possible to build a predictive model for TASP/U=U queries, as the number of questions on this topic did not trend linearly over time.
Requests on Self-Testing have increased over the years; however, this increase was not significant ($p=0.41$).
Questions about PEP remained in the range of 3.11 - 3.79% per year not allowing to observe a substantial change in the number of queries and, consequently, the data were not useful to detect a trend ($p=0.50$).
Conclusions: Despite the experience of lockdown and social limitations due to the Covid-19 pandemic, people that addressed the ANLAIDS forum seems to have a few awareness of the existence of some prevention tools, at least about PrEP.
Questions about the concept of TASP/U=U, the Self-Test tool and PEP have remained relatively stable over time, indicating a serious gap of knowledge. Therefore, prevention strategies should be continuously conceived and managed to people about how to avoid risks for HIV.

Social science, Epidemiology and Prevention

HIV prevention (PrEP and PEP)

P 80 **ANLAIDS IN THE SCHOOLS - WHAT USEFULNESS FOR ADOLESCENTS AND WHAT IMPACT ON THEIR BEHAVIORS**

R. Galipò[1], V. Calvino[1], F. Caramaschi[5], L. Carniato[7], A. De Faveri[6], P. Ferri[2], S. Negri[3], A. Palummieri[1], M. Viscoli[4], B. Marchini[1]

[1]Anlaids, Rome, [2]Anlaids Lazio, Rome, [3]Anlaids Lombardia, Milan, [4]Anlaids Liguria, Genoa, [5]Anlaids Mantova, Mantua, [6]Anlaids Torino, Turin, [7]Anlaids Treviso, Treviso

Introduction: Anlaids believes that information and prevention on HIV/AIDS/STI is important, with particular attention to young people. Since 1993 it has been promoting the School Project which over time has been updated in consideration of epidemiological and social changes and is constantly renewed using new and faster communication tools. The activities are implemented thanks to the operation of the regional offices. Due to direct dialogue with young people (age group 14-19 years) and data collection, the project evolves to become current and effective. But what do teenagers think of these interventions? What impact on them? You can find below an overview provided by the post test analysis.

Method: The interventions in high schools include training courses on related topics, in order to make sexuality safer and more aware. They are carried out within the classrooms and taught by trained operators with different backgrounds, belonging to the various locations (doctors, psychologists and educators). A fundamental premise is the active involvement of young people also through the peer education methodology. Before the interventions, a pre test is administered (relating to the knowledge of the young people on the proposed topics) and then a post test (to evaluate the effectiveness and usefulness of the interventions).

Results: In the two-year period 2019/2020-2020/2021, 6 ANLAIDS offices (Lazio, Lombardy, Liguria, Mantua, Turin and Treviso) involved 43 schools. 3495 students responded to the post-intervention questionnaire, with a median age of 16 years (range 13-21); 61.5% were girls; 26% came from Technical Institutes, 7.4% from Professional Institutes, 66% from High Schools. To the questions, On a scale of 0 to 5, how much do you think "... the intervention was useful", "... could change your behavior" and "... are satisfied with the operators' activity", there were differences in the average scores in the variables: sex (respectively, t = -7.910 p <.001; t = -7.139 p <.001; t = -6.658 p <.001); age of respondents (F = 6.938 p <.001; F = 3.768 p <.001; F = 6.876 p <.001); types of schools attended (F = 39.354 p <.001; F = 3.097 p = .045; F = 59.262 p <.001) and ANLAIDS Sections operating the intervention (F = 9.676 p <.001; F = 6.238 p < .001; F = 9.205 p <.001).

Conclusion: The results show that it is necessary to “intervene” on males who consider the intervention less useful, less able to modify risk behaviors and less satisfactory in its implementation. Furthermore, it should be understood why the older ones think that the intervention can have less influence on the change of risk behaviors. It could be hypothesized that young teenagers, due to fewer opportunities to experience sexuality, are more cognitively prone to change. Finally, more attention is needed on the part of the operators in carrying out the school project in the technical and professional institutes that score lower scores in the analyzed questions.

Social science, Epidemiology and Prevention

HIV prevention (PrEP and PEP)

P 81 **ROLE OF GENERAL PRACTITIONERS IN HIV EARLY DIAGNOSIS AND PREVENTION: AN ONLINE LOCAL SURVEY**

M. Jamhour[1], G. Mancarella[2], S. Garattini[2], A. Carraro[1,2], R. Marocco[1], V. Belvisi[1], M. De Masi[1], M. Lichtner[1,2]

[1]Infectious Diseases Unit, S.M. Goretti Hospital, Latina, [2]Department of Public Health and Infectious Diseases, "Sapienza" University, Rome

Background: Since March 2020 the COVID19 pandemic has impacted heavily on chronic illness management and diagnosis, including HIV infection. Although the overall number of HIV diagnoses is decreasing, we're currently observing an increase in the percentage of people who are diagnosed at an advanced stage of disease. Therefore, there is an increasingly high need to promote the use of the new tools to prevent and detect early infection. Since GPs are known to have a key role in early diagnosis and disease prevention we thought of them to be the target of our study. Hence, the aim of this study was to assess the current knowledge, perceptions, and attitudes of GPs towards HIV testing, counseling, PrEP, PEP and TASP.

Material and Methods: GPs in active service in the province of Latina were invited via email to take part in an online survey made of 20 items directed towards our topics of interest: HIV testing strategies and counseling, PrEP, PEP, TASP.

Results: The median age of the 47 GPs interviewed was 50 years old (min 28 - max 69). 25 (53.2%) of them were female and 22 (46.8%) were male. Our population has been working as GP for a median time of 10 years (min 2 months - max 39 years) and 55,3% of them had over 1500 patients under their care.

Reading through the GPs answers we discovered that 66% of GP's believed that MSM were at greater risk of getting HIV and when asked to rate how comfortable they felt discussing sexual risk behaviors with their patients including MSM, on a scale from 1 to 5, 44.7% of them rated their level of comfort with a 4 and 31.9% with a 5 and most GPs (74.5%) routinely asked their patients about sexual risk behaviors. Yet, when asked the reasons why they tested their patients the most frequent answer was "screening before surgery/invasive procedures".

42.6% of GPs never heard of PrEP, and almost all of them never suggested it to a patient. 34% of GPs are either against the use of PrEP or they do not have an opinion about it yet. 21.3% of the GPs interviewed never heard of PEP and 87.2% never suggested a patient to use it.

36.2% don't know where patients can get tested for HIV anonymously and for free in the province of Latina and almost all of them have never heard of "Latina Checkpoint" or the "Fast Track Cities" initiative.

Conclusions: Analyzing the data collected we observed that even though most of GPs reported to be quite comfortable discussing about sexual risk behaviors with their patients, including MSM, they do not use HIV testing as a mean of at risk population screening. Instead they reported that they test their patients mainly for reasons other than the presence of risk factors.

GPs are not very familiar with the use of ARV medication to prevent HIV and they do not talk about it to their patients. These results show that we need to improve GPs awareness on the topics related to HIV early diagnosis and prevention through large mass screening and the use of PrEP/PEP medication.

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Social science, Epidemiology and Prevention

HIV prevention (PrEP and PEP)

P 82 **TREND OF SEXUALLY TRANSMITTED INFECTIONS IN PATIENTS ON HIV PRE-EXPOSURE PROPHYLAXIS (PREP): THE EXPERIENCE OF TWO ITALIAN CENTRE BETWEEN 2019 AND 2022**

M. Menozzi[1], A.Di Biagio2, G.J. Burastero[1], S. Volpi[1], L. Labate[3], M. Fasce[3], L. Gozzi[1], A. Tili[1], V. Todisco[1], M. Pellegrino[1], C. Mussini[1]

[1]Infectious Disease Clinic, University Hospital of Modena, Italy, [2]Infectious Diseases Unit, Ospedale Policlinico San Martino IRCCS – Genoa, Italy, [3]Department of Health Sciences (DISSAL), University of Genoa – Genoa, Italy

Background: tenofovir disoproxil/emtricitabine (TDF/FTC) is approved as a strategy for HIV pre-exposure prophylaxis (PrEP). It is expected that PrEP users might be more exposed to other sexually transmitted infections (STIs), thus, routinely screening for STIs is also recommended. The aim of our study was to evaluate the trend of STIs in a large Italian PrEP cohort, with particular reference to infections by Neisseria gonorrhoeae (NG), Chlamydia trachomatis (CT), Mycoplasma genitalium (MG), Trichomonas vaginalis (TV) and Treponema pallidum (TP).

Material and Methods: Retrospective multicentre observational study from two Italian university hospitals of Modena and Genova. Demographic data and incidence of STIs were collected between January 2019 and March 2022. Infections due to NG, CT, MG and TV were detected with a polymerase chain reaction (PCR) in urine, rectal and pharyngeal samples. Syphilis was evaluated by TPPA screening followed by standard VDRL. A descriptive analysis was performed using standard deviations and frequencies for continuous and categorical variables respectively. Comparisons were done with Mann-Whitney U test, ANOVA and Chi-square test according to variable distribution and type. A test for trend across ordered groups was done to evaluate differences of STIs incidence during years of follow-up.

Results: Of the 133 persons included in the analysis, 95% were male, 3% female and 1% male-to-female, with median age of 40,3 years (±10,7). In Tab.1 we reported the number of users who started PrEP by year (30 in 2019, 26 in 2020, 49 in 2021 and 15 in 2022). Incidence of NG in was 20,9% 9/43 in 2019, 7,25% 5/69 in 2020, 13,56% 16/118 in 2021 and 6,7% 9/133 in 2022 respectively. The incidence of CT was 13,9% 6/43 in 2019, 8,7% 6/69 in 2020, 13,6% 16/118 in 2021 and 1,5% 2/133 in 2022. No MG diagnosis was done in 2019, while the incidence was 2,9% 2/69 in 2020, 10,2% 12/118 in 2021 and 9% 12/133 in 2021 respectively. No TV positivity was detected in 2019, 2020 and 2022, although in 2021 the incidence was 1,7% 2/118. Syphilis incidence was 6,9% 3/43 in 2019, 1,4% 1/69 in 2020, 0,85% 1/118 in 2021 and 0,75% 1/133 in 2022 respectively (tab 2). In 2019 the proportion of patients with 1, 2 or 3 STIs were 35%, 0,0% and 2,3%, these figures turned to 11,6%, 2,9% and 1,4% in 2020. In 2021, this percentages turned to 20,3%, 5,9% and 2,5% for 1, 2 or 3 STIs respectively and 11,3%, 6% and 0,7% to 2022. No HIV seroconversions were detected. At the test for trend across year groups, no statistical significance was obtained for all the STIs.

Conclusions: STIs incidence in our cohort was similar to others from literature. As previously described, in 2020 the number of STIs was lower compared with 2019 and 2021, maybe as a consequence of COVID19 restrictions (reduction in people contacts and outpatient clinics availability). After the end of lockdown an interesting increase in PrEP users number was recorded (49 users). Although no statistically significant differences were confirmed, a possible incremental trend could be hypothesized regarding NG and CT incidence in 2022. A strict follow-up may be useful to limit the STIs spread in this population.

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Social science, Epidemiology and Prevention

Impact of COVID-19 on HIV care

P 83 **HOME CARE ASSISTANCE: HAS COVID-19 HAD AN IMPACT ON THE COMPLEX MANAGEMENT OF HIV PATIENTS?**

A. Dusina[1], F. Lombardi[1], E. Tamburrini[1,2], F. Onorati[1], M. Petrucci[1], S. Di Giambenedetto[1,2]

[1]Fondazione Policlinico Universitario A. Gemelli IRCCS, UOC Malattie Infettive, Rome, Italy, [2]Università Cattolica del Sacro Cuore, Dipartimento di Sicurezza e Bioetica Sezione Malattie Infettive, Rome, Italy

Background: Adherence to antiretroviral therapy (ART) is one of the key issues in patients living with HIV (PLWH). The COVID-19 pandemic interfered with critical health services for HIV treatment and care so the healthcare systems worldwide adopted different strategies to assist PLWH. Here we describe the activity of "Unità di Trattamento Domiciliare (UTD)" established at our hospital in 1993 with the aim of treating complex or comorbid PLWH. This unit provides different kind of services directly at patients' home in an attempt to overcome poor treatment adherence. The aim of this study is to detremine if SARS-CoV2 pandemic impact on managment of HIV patients by UTD.

Methods: We retrospectively collected the data of patients followed by UTD from 2015 to 2020. We performed a descriptive analysis of the characteristics of population each year and the number/type of services provided. We classified services in 5 categories: blood sample collection, dressing (skin wound and catheter), drug administration, delivery of therapy, others, i.e., adherence support, advanced wound care, electrocardiography, transfusions, aerosol therapy. We evaluated if there was any difference in the viro-immunological parameters and the interventions provided during 2020 with respect to the previous 5 years (2015-2019) and in the percentage of monthly perfomances in 2020 with respect to both 2018 and 2019. To compare categorical variables we used Chi square test, for contiunuos variables reported as median we employed the Kruskal-Wallis test.

Results: The characteristics of the patients according to year are summarized in Table 1. The immunological parameters remained stable over time whreas viral load significanlty decreased (p=0.020). When comparing the median CD4 count, and CD4/CD8 we did not find significant different (p=0.904, p=0.409, respectively). The number of services supplied in 2020 was similar to those provided during the immediately preceding year, 2019 (1,377 vs 1,345) and it was similar to the mean of the total number of interventions carried out over the previous 5 years, (1,377 vs 1,367 – figure 1A). When comparing single interventions in 2020 with their average in 2015-2019 we found a significant increase in delivery of therapy (p<0.001), a reduced drug administratin (p=0.005) and a decrease of other services, (p<0.001) (Figure 1 B). By comparing the percentages of monthly performances in 2020 with those of the immediately preceding years, 2019 and 2018, we observed significant differences that were mostly related to the year 2019, which showed wider fluctuations with respect of the mean of monthly interventions (8.3%). Instead, in 2018 and 2020 the percentages of performance were more consistent over the months remaining around 8.3%.

Conclusions: In conclusion, we observed how this kind of service supplied by the UTD, has been effective in providing a comfortable and continous setting of assistance for complex PLWH even during SARS-CoV2 pandemic.

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Social science, Epidemiology and Prevention

Impact of COVID-19 on HIV care

P 84 **IMPACT OF COVID-19 ON HIV TESTING: OUR LAB EXPERIENCE**

E. Garlatti Costa[1], M. Da Re[2], D.Villalta[2], M. Tonizzo[1]

[1]SC Medicina Interna, Azienda sanitaria Friuli Occidentale, Pordenone, [2]SSD Immunologia Allergologia, Azienda sanitaria Friuli Occidentale, Pordenone

Background and Aims: Human immunodeficiency virus (HIV) testing is important to HIV prevention, treatment, and care. Globally, the coronavirus disease 2019 (COVID-19) pandemic has compromised HIV diagnosis, resulting consequently in excess HIV-related deaths and onward transmission. Friuli Venezia Giulia (Italy) was most affected by this latest SARS-CoV-2 outbreak. Our aim is to assess the impact of pandemic COVID-19 on HIV testing in the Hub Hospital of Pordenone (Friuli Venezia Giulia) comparing 2019, 2020 and 2021.
Material and methods: We retrospectively collected data of simultaneous detection of HIV 1 and 2 antibodies and HIV-1 p-24 antigen referred to our Laboratory from 01.01.2019 to 31.12.2021. We used ADVIA-Centaur® XP HIV Ag/Ab Combo (CHIV) assay.
Results: 9.797, 8.342 and 8.360 subjects were tested for HIV infection respectively in 2019, 2020 and 2021. We registered 40 patients (35 males, median age 49 years old, 22% foreigners) with new onset HIV infection in 2019 while in 2020 we detected HIV infection in 30 patients (16 males, median age 52 years old, 27% foreigners). In 2021, we noted 24 new HIV-infected patients (12 males, median age 50 years old, 46% foreigners).
Conclusions: Following the COVID-19 outbreak, a drop of new HIV infection was showed. According to our Lab experience, interventions to improve HIV screening in key populations in hospital and outside of health care settings are urgently needed.

Social science, Epidemiology and Prevention

Impact of COVID-19 on HIV care

P 85 **HAS COVID-19 PANDEMIC CHANGED THE EPIDEMIOLOGY OF AIDS-DEFINING ILLNESSES? DATA FROM A LARGE ITALIAN CLINICAL CENTER**

V. Iannone[1], A. Dusina[1], D. Farinacci[1], A. D'Angelillo[1], P.F. Salvo[1], A. Borghetti[1], E. Visconti[1], E. Tamburrini[1], S. Di Giambenedetto[1], A. Ciccullo[2]

[1]Fondazione Policlinico Universitario Agostino Gemelli IRCCS UOC di Malattie Infettive, Roma IT, [2]Ospedale San Salvatore Unità di Malattie Infettive, L'Aquila IT

Background: Since the start of the COVID-19 pandemic, the follow-up of PLWHIV in Infectious Diseases Unit has seen a drastic change due to the re-organization of hospitals worldwide. This, together with a reduced compliance by PLWHIV in regularly take their medications during “lockdown” periods, may have had an impact on the rate of AIDS-defining illnesses (ADI) observed. In our study we aimed to assess the real impact of the pandemic on the epidemiology of ADI in our clinical center.

Material and methods: We analyzed data from our center’s database and registered all observed ADI; we divided events in two groups according to calendar years: a pre-COVID group (2018-2019) and a COVID group (2020 -2021). We collected clinical history and viro-immunological parameters of PLWHIV and analyzed data via parametric and non-parametric tests, as appropriate.

Results: We analyzed 122 PLWHIV with at least one AIDS-defining illness (ADI): 87 (71.3%) in the 2018-2019 period and 35 (28.7%) in the 2020-2021 period. Our population was composed predominantly by males (99, 81.1%), with a median age of 41 years (IQR 35-53) and a median CD4+ cell count at the moment of the ADI diagnosis of 67 cell/mm3 (IQR 19-174). Twenty-five PLWHIV had a CD4+ cell count of over 200 cell/mm3 at time of ADI diagnosis; 49 PLWHIV (40.2%) were on a ARV regimen when diagnosed with an ADI, with a median time from ARV initiation of 0.9 years (IQR 0.2-11.9). Full patients’ characteristics are shown in Table 1. In our analysis, we failed to find significant differences between the two analyzed calendar periods in terms of type of ADI, CD4+ cell count at time of ADI diagnosis, ARV regimens, PLWHIV’s sex or age.

Trying to standardize the results and reducing risk of bias, we compared also the number of clinical visits performed in the calendar years. In the 2018-2019 period, 9968 were performed with a rate of 0.9 ADI per 100 visits; conversely, in the 2020-2021 period, 7650 were performed, with a rate of 0.4 ADI per 100 visits.

We observed 11 deaths due to ADI: 10 in the 2018-2019 period and 1 in the 2020-2021 period (p=0.134).

Conclusions: In our analysis we did not observe a significant difference between the two analyzed calendar periods before and after pandemics beginning, in terms of type of ADI. The rate of observed ADI appears to be lower and this is probably due to the changed organization following COVID-19. Further studies are needed to assess the real impact of the COVID-pandemic on the epidemiology of ADI.

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Social science, Epidemiology and Prevention

Impact of COVID-19 on HIV care

P 86 **COVID-19 PANDEMIC'S IMPACT ON THE CLINICAL-CARE MANAGEMENT OF NAÏVE HIV + PATIENTS**

C. Bitello, R. Caprara, S. Vitale, G. Ferraro, L. Appolloni, G. Pensalfine, A. Stancari

IRCCS S. Orsola-Malpighi, Bologna

Background: The COVID 19 pandemic has had a huge impact on the management and on new diagnoses of chronic diseases. In this study, we assessed the impact of COVID-19 in the diagnosis and management of naive patients during 2020-2021 comparing it with 2019.

Materials and Methods: A retrospective study was performed by examining the immunovirological parameters (CD4 + count and HIV RNA viral load) and concomitant diseases at the time of diagnosis in a cohort of patients who started antiretroviral therapy (ART) between 2019 and 2021. Data were collected from specialist reports and tracked in an Excel database, using the CDC guidelines for disease staging.

Results: The study involved 63 patients in 2019 (58 males and 5 females), 57 patients in 2020 (40 males and 17 females) and 67 patients in 2021 (57 males and 10 females) with an average age of 43 years (range 19-76).

In the evaluation of the CD4 + count, the patients in 2019 with CD4 + count < 200 cells/μL at diagnosis were N=13 (21%), in 2020 N=19 (33%) and in 2021 N=23 (34%). In 2019 N=3 (23%) of patients were classified as CDC C3, in 2020 N=15 (79%) and in 2021 N=4 (17%).

N=8 (14%) of the naïve 2019 patients was lost during follow-up, while during 2020 N=5 (9%) and during 2021 N=1 (1%).

Of the remaining patients, virological suppression (HIV RNA <50cp/ml) was achieved in 96% of patients both in 2019 and in 2020, while in 2021 examined patients it has reached the 80%.

Conclusions: In the three-year period considered, the COVID-19 pandemic did not significantly influence the number of HIV + diagnoses which remained almost unchanged, although there were fluctuations in correspondence with the pandemic peaks. Instead, a worsening of the clinical picture with which the patients arrived at the diagnosis was observed.

During 2020, the adoption of more restrictive measures may have influenced the early diagnosis of the disease. Despite this, health care has always been guaranteed by ensuring optimal retention in care with a percentage of virologically suppressed patients of over 95%. Except for the patients taken in charge in the last quarter of 2021 for which there is no definitive data yet.

Social science, Epidemiology and Prevention

Impact of COVID-19 on HIV care

P 87 **IMPACT OF COVID-19 PANDEMIC ON A HIV COUNSELLING AND TESTING SITE AT "D. COTUGNO" HOSPITAL, NAPLES: WHAT LESSONS CAN BE LEARNED?**

F.M. Fusco[1], P. Piselli[2], M. De Cenzo[1], O. Tambaro[1], N. Cuomo[3], F. Borrelli[1], R. Viglietti[1], V. Bruner[1], C. Camaioni[1], N. Sangiovanni[1], A. Mariniello[1], A. Galano[1], A. Laudiero[1], V. Sangiovanni[1]

[1]UOC Infezioni sistemiche e dell'Immunodepresso, "D. Cotugno" Hospital, AOS dei Colli, Napoli, [2]Dipartimento di Epidemiologia e Ricerca Pre-clinica, INMI "L. Spallanzani", Roma, [3]UOC Microbiologia e Virologia, "D. Cotugno" Hospital, AOS dei Colli, Napoli

Background: The COVID-19 pandemic severely weakened HIV-related care services. HIV Counselling and Testing Site (CTS), being generally used by healthy people, may be particularly impaired by the movement limitations and social distancing measures introduced during the pandemic.
At "Cotugno" hospital in Naples, a mono-specialistic hospital entirely dedicated to Infectious Diseases, a CTS is operating since many years. It is a low-threshold, open-access service, where HIV test can be performed anonymously and free-of-charge.
We analysed the impact of COVID-19 on the organization and the performance of the "Cotugno" CTS in the period March 2020-Febraury 2022 (pandemic period), compared with March 2017-February 2020 (pre-pandemic period).
Material and Methods: The number of accesses and the number of HIV+ tests, derived from paper and electronic records, were evaluated during pandemic and pre-pandemic periods. The percentage changes in the 2 pandemic years were compared with the mean of the 3 pre-pandemic years.
Results: During pandemic period, CTS activities were never interrupted, but some limitations were established: access was by appointment, and a negative molecular/antigenic COVID-19 test performed within 48 hours was required.
In the figure, number of accesses, HIV+ tests, and HIV+ rates in both pre-pandemic and pandemic periodsare shown. Accesses have been significantly reduced (-73,1% and -56,5%, respectively in 1st and 2nd pandemic years). Number of HIV+ tests have been reduced too, but less than accesses, and during the 2nd pandemic year reached the pre-pandemic level (-57,4% and +1,4%). Therefore, the HIV+ rates strongly increased (+57,6% and +132,5%, see Table).
Conclusions: As expected, the limitations due to the pandemic, the fear of referring to a hospital dedicated to COVID-19, and the new access rules established for Infection Prevention and Control reasons strongly limited the accesses to the "Cotugno" HIV CTS in the pandemic period. Instead, the number of HIV+ test did not accordingly decrease, and returned to pre-pandemic level in Mar 2021-Feb 2022. Despite more details are needed (for example about demographic and risk factor data of population accessed during the pandemic period) we can hypothesize that people with at higher risk for HIV acquisition accessed anyway to CTS, despite limitations and difficulties.
As preliminary conclusion, we suggest that the primary role of "Cotugno" CTS, that is performing new HIV diagnosis, has been only partially impaired by the pandemic. On the contrary, other activities of our CTS, such as the counselling about HIV risk and prevention, have been severely reduced.

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Social science, Epidemiology and Prevention

SARS-CoV-2 epidemiology

P 88 **SARS-COV-2 INFECTION IN DIALYSIS PATIENTS IN MARSALA HOSPITAL, SOUTHERN ITALY: A SINGLE-CENTRE EXPERIENCE IN A PRE- AND POST-VACCINATION ERA, PRELIMINARY DATA**

G. Marino[1], P. Colletti[2], P. Di Carlo[3], C. Barracco[4], G. Oddo[4]

[1]Medicine and Surgery, University of Palermo (Hypatia), Caltanissetta, Italy, [2]Infectious Disease Unit at "Paolo Borsellino" hospital, Marsala, Italy, [3]PROMISE Departement, University of Palermo, Italy, [4]Dialysis Unit at "Paolo Borsellino" hospital, Marsala, Italy

In March 2020, the World Health Organization (WHO) declared COVID-19 a global pandemic. Since then, Coronavirus has been continuing to spread around the world, causing – to date—more than 6.06 million deaths. During this time, the virus has mutated, resulting in several variants as Beta, first detected in September 2020, Gamma and Delta, both caught in December 2020, and lastly, Omicron noticed in November 2021; this fact – with the development of vaccines—led to changes of the transmissibility and the severity of the disease.

Sars-Cov-2 mainly affects the respiratory system, but clinical evidence shows that it can also affects other organs, such as kidneys: many reports highlighted that people with COVID-19 could develop an acute kidney injury (AKI), and this could happen either in patients with no previous renal pathologies or in patients with end-stage renal disease (ESRD) receiving chronic hemodialysis. These are patients with many comorbidities, such as diabetes mellitus or hypertension, that increase the risk of adverse outcomes. Nevertheless, few studies have investigated the needs of in-patients receiving hemodialysis care during SARS-Cov-2 pandemic in Southern Italy.

This retrospective and observational study – including preliminary data – aims to highlight epidemiology, course, and survival of the disease in a sample of 88 chronic hemodialysis patients with COVID-19 from October 2020 to March 2022. The patients were followed up at the Nephrology and Dialysis Unit of the Marsala hospital. Data were collected by an Italian student to write a dissertation during the Degree Course in Medicine and Surgery, University of Palermo, Italy.

The median age of 88 studied patients was 70 years (51 were males, and 37 were females), hospitalizations in Covid Area have been 37/88 (42%), and Intensive Care Unit admissions have been 13/88 (14,77%). Deaths have been 24. Comorbidities in dead patients were hypertension (7), diabetes mellitus (2), both hypertension and diabetes (10), while 5 deceased patients didn't have any comorbidity. No one of the HIV patients in chronic hemodialysis showed Sars-Cov2 infection.

In-center hemodialysis patients are a unique population with multiple risk factors for severe course of SARS-Cov-2 infection, including repeat exposures to a health care setting. The higher incidence of disease and mortality is concerning and calls for evidence-based interventions of infection control that help mitigate the spread of the virus. The management of this population at risk includes home care, district and hospital protocols, measures during transportation of patients, and education of the community.

We hope to continue to learn more about SARS-Cov-2 infection in vaccinated dialysis patients as the pandemic evolves and incorporates the knowledge to develop best practices and protocols to prevent serious illness in this group of patients.

Social science, Epidemiology and Prevention

SARS-CoV-2 epidemiology

P 89 **DISTRIBUTION OF SARS-COV-2 VIRAL VARIANTS IN A COHORT OF SUBJECTS TREATED WITH MONOCLONAL ANTIBODIES TARGETING SPIKE PROTEIN IN CAMPANIA**

A. Di Fraia[1], M. Pisaturo[1], M. Starace[1], C. Minichini[1], L. Occhiello[1], I. Gentile[2], L. Atripaldi[3], C. Tiberio[3], I. Cavallaro[3], F. Ferrentino[3], N. Coppola[1]

[1]Infectious Diseases Unit, Department of Mental Health and Public Medicine, University of Campania "Luigi Vanvitelli", Naples, Italy, [2]Department of Clinical Medicine and Surgery, University of Naples "Federico II". Napoli, Italy, [3]Cotugno Hospital, AORN Ospedali dei Colli, Napoli, Italy

Aims: evaluate the distribution of SARS-CoV-2 variants in subjects treated with monoclonal antibodies targeting spike protein in Campania.

Material and Methods: all patients with Sars Cov 2 infection who received anti-SARS-CoV-2 monoclonal antibodies (mAbs) targeting Sars Cov 2 spike proteine as early therapy against Covid 19 at two University Hospitals in Naples (AOU Vanvitelli and AOU Federico II) from 17 December 2021 to 29 January 2022 were enrolled. At enrollment for each subject was collected a nasopharyngeal swabs.

Virus extraction was performed on nasopharyngeal swabs with QIAamp Viral RNA Mini Kit, real-time PCR and variants detection were performed with Allplex SARS-CoV-2 Master Assay.

Results: 160 patients were included in this study, 78 (48.8%) were male. 105 patients had these comorbidities: 17% were obese, 20% had cardiovascular disease, 5.7% diabetes and 10.5% were immunosuppressed. In December 2021, 50% of the patients had the delta variant and the 50 % the omicron variant. In december alpha variant was not detected. In January 2022, 5 % of the subjects had the delta variant and 98% the omicron variant, alpha variant was not detected (figure 1).

Conclusions: this study showed that in december both the delta variant and the omicron variant circulated, while in January 2022 the predominant viral variant was omicron, as confirmed also worldwide.

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Social science, Epidemiology and Prevention

Social and behavioural science, marginalized groups, community aspects and community surveys

P 90 PERCEPTIONS OF AN ONLINE SERIOUS GAME ACTIVITY AS FORMATIVE ASSESSMENT IN HIGHER EDUCATION APPLIED TO A LECTURE ON HIV AND SEXUAL HEALTH

S. Licchelli, L. Barnett

University of Surrey, Guildford

Background: During the last decade there has been a focus on a new way to use games for learning purposes (Rosas et al., 2003; Haruna et al., 2018; Campillo-Ferrer et al., 2020; Fernandez-Antolin et al., 2020) which has seen different developments such as gamification of the learning experience, game-based learning (GBL) or serious games. However, we do not know enough about the use of games as a form of formative assessment in higher education settings. The perception of the use of games as a way of applying knowledge and fostering learning and independence will be explored in a cohort of students from the School of Psychology following a lecture on health psychology applied to HIV and sexual health where students will be invited to complete an online escape room (OER).

Materials and Methods: A qualitative methodology will be used to answer the research question using thematic analysis. Participants are recruited from the cohort of the MSc students after attending a lecture on HIV and completing a serious game activity. After that, students are invited to answer an online qualitative survey of 10 questions shared through Qualtrics. The online qualitative survey will cover different areas such as the perception of the OER as an educational activity, the perception of how well the OER was built and general opinions towards using serious games in higher education. The activity will be conducted in groups and students will need to clear three different “rooms” to complete the OER. Students will be able to complete each room by applying knowledge acquired during the lecture on HIV and sexual health conditions as well as elements of prevention and testing in sexual health. At the end of the activity the lecturer will provide an explanation of each activity and will answer any questions that may arise. Students will receive a £10 Amazon voucher for their time. This study has received ethical approval from the University of Surrey FHMS 21-22 048 EGA. For this study, I aim to recruit 30 students who will attend the lecture on HIV from the 4th of May 2022 to the 3rd of June 2022.

Results: Answers to the online qualitative survey will be analysed using thematic analysis (Braun & Clarke, 2006) through an inductive process. The researcher will analyse the answers, highlighting the main themes and producing a thematic map linking the different themes together as part of the data analysis. Participants will be invited to provide feedback on a first draft of the thematic map.

Conclusions: This study is going to further advance our knowledge and understanding of how serious games are perceived in higher education settings. Furthermore, this study is going to provide an analysis of how to improve this alternative form of assessment applied to a lecture on HIV and sexual health.

Social science, Epidemiology and Prevention

Social and behavioural science, marginalized groups, community aspects and community surveys

P 91 DETERMINANTS OF QUALITY OF LIFE IN PLWH EFFECTIVELY TREATED WITH ART

F. Maggiolo[1], E. Di Filippo[1], P. Meli[2], D. Valenti[3], F. Radici[4], I. Mercurio[5], L. Comi[1]

[1]ASST Papa Giovanni XXIII, [2]Comunità Emmaus & Caritas Bergamasca, [3]Associazione FROM, [4]Arcigay Bergamo Cives, [5]CRI-Comitato di Bergamo, Bergamo

Background: Measuring progress towards the HIV care cascade allows to identify processes that should be improved to achieve UNAIDS 95-95-95 goal. We focused our attention on the fourth “95”: health related quality of life (HRQoL).

Methods: We calculated the number of PLWH using the eCDC HIV modeling tool (version 1.3.0) that estimates the size of the undiagnosed population. Data on the diagnosed and treated populations were derived from the clinical database of the only Provincial Center authorized to treat HIV infection. Virologic response to ART was defined according to the last available HIV-RNA measure. HRQoL was assessed by EuroQol 5 Dimensions (EQ -5D) patient questionnaire using EQ-5D index score responses (scale - 0.594 to 1; worst to best health status). We defined as good an HRQoL status with an index score >0.75 that is no more than a modest discomfort in no more than 1 domain. A probit model was used to assess the outcome in relation to baseline variables.

Results: At January 2022 the estimated number of PLWH was 3225 . All subjects on active FU (2834) were actively taking ART and 98.5% of them had their last viral load < 200 copies/ml, for a final proportion of PLWH virally suppressed of 86.45% just above the 95-95-95% goal. We focused our attention on PLWH with suppressed viremia. Their mean HRQoL was 0.88 (95%CI 0.87-0.909) with 82.6% of persons indicating an index >0.75 thus reaching the threshold for the UNAIDS fourth “95” goal. A severe discomfort was reported by no more than 2.3% of persons in the “usual activities”, “pain” and “anxiety/depression” domains (figure), The “pain” and “anxiety/depression” domains resulted those with the greatest negative impact on HRQoL (figure). However, 56% of people indicated a perfect HRQoL status (index 1). Some co-pathologies were specifically associated with a reduction of HRQoL: osteo-articular diseases (P = 0.002), neurological disorders (P = 0.011), psychiatric disorders (P = 0.001), neoplastic diseases (P = 0.049) and gastro-enteric diseases (P = 0.033)(figure). Having multiple co-pathologies was negatively associated to the outcome, too (P < 0.0001). According to probit analysis, neither age, gender or any characteristic of HIV infection including last CD4 or CD8 counts, nadir of CD4, CDC category, number of ARV drugs significantly influenced HRQoL that was significantly linked only with the number of chronic co-pathologies (P = 0.002)(figure).

Conclusions: Reported HRQoL was completely independent from the classical tools for describing HIV infection or from the type of ARV therapy. Much more relevant was the weight of some concomitant chronic diseases especially if they could influence specific domains such as “pain/discomfort” or “anxiety/depression” which have the greatest negative impact on HRQoL. Chronic co-pathologies with potential impact on these domains should be addressed carefully.

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Social science, Epidemiology and Prevention

Social and behavioural science, marginalized groups, community aspects and community surveys

P 92 **A THEATRE-COUNSELING WORKSHOP ON CHEMSEX: THE EXPERIENCE OF PLUS ROMA**

A. Infante, F. Leserri, G.M. Corbelli

Plus Roma, Roma

Background: Chemsex is a common way for MSM community to socialize and it is often analysed only from a phenomenological point of view, as substances use during sex. A partial approach may be perceived as blaming, since it focuses on problematic aspects at the expenses of recreational ones, perceived by most chemsex users. Chemsex needs a more complex analysis as a socio-cultural phenomenon based on personal stories situated in between the recreational and the problematic modality.

Methods: In October 2021, Plus Roma launched a Theatre-Counseling workshop directed by the counselor Angela Infante. The workshop is a journey for a group made by gay and bisexual men who gather their energies to improve their way to explore pleasure, taking care of their sexual health and wellbeing. This project aims at creating a space where those who share this practice can tell their experience in a protected environment, without any judgement, thanks to theatrical expression. The workshop is aimed at exploring one's idea of pleasure, and at acknowledging with ourselves what really makes us feel better and what we want to reject, facilitating the construction of a higher form of self-respect, outside culturally determined constructions. Each meeting of this workshop is a place for exploring our physical and perceived bodies, a place for testing and showing our emotions and a place for telling our sexual pleasure, in an authentic way. Methodology based on circularity of experiences, exchanging information within the group, with no fear for judgement and without self-judgement, creates in each person empowerment and awareness.

Results: Here are some feedbacks collected during the workshop: "I can speak about myself, with freedom, acknowledging also conflicting emotions after chemsex" – "I never did chemsex, but I can never rule out the possibility of an experience, listening to others gives reestablish dignity to that same experience" – "I don't feel embarrassed… I know other men are there, in this group, I had sex with, but I do not judge myself and I don't feel judged… I express myself" – "I wish more experiences of this kind were available, where you can talk about HIV, chemsex and our sexuality".

Conclusions: Chemsex is a real phenomenon which, as well as HIV, represents an opportunity for the whole LGBT+ community to investigate topics such as pleasure, wellbeing, and quality of life, where sexuality plays a critical role. To describe this in an inclusive way, we need to observe it from different points of view, understanding aspects related to information, narration, psychology, relations, sociality as well as those potentially problematic. According to Plus Roma experience, Theatre-Counseling can be an effective tool to facilitate people ability to develop awareness related to the dynamics of practice and idea of pleasure.

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Social science, Epidemiology and Prevention

Social and behavioural science, marginalized groups, community aspects and community surveys

P 93 PAMP: PREVENTION AMONG MIGRANT PEOPLE: A PILOT PROJECT

G.V. Calvino[1], C. Sforza[2], C. Vajro[3], C. Sfara[4], S. Ondedei[5], E. Teti[6], B. Rossi[6], V. Barchi[6], L. Ansaldo[6], L. Campogiani[6], S. Tedde[6], A. Cavasio[6], M.L. Minardi[6], D. Kontogiannis[6], M. Andreoni[6], B. Marchini[1]

[1]Anlaids Onlus-Ets, [2]Consiglio Italiano per i Rifugiati, [3]Cooperativa Famiglia Nuova, [4]Anlaids Umbria, [5]INMI L. Spallanzani, Roma, [6]UOC Malattie Infettive Policlinico Tor Vergata, Roma

Background: PAMP Project was realized thanks to Getting To Zero Grant by Gilead Sciences and was carried out by Anlaids in partnership with CIR – The Italian Council for Refugees and Famiglia Nuova Cooperativa Onlus.
The Monitoring implementation of the Dublin Declaration on Partnership to Fight HIV/AIDS in Europe and Central Asia in 2017 highlights how the decrease in new infections in European countries does not correspond to an equal figure for the migrant population, which remains highly at risk, especially of late presenters. The reasons for this gap are indicated in the lack of dedicated prevention and screening services, especially for undocumented foreign people, in the stigma and discrimination among the foreign communities themselves and health professionals and in the linguistic and cultural barriers that prevent the approach to healthcare facilities and information related to prevention.
Material and methods: The project aimed at preventing HIV infection among foreign and refugees population in the regions of Lazio and Umbria, enhancing awareness on prevention, promoting access to Test and to health facilities and facilitating the early diagnosis and linkage to care.
The Project started on February 2021. The first step was the training of eight cultural mediators about Hiv, transmission, strategy of prevention, testing, treatment, ecc.
We also created and printed information material in three languages (English, French and Arabic) to be distributed during the meetings.
The second step involved the dissemination of information to the foreign population on HIV transmission and the possibility of taking the rapid test in center for asylum seekers and in informal settlements.
The third step involved the elaboration of a tailored path in order to accompany the person eventually found positive at rapid test to health facilities.
Results: 8 cultural mediators were trained of the following nationalities: Nigerian, Moroccan, Eritrean, Malian, Tunisian, Somali, Ivorian
6 meetings took place in Lazio and 8 in Umbria in centers for asylum seekers and beneficiaries of international protection with the collaboration of medical staff of UOC Malattie Infettive Policlinico Tor Vergata of Rome and Clinica Malattie infettive di Perugia. Furthermore, two meetings were held in Umbria in informal meeting points with the dissemination of leaflet and condoms.
262 people were reached with meetings in the centers and in informal places
105 rapid test were performed all non reactive exept one
Conclusions: PAMP was a pilot project that aimed to carry out the objectives set, but also to study a modality of intervention that can be reproduced in the future. Despite the difficulties given by the approach of different cultures to a "hot" topic such as the one proposed, we received a good interest so much that we decided to present PAMP2 project that has already started, whose focus is on women victims of trafficking and to young adults.

Social science, Epidemiology and Prevention

Social and behavioural science, marginalized groups, community aspects and community surveys

P 94 MAPPING ITALIAN HIV CHECKPOINTS AND TESTING CENTERS: THE CHECK POINT INDEX

M. Carlevari[1], S. Mattioli[2], P. Meli[3], M. Viscoli[4], G.M. Corbelli[5], L. Saracini[6], D. Calzavara[7]

[1]Director Public Affairs Gilead sciences Italy, [2]BLQ Checkpoint, [3]Bergamo Checkpoint, [4]Checkpoint IOC'ENTRO Genova, [5]Roma Checkpoint, [6]Ancona Checkpoint, [7]Milano Checkpoint, Elma Research Srl

Background: Checkpoints are community-based peer-oriented centers, linked to the NHS in terms of horizontal subsidiarity. Checkpoints provide services to promote a conscious sexuality and free peer counselling, free prevention, early diagnosis and care services for HIV, HCV and other STIs, through the support of peer counselors, psychologists, and health care providers. Checkpoints have long been considered the points of reference for the communities most vulnerable to STIs, facilitating free access to screening and counselor services, especially for key populations, who have difficulty accessing the health care system. The Check Point Index was created with the aim of providing an up-to-date map of the Italian Checkpoints organization.

Material and methods: The survey involved 6 Italian Checkpoints, a representative sample for the Italian scenario, each with a specific background and target: Ancona, Bergamo, Bologna, Genoa, Milan, Rome. The survey was conducted through remote interviews, between Dec 2020 and Jan 2022. The interviews were structured in such a way as to delve into background, communication channels, users, testing, activities, networks, needs and perspectives of each Checkpoint.

Results: The 6 Checkpoints are protected and welcoming places where to carry out counselling and free and anonymous STI tests, and where qualitative advice can be provided through conversations with peer experts. The checkpoints differ in two main characteristics: identity and historicity. In terms of targeting, some Checkpoints (mainly Bologna, Milan and Rome) explicitly target the LGBT community (with a majority of MSM), while other centers promote initiatives addressed to a general population (mainly young people: high school and university students). Longer-established Checkpoints (Bologna and Milan) offer a variety of services (including PrEP provision), are internationally recognized, and have become a point of reference for newer Checkpoints (Ancona, Genova) which are still promoting their presence on the territory, through social networks and by starting free testing. Considering this commitment Checkpoints, currently supported by private sponsors, call for a bold recognition from the NHS both when it comes to financials, through access to public funding, and in terms of professional qualification for peers and volunteers

Conclusions: Thanks to a community-based peer-oriented approach, the Italian Checkpoints are contributing proactively to the creation of a culture of acceptance of one's own sexuality, without judgments and in a logic of prevention of STIs. An approach that favors early diagnosis but, above all, allows for the establishment of a close relationship with users as members of the community.

Acknowledgments the research has been conducted by Elma Research upon specific commission by Gilead.

Social science, Epidemiology and Prevention

Social and behavioural science, marginalized groups, community aspects and community surveys

P 95 PEOPLE WITH HIV - THE PSYCHOLOGICAL AND SOCIAL INTERVENTION OF ANLAIDS LAZIO

R. Galipò[1], V. Calvino[2], M. Falaguasta[2], P. Ferri[1]

[1]Anlaids Lazio, Rome, [2]Anlaids, Rome

Introduction: The advancement of science in relation to the effectiveness of therapy have greatly improved the prognosis of the pathological pictures resulting from HIV infection, with a drastic reduction in mortality and an improvement in the quality of life of people with HIV, transforming the infection into a chronic pathology. However, the psychological and social reality of people with HIV is very complex, both for the meanings it still represents on a social level and because of the difficult path that the person faces. In the person with HIV, a transformative process is set in motion with psychological and behavioural implications that affect both identity and the project dimension. How does Anlaids Lazio support the mental wellbeing of people with HIV?

Method: There is a counseling and support service aimed at people with HIV which is carried out both through telephone counseling, operating from Monday to Friday from 9. a.m. to 4 p.m. and face-to-face by appointment. The contacts of Anlaids Nazionale also belong to Anlaids Lazio, which is located in the same headquarters. The service is coordinated and managed by a psychologist. The telephone interventions are managed according to the counseling intervention: calls mainly come from people in the grip of anxiety or those who need to be oriented in the overall management. Face-to-face consultations, adapted to the emerging need, are required for continuous psychological support and for a generalized state of anxiety linked to infection through a cycle of meetings that take place weekly, in which the sense of anguish linked to the fear of what could happen, loneliness and stigma is manifested.

Results: In the period going from 2011 to 2021, 313 calls were received from people diagnosed with HIV (4.3% of total calls that is 7300 received by the counselling service), of which 32% declared a newly acquired diagnosis. The total includes repeated calls. 65% of the calls come from the Centre and the age group for new diagnoses is 25-29, while for non-new HIV diagnoses it is 50-54. The number of consultations required face to face over the same years is 25, of which 9 are new diagnoses: age group 25-29 years.

Conclusion: Despite the fact that there has been a considerable improvement in the quality of life and increased survival, the news of being HIV positive is still one of the most difficult moments in care, with psychological, interpersonal and social repercussions. It is necessary for carers of people with HIV to pay attention not only to the general level of health but also to psychological well-being. In order to respond to the request not to feel alone, to face and share experiences, Anlaids continues its path of psychological support, implementing, from March 2022, its service with the activation of an online self-help group Altrevoci designed as a space for sharing and listening, a support network that promotes the emancipation of the person with HIV and a reference point for the practical aspects

Social science, Epidemiology and Prevention

Social and behavioural science, marginalized groups, community aspects and community surveys

P 96 **A PROTOCOL FOR A SYSTEMATIC REVIEW OF PREDICTORS OF QUALITY OF LIFE AND HEALTH-RELATED QUALITY OF LIFE IN OPLWHIV**

S. Licchelli, K. Smith, A. King, F. Trevisan

University of Surrey, Guildford

Background: People living with HIV (PLWHIV) are getting older due to more efficient pharmacotherapy that is effective in stopping the spread of HIV and the progression of the virus in AIDS (Trickey et al., 2017), therefore increasing survival rate and the lifespan in this population. However, living longer does not necessarily mean living well. For this reason, it has been suggested to add health-related quality of life (HRQoL) as a fourth 90 (Lazarus et al., 2016) in the international strategy that aims to stop HIV by 2030 developed by UNAIDS (2014). Lazarus et al. (2016) suggested to add a fourth 90, indicating that 90% of virally suppressed people experience good HRQoL. The aim of this systematic review is to determine what variables are identified as predictors for quality of life (QoL) and health related quality of life in OPLWHIV.

Material and methods: To conduct this systematic review, the following databases will be searched: CINHAL, MEDLINE, ASSIA, Web of Science and PsycARTICLES. The search will be conducted selecting only articles published from 2000. Cross-sectional studies, observational studies and longitudinal studies will be included. Also, studies where OPLWHIV are analysed as a subgroup and are not the main focus of the study. First reviewer (SL) and second reviewer (FT) will screen the articles for duplicates and against the selection criteria. After that, the Data Extraction process will start and a piloted data extraction form is going to be used and discussed by first (SL) and third (KS) reviewer. Once the articles have been selected, they will be put forward for quality assessment by consensus using the NIH study quality assessment tool for the first 25% of articles and this will be reviewed by the third reviewer (KS) for consensus. Any discrepancy will be resolved by consensus or by arbitration by fourth reviewer (AK).

Results: A descriptive summary of the included studies will be provided presenting characteristics and results of the studies selected. A narrative synthesis will also be provided reporting firstly a preliminary analysis of the main results of studies selected in relation to the research question. After that, the relationship between and within studies will be analysed considering subgroups and creating a conceptual mapping where possible to provide a visual synthesis. Lastly, the robustness of the analysis will be presented considering the quality of the studies selected and a critical appraisal of the synthesis process.

Conclusions: This systematic review aims to synthetise and report the main variables related with QoL and HRQoL in OPLWHIV. In doing so, this review can inform possible interventions to improve QoL and HRQoL in this population. Also, this review is going to highlight how variables affect the outcomes mentioned above in different subgroups.

Social science, Epidemiology and Prevention

Social and behavioural science, marginalized groups, community aspects and community surveys

P 97 HIV AND STI AWARENESS PROJECT AMONG ADOLESCENT POPULATION

F. Rossi[1], A. Bianchi[1], P. Testoni[1], D. Zagato[1], R. Repossi[1], A. Antonino[1], E. Garavaglia[1], D. Pennisi[1], M. Cernuschi[2]

[1]ASA Associazione Solidarietà AIDS, Milano, Italy, [2]San Raffaele Hospital, Milano, Italy

Background: ASA, Associazione Solidarietà AIDS, is a charity founded in 1985 in Milan active in HIV and STI prevention field and in the support of HIV- positive people.
The school project aims to bring the topic of HIV and STI within the school context because we realized that very often teenagers lack in information about prevention topics in a particularly vulnerable stage of life as they are involved in their first sexual experiences.
Methodology: school project was active starting November 2022 through all March 2022, involving 15-17 years old students of four different high schools in Milan.
Due to the outbreak of COVID-19, it was not possible to hold all meetings in attendance, so Google Meet was for virtual classes.
Each meeting, lasting two hours, was conducted by a psychologist and a volunteer. The psychologist gave the students information about the infection (ways of transmission, testing, antiretroviral therapy), its history and the current status of the situation. The volunteer told about his life experience with the virus.
Before each meeting participants were sent a link to an anonymous form consisting of ten multiple-choice questions, with the aim of assessing the degree of previous knowledge on the subject. After the meeting a second questionnaire was sent with the same questions, to evaluate the effectiveness of the activity.
In addition, a satisfaction survey was also sent out to investigate several areas of usefulness and effectiveness of the meeting.
Results: out of a total of about 600 students involved (9 school classes), 424 students filled in the pre-meeting survey scoring an average of 75.5% correct answers. The post-meeting survey, completed in the days following the meeting, was answered by 193 students of the initial group (with a decrease of 54.5% of the initial participants). This decrease could be explained by the fact that only those students who were more involved and interested in the topic or those who were scholastically more diligent answered the post-meeting survey. In addition, we could hypothesize that some children struggle to complete tasks that go beyond the school context.
The 193 students who completed the final survey scored 83% of correct answers: this data indicates how the activity carried out has a positive effect in terms of effectiveness and usefulness of learning.
The analysis of the 131 satisfaction surveys collected shows that all the interviewees evaluated the meeting positively (18% considered it extremely informative, 60% very informative and 22% quite informative). Nearly all respondents agreed that the meeting was useful (30% extremely useful, 49% very useful, 21% quite useful), only 1% saw no usefulness in it.
Conclusion: given the positive impact of the project, we will continue to offer this kind of meeting in schools, optimizing the methodology used so far in order to avoid the dispersion of the interviewees by having them fill out the final survey at the end of each meeting.

Social science, Epidemiology and Prevention

Social and behavioural science, marginalized groups, community aspects and community surveys

P 98 **NATHAN NEVER CHARACTER BY BONELLI EDITORE COMBATS AIDS AND STIGMA**

G. Dessì, V. Mascia, B. Mocci, A. Pontis

Lila Cagliari OdV, Cagliari

In 2021 LILA Cagliari (NGO affiliated with LILA-Italian League for the Fighting AIDS) conceived and implemented an information campaign in partnership with Sergio Bonelli publishing house. Being aware of how much the youth imagination is influenced by comics, we created a campaign based on the popular character Nathan Never who is depicted in 3 different comic boards: encouraging the use of condoms, inviting people to get tested, the concept U=U to promote a culture of non-discrimination towards PLWHIV.

We worked remotely for a year with Sergio Giardo (official Nathan Never illustrator), the editorial staff and the Bonelli press office, to discuss the contents: the use of condoms, HIV testing and the fight against the stigma that surrounds HIV. That communication became even more crucial when the Covid19 pandemic was the focus of public opinion's attention for over two years. The campaign was designed to hinder some issues: the media lack of interest on HIV and access to HIV testing; the awareness that doctors do not communicate the U=U scientific evidence to their patients who, as a result, often refuses emotional and sexual relations; the remote possibility for all population to learn about something which, as well as improving the quality life of the person with HIV, eradicate the stereotype and shared stigma that still perceives them as dangerous. In this social awareness campaign, Nathan Never represents a "Space Hero", who lives in a future time destroyed by terrible disasters, but he owns the futuristic tools and weapons with which he creates messages of great impact and hope on the subject of HIV.

The previously unknown panels are colourful and with a strong visual impact. In one of them, Nathan Never floats in space with a helmet to protect himself from viruses, which reminds us about the importance of using condoms. In the second one, he uses one of his futuristic weapons to highlight that the most powerful weapon is knowledge. In the last board, he uses the radar scan's screen of a spaceship on which we read the reassuring message: Undetectable=Untrasmittable. The production of the 3 different campaign's subjects was released in various formats: postcards, large posters affixed in town, dynamic advertising on the external sides of local buses. The campaign has been spread on all social networks and online newspapers. Moreover, a digital video version was distributed through monitors on local buses and a paper version was printed on 15x20cm coloured posters, which were hung inside the buses. These posters have become a "must-have" and have literally been snapped up by collectors and comics enthusiasts.

This campaign has achieved resounding success, with particular appreciation from those who know comics and Nathan Never character. We believe the set goals have been accomplished, namely to bring back attention to HIV, encourage people to use condoms and help to combat discrimination and stigma through an important message such as U=U.

Attach: https://www.icar2022.it/public/abstract/Attach_ABS_39.png

Social science, Epidemiology and Prevention

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P 99 VILLA MARAINI: SYNDEMIC APPROACH AGAINST SOCIAL STIGMA

T. Di Giovanni[1], P. Sammarco[1], D. Masci[1], G. F. M. Direnzo[1], E. Teti[2], B. Coladarce[1], G. Rodoquino[1], M. Andreoni[2], E. Rossi[1], M. Barra[1]

[1]Fondazione Villa Maraini, Rome, Italy, [2]Infectious Disease Clinic, Tor Vergata University, Rome, Italy

Background: The Covid-19 pandemic has caused a severe limitation of access to care and the overshadowing of other diseases such as HIV and Hepatitis C, and it's likely to have of the deeper and more significant consequences related to social stigma, which could constitute a further barrier for new diagnoses and subsequent treatment pathways.
This stigma hits our target populations even harder, that even before the Covid they often found themselves living in conditions of marginalization and social isolation.
Villa Maraini Foundation, which has always been involved in the fight against stigma, with daily work of meeting and accompaniment to the care of frail people, never interrupted testing work for HIV and HCV.
Material and Methods: The team is represented by a doctor and a psychologist/socio-health worker, frequently a former drug addict. Rapid tests are on a capillary blood sample. PPE are used: ffp2 mask and sterile gloves for the doctor and surgical mask for the patient. The rooms are sufficiently ventilated and the surfaces are disinfected regularly. Tests were also carried out outdoors, in the Foundation's green spaces or at the Tor Bella Monaca park where the Road Unit operates. First of all the patient's temperature is taken, then a pre-test counseling is carried out through a questionnaire regarding clinical history and risk behaviors in the previous 6 months. The doctor carries out the test and communicates the results: in case of negativity, the patient is informed about the possibility of repeating it or not. In case of preliminary positive test the patient is sent/ accompanied to a center for the confirmation test and the start of treatment with a view to “Continuum of care”.
Results: From July 2021 to April 2022 235 people were tested: 74 women, 146 men 13 Trans, 1 Non-Binary.
Of the women, 72 had the HIV test, all negative; 63 had the HCV test of which 4 with positive results.
Of the men, 138 had the HIV test of wichh 2 with positive results, 137 had the HCV test of which 5 with positive results.
Of the Trans, 13 carried out the HIV test and the HCV test, all with negative results.
The Non-Binary patient had HIV and HCV tests, both negative.
Conclusions: Villa Maraini Foundation continued throughout the pandemic to ensure the execution of rapid tests for HIV and HCV, and accompanying hundreds of fragile people to care, reducing the impact of social stigma on the possibility of access to care.
All this was possible thanks to the presence of 24-hour services, of operators ex drugs users, doctors and psychologists adequately trained and able to establish an empathic contact.
The experience of the Villa Maraini Foundation has shown how it is possible to adopt a syndemic model oriented towards prevention, effective deterrent against social stigma. With the relaxation of restrictions, it will be possible to resume and implement testing work on the road, which will allow us to contact, test and accompany an even larger number of people to the treatment.

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P 100 THE RISE AND FALL OF THE NEWS MEDIA INTEREST FOR HIV/AIDS IMPACT ON PEOPLE'S LIFE: AN OBSERVATIONAL STUDY OF THE ITALIAN PRESS

C. Capelli[1], M. Pasquali[1], G.M. Corbelli[2], P. Lalli[1]

[1]Department of Political and Social Sciences, University of Bologna, [2]Plus, Network persone LGBT+ sieropositive

Background: HIV and AIDS are not just biomedical conditions. Their trajectories intertwine sociocultural, political, economic, religious, and ethical issues, and the news media are a good indicator of the selected aspects involved in the process of their construction as a public problem. An analysis of media representations of people living with HIV/AIDS (PLWH) can provide insights on how society addresses the topic of HIV/AIDS and its related stigma.
Material and methods: Thanks to an unrestricted grant from ViiV Healthcare, we are conducting a research aimed at analyzing the media representations of PLWH between 1999 and 2019 in Italy. Our study addresses the following questions: a) has the newsworthiness of people living with HIV/AIDS decreased or increased over time? b) Does the development of the news coverage reflect specific key news-generating events? c) How has the coverage changed, and does it still include stigmatizing representations of minorities or marginalized groups? d) What are the characteristics of the news stories that have been selected to be shared on the outlet's social media pages?
At present, our data consist of content searches of the Italian newspaper with the largest national circulation – Corriere della Sera. A similar search is planned for La Repubblica. Articles were collected through a keyword search within the newspaper's archives and coded for themes, frames, and main actors. At present the corpus consists of 3725 news stories that cover the period from 1999 to 2019. We also monitored the Twitter and Facebook profiles of the newspaper since the date of their creation (2011, 2010) obtaining 113 and 129 posts.
Results: Preliminary results show that coverage of HIV/AIDS constantly decreased over the period analyzed, consistent with the "AIDS fatigue" observed in the Western media since the mid-1990s and with the general disappearance of the issue from the public discourse. A shift is also observed from a predominantly domestic coverage to an increase in the coverage of the global epidemic, with a focus on Africa. News media on PLWH are often driven by specific events (World AIDS day, sporadic episodes of moral panic concerning supposed "plague spreaders", individual recoveries, or medical breakthroughs) as well as by celebrity activism. The media appear to be interested in new, more effective drugs, possibly pointing to a tacit belief that the epidemic is no longer a matter for public concern.
Conclusions: Further analysis is still ongoing to better identify which frames and high-risk groups are placed at the center of the HIV/AIDS news coverage and whether this reveals the emergence of new forms of stigma or social acceptance, as well as any correlation to the extent to which groups might be effectively affected by the epidemic.

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P 101 COVID 19: LET'S GO WITH THE VACCINE ACCOMPANYING THE BOOKING OF THE ANTICOVID-19 VACCINE FOR MIGRANTS AND LGBTI MIGRANTS + APS ARCIGAY CASSERO

R. Cerbo, S. Degasperi

APS Arcigay Cassero, Gruppo Salute, Bologna

Background: In Emilia Romagna one person out of every 11 is foreign, in Bologna there are 60,698 resident * foreigners *. The Emilia Romagna Region provides a lot of useful information, also available online, for everything concerning the prophylaxis to be adopted to avoid contagion from Covid-19, the materials are translated into many languages. The information most difficult to find online is that relating to vaccination for non-resident foreigners who do not have a valid tax code, the same applies to obtaining the Green Pass.
The aps Arcigay il Cassero set out to carry out research and awareness activities on the subject of vaccination against the Covid-19 virus for migrants and LGBTI migrants. The goal is to systematize existing information and make it usable for migrants to increase accessibility to the health system.
Material and methods: The management and development of the “Covid 19: let's go with the vaccine” project was coordinated by the Health Sector of the Cassero lgbti + center. The funds for the realization of this project were obtained thanks to funding from Intersos (https://www.intersos.org/).
To convey the information it was decided to use short videos in which we explained how to access the service and how to ask the Health group for help to get support.
The calendar of activities was as follows:
A phase of mapping the services already present in the area for access to vaccination for migrants regardless of their legal status (4 weeks in October and 1 week in November)
The creation of informative material / a reduced billboard campaign / landing page with qr code, telephone number to call and creation of films (30 days in October and first week of November). Material available in language / English / French / Arabic
The setting up of information points with telephone counter activities and accompaniment to the administration of the vaccine (2 months November and December)
The dissemination of information materials at facilities, banquets and events for migrants and LGBTI migrants (2 months November and December)
Results: On 31/12/2021 the people supported in booking the vaccine are 75, of which 20 physically accompanied to the vaccine by a volunteer from the Cassero Salute group;
on 12/31/2021 the people reached through the analysis of the data of our social channels are 1500.
Conclusions: Currently, the Health group is able to provide information on how to access the vaccine (first, second and third dose), provide useful contacts and information about obtaining the Green Pass even in situations where there is no documents.

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P 102 MEASURING IMPACT OF A SCALABLE PEER EDUCATION-BASED SEXUALITY EDUCATION PROGRAMME IN MULTIPLE ARCIGAY LOCAL COMMITTEES

B. Allegretti, A. Barretta, A. Biondi, W. Bravi, M. Breveglieri, G. Cioffi, G. D'Ambrosio, B. Diana, D. Enicchiaro, M. Marocco, I. Mele, F. Merolle, N. Piazza

Arcigay, Caserta

According to UNESCO, sexuality education (SE) is a key component of the global strategy for HIV and sexually transmitted infections' (STIs) prevention in Europe. Nevertheless, in Italy, informational programmes concerning HIV and STI prevention addressed at the general population are still scarce or have little effectiveness.
"Healthy peers" is a national project funded by the Italian Ministry of Labour and Social Policies and organized, among other subjects, by Arcigay. The aim is to promote a culture of sexual health and wellness, sex positivity and HIV/STI prevention through peer education. A SE programme, consisting of asynchronous learning of 10 educational units followed by two weekends of peer education in-person sessions, was offered to staffers/volunteers of Arcigay Roma, Caserta, Torino and Palermo enrolled in the "Healthy peers" project.
We developed a questionnaire on HIV/STI knowledge to measure the impact of our SE programme, and hereby present the results.
Material and methods: The questionnaire was created based on the educational units and training material developed for the "Healthy peers" project, approved by organizers and peer educators, and administered to participants of the Arcigay Caserta and Roma SE courses.
It consists of 20 multiple-choice questions, scored as follows: 1 point for correct answer; 0 points for wrong answer.
The control group was composed of members from the general population who did not attend the SE programme before filling out the self-administered questionnaire.
Normal distribution of the two datasets was calculated using the Kolmogorov-Smirnov test, and then T-test was used to verify result significance.
Results: Among the two SE classes (Arcigay Roma and Caserta) making up the intervention group, a total of 30 participants filled out the questionnaire. Also from the naïve population, 30 volunteers filled out the questionnaire.
The mean and median values of the intervention group were, respectively, 17.97 and 18.00, with SD = 1.81.
The mean and median values of the control group were, respectively, 12.57 and 12.50, with SD = 4.01.
Using the T-test, we obtained a t-value = -6.71671 and a p-value < .00001, indicating that the score difference between the test and control groups is significant.
Conclusions: The results of this study indicate the importance of effective SE in improving knowledge regarding STIs, which in future developments we hope to show to be a proxy for improvements in incidence of STIs in the general population and in target populations (e.g. by segmenting them in clusters by age, level of instruction or sexual habits).
In the future, other Arcigay local committees in Italy will start peer education-based SE programmes, and use of this questionnaire, along with other indicators (e.g. demographic data, real-life STI

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P 103 IN AND OUT TESTING/COUNSELING APPROACH IN PANDEMIC ERA: A NINE MONTHS EXPERIENCE AT CHECKPOINT AND HOSPITAL CENTER

G. Mancarella[2], M. Jamhour[1], A. Carraro[1,2], S. Garattini[2], A. Pontrelli[2], A. Gasperin[2], D. Di Trento[2], R. Marocco[1], A. Petrillo[3], V. Vitale[3], D. Coletta[4], M. Lichtner[1,2]

[1]Infectious Diseases Unit, S.M. Goretti Hospital, Latina, [2]Department of Public Health and Infectious Diseases, "Sapienza" University, Rome, [3]Arci Gay Latina/Sei come sei, [4]Municipality of Latina

In the last two years, the SARS-CoV2 pandemic had an heavy impact on chronic illness management and diagnosis, HIV infection being one of them. On a national and local level, the majority of the newly diagnosed people are late presenters, so it became mandatory to increase our effort to create structured screening campaigns and obtain early diagnosis. The city of Latina recently joined the Fast Track Cities network and the Checkpoint initiative, a place outside hospital where everyone can be tested for sexually transmitted disease and receive sexual health education with particular attention on PrEP and PEP.

People wanting to be tested in our Checkpoint need to schedule an online anonymous appointment and choose between the available rapid capillary blood tests: HIV, HCV, syphilis or all of them. At first we administer a community-based counseling and then perform the HIV test(Ab and p24 antigen detection), HCV(Ab Detection) and Syphilis(Ab detection). Results are given in 15 minutes and uploaded on the COBATEST website.

On the other hand, HIV testing in our clinic does not need a scheduled appointment, requires a phlebotomy and results are available in 3 days. Counseling is conducted by ID specialists and written in the patient's anonymous medical record. HCV and syphilis tests are not offered. Data was collected through the COBATEST export tool and compared with the one from our HIV clinic.

To this day, in our Checkpoint 194 people have been tested for HIV, HCV and syphilis. All HIV and HCV tests resulted negative, instead 9 syphilis tests resulted positive as serological scar. The population was characterized by 112 male, 82 female, median age 31 years (compared to the median age in the new HIV diagnosis in Latina being 50 years). 74 people had risk exposure (71,6% for unprotected vaginal sex, 19% for unprotected anal sex and 6,7% for unprotected oral sex).18% were MSM, 53% were heterosexuals. According to the latest report, 56% of new HIV diagnosis in Latina were found in MSM and only 43% in heterosexuals. 74% of all says it did not use condoms in the last penetrative sex. 4 people had an STI diagnosed in the last 12 months. No IDU or risk from sharing injection materials was found. Most of the subjects have heard of PrEP but never considered using it. Almost nobody has ever heard about PEP.

These first few months of testing and counseling in our checkpoint highlighted the great role that this service has in the community in terms of prevention and sexual health education. We need to better address the key populations, such as MSM and people >31 years old, which contribute to the majority of the new HIV diagnosis in our district. We also should put our effort in educating people about the tools we now have to prevent HIV transmission such as PrEP and PEP. Improving the activities of our checkpoint, working side by side with Arcigay volunteers, will certainly help us getting closer to the Fast Track Cities goal of ending the HIV epidemic.

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P 104 HIV WRITTEN INFORMED CONSENT: TIME TO RECONSIDER THE ITALIAN STANDARD?

J. Testa[1,2], N. Cocco[2,3], F. Nicoli[2,4], D. Radrizzani[1], C. Abeli[1], M Farinazzo[1,2], B. Menzaghi[1]

[1]Infectious Diseases Unit, ASST Valle Olona, Busto Arsizio, [2]Research Group of Italian Society of Migration Medicine (SIMM), [3]Infectious Diseases Service, Penitentiary Health System, ASST Santi Paolo e Carlo, Milan; [4]Clinical Ethics Service "Domus Salutis" Clinic, Teresa Camplani Foundation, Brescia

Issues of social stigma towards people living with HIV (PLWH) are still common in many parts of the world. In the 1980s and 1990s, before therapies could alleviate the social burden of HIV/AIDS diagnosis, the stigma was very common even in Western countries, particularly in the USA and in the European Union. In Europe, HIV-testing had to be conducted differently from other blood tests, requiring voluntariness, confidentiality and preferably written Informed Consent (IC) Forms.

Since 1990 the Italian law requires written IC and pre- and post-test counselling for HIV testing. This procedure was mainly established to protect individual rights at risk of being jeopardized, especially in the workplace. As time went by, things changed and thanks to Highly Active AntiRetroviral Therapy (HAART) HIV-infection should now be compared to other chronic diseases.

We intend to investigate whether it is time to reconsider the Italian standard written procedure to obtain IC, at least within healthcare facilities.

A simplification of HIV testing procedures occurred in some countries thanks to the improvement of quality-of-life for PLWH achieved through HAART. Revised recommendations from the Centers for Disease Control and Prevention (CDC, 2006) as well as the 2014 European Guideline on HIV testing suggest that, in routine care, verbal communication to subjects can replace a dedicated procedure to obtain a valid written IC. This seems to lead to increased early HIV-infection diagnoses.

In any case, the explicit consent or refusal of HIV screening must always be obtained and documented in medical records. According to CDC's "Opt-Out Testing", all patients are verbally informed that they will be tested for HIV; they can then decline, or "opt-out". Counselling on HIV should be guaranteed to all patients in their mother tongue.

In Italy, we are still anchored to procedures established in the 1990s, when the HIV epidemic had very different clinical and social characteristics from today, even though issues related to social stigma are yet to be resolved.

We believe that in Italy the fight against residual stigma must involve the strengthening of communication between healthcare providers and patients. Moreover, we need an upgraded widespread dissemination of awareness about HIV, both at a macro-level (within the community) and micro-level (patient-provider relationship): a great deal of efforts must be made to implement both extensive educational programs about HIV-related risky behaviours and public awareness campaigns aimed at removing HIV social stigma. Fear of being identified as HIV-positive may discourage people from getting tested and accessing medical services. The use of a specific written IC form could also be an obstacle in fighting the stigma, which has indeed a pivotal role in the spread of the AIDS epidemic. Easier HIV testing procedures may contribute in normalising HIV as a chronic condition and may be beneficial to individuals as well as public health.

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P 105 CHEMSEX IN MILAN

S. Giacalone[2], S. Ramoni[1], M. Cusini[1]

[1]UOC Dermatologia, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, [2]Dipartimento di Fisiopatologia Medico-Chirurgica e dei Trapianti, Università degli Studi di Milano, Milan, Italy

Introduction: The term Chemsex is used to describe the intentional intake of psychoactive and non-psychoactive drugs during planned sexual activity to sustain, enhance, disinhibit or facilitate the experience. It is a specific form of recreational drugs use associated with multiple partners, extended sexual sessions lasting many hours/several days, extreme sexual practices and poor condom use. This identifies a category of patients more susceptible to transmission of common sexual infections, consumption abuse and drugs interaction. For the reasons listed above, recent UK studies underline the need to consider Chemsex a public health priority. Epidemiologic data show that in northern Europe and the USA, it is a widespread practice, but little is known on the Italian situation, which is the reason we decided to propose our research.

Materials and Methods: In the period from 1 July 2021 to 31st January 2022, we distributed 534 paper questionnaires to volunteer patients attending the Sexually Transmitted Infections (STI) Department of the City. The research team designed an anonymous multiple choices survey with the following categories: sociodemographic data (age, sex, educational level, working status, self-reported sex orientation), STI history, sexual risk behaviour (testing history, number of sexual partners, participating to sex-parties or orgies, use of condom with occasional partner, frequency of dating app use), Chemsex experience

Results: 132 (25 %) patients reported having Chemsex during the last year – 107 (81 %) men and 25 (19 %) women. Of those, 57.5% declared a LGBQT+ self-sexual orientation vs 42.5% of heterosexuals, 74 % of the people had had this more than once and the 48% of patients expressed doubts about desire to stop. Altogether, Cocaine was the most frequent drug (33.3 %) used, while a 23% of participants mixed substances. Desire to increase both pleasure and arousal was the main reason (81%) to practise Chemsex. Compared with non-chemsex users, chemsex users reported higher incidence of STI (56% vs 3%), increased number of sexual partners (62.2 % vs 37.5 had more than 5 partners) and lower condom use (22% vs 8% declared to don't use it with occasional partners). We found no major differences in sociodemographic characteristics among the two groups in our sample: the majority of people had higher education, were in employment and the average age was equal to 30.

Discussion: This study, even if with some limitations, showed that Chemsex is common among patients attending our STI centre, which is the first centre in terms of attendance and number of services in the City. In this way, a subgroup of patients at higher risk of STIs was identified, highlighting the importance of adequate training in this regard.

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P 106 BRINGING COMPREHENSIVE SEXUALITY EDUCATION INTO ITALIAN LOWER SECONDARY SCHOOLS' PRACTICE: A PILOT STUDY

E. Torri[1], A. Chinelli[1], L. Ceccarelli[1], L.Rancilio[6], M. Farinella[7], R. Galipò[3], P. Meli[4], A. Camposeragna[5], L. Colaprico[8], M. Oldrini[9], M.C. Salfa[10], A. Cellini[11], M. Ubbiali[12], A. Caraglia[13], L. Mortari[12], A.T. Palamara[11], B. Suligoi[10], L. Tavoschi[1], D. Martinelli[2]

[1]University of Pisa, Department of Translational Research on New Technologies in Medicine and Surgery, [2]University of Foggia, Department of Medical and Surgical Sciences, [3]ANLAIDS - National Association for the Fight against AIDS, Rome, [4]CICA - Italian Coordination of HIV/AIDS Housing Homes, Bergamo, [5]CNCA - National Coordination of the Hospitality Community, Rome, [6]Caritas Ambrosiana, Milan, [7]Circolo di cultura omosessuale Mario Mieli, Rome, [8]Italian Red Cross, Rome, [9]LILA - Italian league for the fight against AIDS, Rome, [10]Italian National Institute of Health, Rome, [11]Sapienza University of Rome, [12]University of Verona, Department of Human Sciences, [13]Ministry of Health, Department of Prevention, Rome

Background: Sexual and reproductive health (SRH) is a key dimension of health and well-being. School plays a central role in the learning about health and health promotion skills, including sexual health. Available theoretical and research evidence indicates that Comprehensive Sexuality Education (CSE), especially when delivered in a school-based context, positively impacts on the behaviour and attitudes of young people, by improving SRH outcomes and empowering them to make free and informed choices. This study aims to describe the features of a pilot activity designed to deliver CSE into lower secondary schools (LSS) within the context of EduforIST project. EduForIST is funded by the Italian Ministry of Health and involves academics, the Italian National Institute of Health and HIV/AIDS civil-society organisations (CSOs).

Methods: A desk review was conducted to collect information about regional and national normative documents, international literature and guidelines on the topics of sexually transmitted infections (STIs), affectivity and sexuality education (SE). An online survey was developed to collect information on duration, content and methods used to implement school-based SE (SBSE) in Italian secondary schools from 2016 to 2020. The results of the survey and desk review, along with focus groups and open discussions involving all partners were used to define objectives, contents, methods of delivery and evaluation of the pilot activity. Additional information was added after feedback from an expert advisory board.

Results: A pilot activity was designed and targeted at LSS students, belonging to 4 target regions, with a total of 20 schools involved. The educators delivering the activity belong to CSOs and have been trained during a 2-day intensive workshop. The activity consists of 5 interactive interventions of 2 hours to be conducted in each classroom: 4 theoretical and practical modules and 1 intervention dedicated to deepening topics requested by the students. Each module consists of 3 parts: a syllabus, a set of theoretical slides, and a list of activating tools. The modules address the following dimensions: A) acknowledging changes in adolescence, B) handling emotions and relationships, C) sexual identities and diversity, D) sexual consent, STIs/pregnancy prevention, sexual health services. The evaluation will be carried out on educators' level (through SWOT analysis and field diary) and students' level (pre/post tests and satisfaction questionnaires).

Conclusions: SBSE is the most effective way to positively impact on young people's behaviour and attitudes towards sexuality. However, SE is not included in Italian school curricula and very rarely the students are provided with rightful, appropriate, and accurate information about their sexuality. This pilot activity represents a first step towards the implementation of an evidence-based approach to SBSE, to be promoted and implemented equally across the country.

Social science, Epidemiology and Prevention

Social and behavioural science, marginalized groups, community aspects and community surveys

P 107 SEXUAL HEALTH IN MIGRANT POPULATION: ANALYSIS OF THE RISK OF CONTRACTING HIV AND STDS

V. Manca[1], V. Fiore[1], A. De Vito[1], N. Geremia[2], E. Princic[1], G. Madeddu[1], S. Babudieri[1]

[1]Unit of Infection Diseases, Department of Medical, Surgical and Experimental Sciences, AOU, Sassari, [2]Unit of Infection Diseases, Department of Clinical Medicine, Ospedale dell'Angelo, Venezia

Background: Migration has a direct influence on sexual health. Differences both in sexual networks and the risk of sexually transmitted diseases (STDs) between racial/ethnic minorities and the native population have been described in the literature.

Methodology: We collected data on medical history, physical examination, and HIV/STDs tests. Screenings were proposed basing on CDC 2018 guidelines on STDs. Patients underwent peer-to-peer counselling before screening offer.

Results: We included 391 patients (both outpatients and migrants living in facility centers), median age was 29 (23 -37) years, and the most part were male (198/391; 50.6%). Of them, 389 (99.4%) were counselled and 371 (94.8%) accepted the screening. We found 157 (40.1%) HBsAg/Anti-HBc positivities, 4 (1%) HIV positive screenings, 1 HCV infection, 47 (12%) HPV-related genital warts, 29 (2.3%) cases of syphilis, 13 (3.3%) Molluscum contagiosum.

Conclusions: Migrants have high-risk sexual behavior. Despite this, they have a low perception of risk and healthcare needs. A peer-to-peer counselling demonstrated to be useful increasing the screening acceptance. However, the retainment in care was low, as in previous studies. The access to HIV/STDs screening and treatment should be implemented. The development of specific retainment in care pathways is still needed to reduce the lost to follow-up.

The access frequency of the follow up is estimated at 15%.

Virology and Pharmacology

HIV virology

P 108 **EVALUATING THE DUAL-TARGET APTIMA HIV-1 QUANT DX ASSAY: COMPARISON BETWEEN VIRAL LOADS MEASURED WITH THE POL AND LTR TARGETS IN THE SAME SAMPLES**

G. Sberna[1], S. Sarti[1], A. Antinori[2], S. Cicalini[2], A.R. Garbuglia[1], A. Amendola[1]

[1]Laboratory of Virology, National Institute for Infectious Diseases "Lazzaro Spallanzani" IRCCS, Rome, Italy, [2]HIV/AIDS Department, National Institute for Infectious Diseases "Lazzaro Spallanzani" IRCCS, Rome, Italy

Background: For the correct and the effective management of HIV-1 patients, accurate measurement of HIV-1 RNA viral load (VL) is fundamental. The latest generation molecular assays for monitoring of VL perform simultaneous detection of two regions of the viral genome, however without specifying the target used for VL quantitation.

Material and methods: Five-hundred VL data from chronically HIV-1 patients under ART were analysed for intra-assay evaluation of values measured by pol and by LTR targets in the same specimens by using the "open" software (RUO=Research Use Only) of Aptima HIV-1 Quant Dx Assay, which shows the two results separately. Correlation and concordance between pairs of results and potential clinical implications were described.

Results: By stratifying VL into two groups (<30 and ≥30 copies/mL HIV-1-RNA) according to pol-based results and matching them with their respective LTR values, the concordance was substantial (κ=0.635; 95%CI: 0.569-0.700). Considering the specimens (n=224) with VL exactly quantified (i.e. ≥30 cp/mL) with both pol and LTR targets, an optimal correlation subsisted (r=0.8882; p<0.0001) and Bland-Altman plot showed not significant mean difference between them. However, by stratifying these data in three ranges (30-200, 201-1,000 and >1,000 cp/mL), concordance analysis showed fair agreement (κ=0.344; 95%CI: 0.257-0.432). When all mutually concordant VL values in each range (n=134) were excluded, the remaining samples (n=90; 40.1%) showed an increased LTR expression gradient compared to the corresponding pol value (Figure 1). In particular, in samples with pol values >1,000 cp/mL, mean difference (pol minus LTR VL values) was +0.9 Log10 cp/mL (min-max difference: +0.5 and +1.5 Log10 cp/mL, respectively); in samples with pol values 201-1,000 cp/mL, mean difference was -0.3 Log10 cp/mL (min-max difference: -1.7 and +1.2 Log10 cp/mL, respectively); in samples with pol values 30-200 cp/mL, mean difference was -1.1 Log10 cp/mL (min-max difference: -1.9 and -0.4 Log10 copies/mL, respectively).

Conclusions: With "open" version Aptima software, in a previous study [1], we reported that 6% of plasma samples from chronically HIV-1 infected patients under effective ART, show absence of pol signal with viremia values calculated exclusively on the basis of LTR amplification. Here, we reported that, in 40.1% of samples with VL quantified with both target, LTR based VL are on average 0.5 Log10 cp/mL higher than that measured with pol. Further studies on these discrepancies and nature of viral RNA elements detected only with the LTR in HIV-positive patients despite efficient ART are needed to identify possible clinical implications.

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Virology and Pharmacology

HIV virology

P 109 **INHIBITORY ACTIVITY OF THE POLYPHENOLIC EXTRACT OF CISTUS MONSPELIENSIS L. AGAINST HIV-1 UNDER CELL CULTURE CONDITIONS**

M. Tamburello[1], V. Ferraro[1], S. Vituliano[1], A. Morellini[1], A. Primavera[2], A. Bertoldi[2], M. Mandrone[3], F. Poli[3], G. Gallinella[3], T. Lazzarotto[1,2], I. Bon[2]

[1]Section of Microbiology, Department of Experimental, Diagnostic and Specialty Medicine, University of Bologna, Bologna, [2]Microbiology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, [3]Department of Pharmacy and Biotechnology, University of Bologna, Bologna

Background: The research of alternative pharmacological approaches, as topical microbicides, is fundamental in HIV infection treatment to avoid or reduce sexual transmission across epithelial cells of genital and rectal mucosa, the most common pathway of HIV entry. Plants are a rich source of new promising antiviral agents; in this context, we analysed the antiviral properties of the natural compound Cistus Monspeliensis L. (Cim) that belongs to the family Cistaceae and consists of a polyphenolic mixture with a broad range of antioxidant, anti-inflammatory and antimicrobial activities.

Material and Methods: Cim, extracted from fresh leaves of aerial parts, was employed in attachment, pre-attachment and post-attachment assays in order to investigate its antiviral mechanism in vitro, using HIV-1 strains with different coreceptors tropism. Scalar concentrations of the compound (20-10-5 µg/mL) were pre-incubated with 5 ng/mL HIV-1 gag p24 of HIV-1IIIb (X4-tropic), HIV-1Bal and HIV-1Ada (R5-tropics), added to a cell line C8166 and activated PBMCs respectively and seeded into fresh medium at 37°C. Cells exposed to virus without compound (100% infection) and unexposed cells (background) were used as controls. Each Cim concentration was tested in at least 3 replicate wells in 3 separate experiments. After day 7 post-infection, genomic RNA was isolated from cells, cDNA was generated by reverse transcription and quantified by qRT-PCR using HIV-1 pol gene specific probe and primers. The inhibition of viral replication was confirmed by measuring HIV-1 gag p24 antigen enzyme-linked immunosorbent assay (ELISA) in cell supernatants. LDH detection kit was used to evaluate the cytotoxicity of Cim on cell cultures.

Results: The antiviral activity of Cistus Monspeliensis was tested in C8166 infected with HIV-1IIIb laboratory isolate and in activated PBMCs infected with HIV-1Bal and HIV-1Ada strains. Three different assays were performed. In the attachment assay, Cim extract inhibited infection of cells by all 3 viral strains; in particular, the concentration of 20 µg/mL displayed a decrease of 93% ($p<0.05$; Two-tailed Student test) of viral replication, expressed as a reduction of HIV-pol RNA detection, compared to infected and untreated controls. The results were confirmed by a significant decrease in the p24 protein in a Cim concentration-dependent way. In pre and post-attachment assays no effect on viral infection was observed at the 3 concentrations of the compound tested, demonstrating that Cim inhibits a very early step in HIV-1 replication cycle. No cytotoxicity of the compound was highlighted by LDH assay.

Conclusions: Cistus Monspeliensis L. exhibits a good inhibitory power of HIV-1 replication. These preliminary data suggest that Cim blocks attachment of viral particles to cells and thus inhibits viral entry. Evaluation of the potential use of Cim extract as topical microbicide, to prevent sexual transmission of HIV, requires extensive future investigations.

Virology and Pharmacology

HIV virology

P 110 **EVALUATION OF A NEW REAL-TIME PCR COMMERCIAL TEST FOR HIV-DNA QUANTIFICATION IN PBMC**

T. Allice, M.G. Milia, E. Burdino, G. Gregori, F. Cerutti, S. Crisavola, S. Monteleone, E. Scuccimarra, V. Ghisetti

Laboratory of Microbiology and Virology, ASL Città di Torino, Italy

Introduction: Quantification of total HIV-1 DNA from peripheral blood mononuclear cells (PBMC) of patients via polymerase chain reaction (PCR) provides a useful tool to monitor the size of the viral reservoir. Total HIV-DNA (integrated and unintegrated forms) is a marker of disease progression and survival, a potential indicator for the initiation of antiretrovirals in treatment-naïve patients, a predictor of virological rebounds in treatment-patients, and could be a predictor of the presence and severity of some HIV-1 associate disorders. Standardized methods for the total HIV-DNA quantification are currently lacking and several discordant results are still present in different studies.

Aim of this work was to analyze the performances of a commercial total HIV-DNA kit based on real-time PCR (qPCR) for the measurement of total HIV-DNA in PBMCs samples from HIV positive patients.

Materials and Methods: Twenty plasma samples derived from 20 HIV-1 patients (18 patients with viremiae below 20 copies/ml and 2 with HIV-RNA 53 and 126 copies/ml, respectively) were tested with Generic HIV DNA Cell (GHDC, Biocentric, France) a commercial total HIV-DNA real time PCR quantitative assay and compared with the “in house” qPCR test routinely used in our laboratory.

The GHDC test target a consensus sequence in the highly conserved long terminal repeat (LTR) region among HIV-1 group M subtypes and includes a standard curve used for the quantification of total HIV-1 DNA in PBMC expressed in copies/10^cells . The “in house” HIV-DNA quantitative assay is a qPCR test designed to target LTR regions (Viard et al., AIDS 2004) and that use as standard curve a serial pNL4-3 HIV-1 plasmid dilution (from 10^5 to 10 copies/reaction). PBMCs were obtained with separation of lymphocytes and peripheral mononuclear cells by using the Leucosep tubes (Greiner Bio-one, RM, Italy).

Results: The GHDC test was able to detect and quantify total HIV-DNA of 18 patients (from 6 to 4.285 copies/10^6 cells) while the in house assay detected HIV-DNA in 19 patients (from 3 to 731 copies/10^6 cells). Correlation between in house-HIV DNA and GHDC, was 0.74. With the Bland-Altman analysis the mean difference between the two test was 0.39.

Conclusions: In this study, we analyzed the performance of the Generic HIV DNA Cell a commercial total HIV-DNA kit based on real-time PCR (qPCR) for the measurement of total HIV-DNA in PBMCs in comparison with an in-house real-time PCR test. The GHDC test showed a good performance in the quantification of total HIV-DNA and reported an good correlation with the in-house method. Therefore, this commercial assays could be interesting in the standardization method for total HIV-DNA quantification and to better understand clinical implication of this marker.

Virology and Pharmacology

Pharmacology, pharmacogenomics and drug interactions

P 111 **EXPLORATORY ANALYSIS OF POTENTIAL DRUG-DRUG INTERACTIONS BETWEEN MOLNUPIRAVIR AND HAART IN PLWH WITH COVID-19 IN UDINE**

D. D'Elia[1], A. Londero[1], F. Prataviera[1], L.M. Ditaranto[1], M. Fusi[2], C. Resnati[2], C. Tascini[1], D. Cattaneo[2]

[1]Unit of Infectious Disease, Santa Maria della Misericordia University Hospital, Udine, Italy, [2]Unit of Clinical Pharmacology, Luigi Sacco University Hospital, Milano, Italy

Introduction: Molnupiravir was the first oral antiviral drug approved in Italy against COVID-19. Based on in vitro studies, molnupiravir is not inhibitor or inducer of major drug metabolising enzymes or major drug transporters. Therefore, the potential for molnupiravir interact with concomitant medications is considered unlikely. However, no clinical interaction studies have been performed with molnupiravir. Here, we aimed to evaluate potential drug-drug interactions (DDIs) between molnupiravir and antiretroviral therapy in people living with HIV (PLWH) and COVID -19.

Materials and Methods: The study was conducted from January to March 2022 at Udine Infectious Disease outpatient clinic. Therapeutic Drug Monitoring (TDM) of antiretrovirals trough concentrations was performed before and after last use (on the 5th day) of molnupiravir treatment. Non hospitalized PLWH, older than 18 years, with early onset of mild or moderate COVID-19 disease completing the treatment with molnupiravir were considered.

Results: Nine PLWH (2 women, 7 men, median age 37 years) were enrolled in our study. About 22% of our sample was in a dual antiretroviral therapy: dolutegravir/lamivudine or dolutegravir/rilpivirine. Instead 78% took a triple antiretroviral therapy: 86% of these patients had as backbone therapy emtricitabine/TAF and 14% abacavir/lamivudine. Integrase inhibitors were included as third drug in 86% of triple therapies (33% dolutegravir, 17% elvitegravir, 17% raltegravir, 33% bictegravir), against 14% of protease inhibitors (atazanavir/cobicistat). As shown in Table 1, no relevant DDIs between molnupiravir and antiretroviral therapy was observed, as documented by no significant variations in the trough concentrations before and after molnupiravir treatment. Remarkably, a not significant trend for a reduction of dolutegravir trough concentrations (2686±989 vs. 1639±492 ng/mL, difference: -34%, p=0,104) was observed during molnupiravir treatment. Converseley, molnupiravir had no effects at all on tenofovir trough concentrations (17±11 vs. 14±4 ng/mL, difference: -11%, p=0,345).

Discussion: Our preliminary data are the first that provide clinical information about potential DDIs in molnupiravir tretament. Although our analysis has some limitations such as the small proportion of patients, some observations can be produced. In the struggle against COVID-19 pandemic, molnupiravir demonstrates a safe DDI profile in PLWH and in highly active antiretroviral treatment. The potential effect of molnupiravir on dolutegravir trough concentrtions seems to be of negligible clinical relevance and deserves further investigations.

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Virology and Pharmacology

Pharmacology, pharmacogenomics and drug interactions

P 112 DOLUTEGRAVIR PLASMA AND INTRACELLULAR PHARMACOKINETICS IN THE CLINICAL SETTING

F. Alladio[1], M. Ferrara[1], G. Accardo[1], S. Fantino[1], G. Trevisan[1], E. Drappero[1], A. Serra[1], L.Trentini[1], M. Tettoni[1] , E. De Vivo[2], A. Ianniello[2], J. Mula[2], A. De Nicolò[2], A. D'Avolio[2], A. Calcagno[1] , G. Di Perri[1], S. Bonora[1]

[1]Unit of Infectious Diseases, Department of Medical Sciences, University of Torino, Torino, [2]Laboratory of Clinical Pharmacology and Pharmacogenetics,, Department of Medical Sciences, University of Torino, Torino

Background: Dolutegravir (DTG) is currently used in association with different drug companion as a third drug in the standard of care triple regimen and as part of dual regimen. DTG plasma and intracellular (IC) pharmacokinetics (PK) has been reported to have a higher plasma and IC exposure in lamivudine (3TC)-including vs TAF/FTC-including regimen. CD4+/CD8+ ratio has been discussed as a potential biomarker of inflammation and its role on antiretroviral (ARV) plasma and IC exposure. Aim of the study was to evaluate factors affecting DTG plasma exposure in the clinical setting.

Methods: Patients (pts) administered with DTG 50 mg plus abacavir/lamivudine (ABC/3TC), tenofovir alafanamide/emtricitabine (TAF/FTC), 3TC, rilpivirine (RPV) and protease inhibitors (PIs) were included, after informed consent given. Plasma and IC (PBMC) DTG concentration were measured as Ctrough by means of UHPLC-MS validated method at the end of dosing interval (24+/-4 hours after intake). DTG plasma Ctrough previously reported in literature (1110 ng/mL) was used as cut-off to evaluate plasma exposure. Non-compartmental PK parameters were expressed as geometric mean (CI95%). Pts characteristics were analysed by Kruskall-wallis and Chi-square test and Binary Logistic Regression analysis, as appropriate.

Results: 133 pts were included in the study: 19% on TAF/FTC, 17% on ABC/3TC, 29% on 3TC, 26% on PIs, 9% on RPV. 78.9% of them were male, age and BMI were 51 years (49-53) and 24.2 kg/m2 (23.4-25). Geometric mean DTG plasma Ctrough plus TAF/FTC, ABC/3TC, 3TC, RPV and PIs resulted to be respectively 1107.3 (830.8 -1383.8), 2051 (1597.0-2505.6), 1987.0 (1554.8-2419.3), 1407.8 (854.6-1960.9) and 1647.0 (1043.8-2250.0) ng/mL (p=0.002). DTG IC Ctrough resulted to be 244.5 (179.6-309.5), 485.8 (323.4-648.1), 490 (387.0-593.1), 390.5 (156.0-624.9) and 277.4 (202.2-352.5) ng/mL (p<0.001), and IC/plasma ratio 0.237 (0.188-0.287), 0.231 (0.185-0.278), 0.261 (0.230-0.292), 0.331 (0.172-0.491) and 0.259 (0.190-0.329) ng/ml (p=0.192). On multivariate regression analysis lower CD4+/CD8+ ratio (p=0.012) resulted to be indipendently associated with reduced DTG plasma exposure while 3TC-including regimens (p=0.013) with increased exposure.

Conclusions: In our study, DTG exposure showed to be affected by CD4+/CD8+ ratio. Chronic inflammation has been shown to upregulate efflux pumps, potentially impairing drug distribution. Further studies are needed to evaluate the role of inflammation on DTG PK.

Virology and Pharmacology

Pharmacology, pharmacogenomics and drug interactions

P 113 **ISOENZYMES SUBFAMILIES AND SYMPTOMATIC ADVERSE EVENTS: IS THERE A LINK?**

E. Gentilini Cacciola, A. Lazzaro, P. Vassalini, C. Borrazzo, C.M. Mastroianni, G. d'Ettorre

University of Roma "LaSapienza", Roma

Background: People living with HIV-1 (PLWH) are exposed to a large amount of drugs, concerning not only antiretroviral regimen (ART), but also therapies for their non-AIDS comorbidities. Thus, enzymes involved in transportation and metabolic pathways are overloaded, leading to potential safety problems.
This case-control study collected symptoms of a 50 PLWH cohort, treated with 5 or more drugs including ART therapy, by the patient-reported PRO-CTCAE® questionnaire, developed by the National Cancer Institute to capture symptomatic adverse events. The survey characterizes frequency, severity and presence/absence of symptomatic toxicities reported from the patient perspective. Data about enzymes involved in drugs metabolism, like cytochromes (CYPs); UDP-glucuronosyltransferases (UGTs); organic anion-transporting polypeptide (OTPs); multidrug and toxic compound extrusion proteins (MATEs) and breast cancer resistance protein (BCRP/ABCG2) were collected thanks to DrugBank, a comprehensive resource for in silico drug discovery and exploration. Primary objective was to evaluate which are the common adverse events in our population and association to drug metabolism enzymes, frequently involved in patients polypharmacy. Secondary objectives were to find: an enzymes involvement burden for symptoms onset and severity; ART regimen more frequently involved in symptoms onset. Baseline characteristics are described as mean values ± standard deviation (SD), simple frequencies (n) and percentages (%). P-values (p) < 0.05 were considered statistically significant.
Results: Baseline demographic, immunovirological and therapeutic data shown a mean age of 61 (±1.2 S.D.); nadir CD4 243 (44.3 S.D.); current mean CD4 count 761 (±51 S.D.) years of HIV infection 22 (±14 S.D.), years of TARV 20 (±14 S.D.), undetectable RNA in 70% of patient, NRTI in 86% of TARV regimens, NNRTI 20% of TARV regimens, PI 16% of TARV regimens, INSTI 76% of TARV regimens, Cobicistat 14% of TARV regimens. The most common symptoms are shown in Figure 1.
Relationships were found: numbness and tingling associated with inhibition of CYP2B6 (95% CI 1.01-7.3; P 0.022); heart palpitations with inhibition OATP1B1/SLC01B1(95% CI 1.12-9.6; P 0.001), CYP2E1(95% CI 1.4-137; P<0.001), BCRP/ABCG(95% CI 1.21-18.5, P 0.021); achieving and maintaining erection with OAT3/SLC22A8 inhibition (95% CI 1.01-14.9; P 0.012); dry skin associated with CYP2B6 (95% CI 1.01-17.3; P 0.022) and CYP2D6 (95% CI 1.44-18.8; P<0.001). About relationship of symptoms and ART regimen, Non Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) are the most frequent drug involved in symptoms onset (20%) following Nucleoside Reverse Transcriptase T-Inhibitors (NRTIs 14%), Protease Inhibitors (PIs 10%) and Integrase Strand Transfer Inhibitors (INSTIs 9%).
Conclusions: We found several associations of symptoms with metabolic pathways; we found a burden of enzymes involved in the symptoms onset and ART drugs associated with presence of symptoms.

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Virology and Pharmacology

SARS-CoV-2 virology

P 114 **DISCERNING THE MOLECULAR MECHANISM BEYOND THE UV-PHOTOINACTIVATION OF SARS-COV-2**

S. Strizzi[1], L. Bernardo[2], A. Bianco3, D. Trabattoni[1], A. De Palma[2], G. Pareschi[3], P. D'Ursi[2], M. Clerici[1], P. Mauri[2], M. Biasin[1]

[1]DIBIC University of Milan, [2]Proteomic Unit of Institute for Biomedical Technologies – CNR, Segrate (MI), Italy, [3]INAF- Brera Astronomical Observatory Merate

Background: All airborne RNA viruses are highly susceptible to UVA-B-C light photoinhibition, as recently demonstrated for SARS-CoV-2, but the mechanisms beyond this effect are still unclear. Such information could be useful to design and develop new photoinactivating devices as well as to identify new molecular targets. We faced this exciting scientific with an in-depth analysis on the molecular modification caused by UVC exposure on the Spike protein of SARS-CoV-2, which represents the key to enter human cells; in parallel, we assessed the effect of UV-A -B -C radiations on different SARS-CoV-2 Variants of Concern (VOC) to highlight differences and to validate the model.

Material and methods: Following Spike protein exposure to UVC radiation the molecular modifications were assessed by means of nano-liquid chromatography coupled to high resolution tandem mass spectrometry (nLC-hrMS/MS) after enzymatic digestion. The altered protein domains were further investigated by computational analysis to evaluate potential changes of the 3D structural folding and functions.

In order to validate the UV-inhibiting effect on different SARS-CoV-2 VOC (B.1.617.2, BA.1), an established viral concentration was exposed to each UV light source and viral titers were determined by TCID50 endpoint dilution assay.

Results: Our preliminary tests evidenced modifications in five peptide sequences of wild type (WT) SARS-CoV-2 Spike protein following UVC treatment. Such modifications include oxidations and the cleavage of specific disulfide bonds. By computational analyses they were correlated with conformational changes in functional domains of the viral receptor protein.

TCID50 data confirmed that SARS-CoV-2 VOC Delta (B.1.617.2) and Omicron (BA.1) are inactivated at the same extent of the WT strain by applying similar UVA, UVB and UVC doses.

Conclusions: These data endorse the broad mechanism of action exerted by UV on SARS-CoV-2 and its VOC and allow to identify the specific molecular modifications induced by UVC exposure on the Spike protein.

Further analyses on UV-induced inactivation on other viral structures will allow to achieve a thorough understanding of the natural mechanisms of UV/Solar-inhibiting effect, and how to exploit them in fighting future epidemic against SARS-CoV-2 and new emerging airborne viruses.

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Virology and Pharmacology

SARS-CoV-2 virology

P 115 QUALITATIVE AND QUANTITATIVE APPROACH TO SARS-COV-2 RNA DETECTION

C. Orlandi[1], A. De Maria[2], M. Magnani[1], A. Casabianca[1]

[1]Department of Biomolecular Sciences, University of Urbino Carlo Bo, Urbino, Italy, [2]Department of Internal Medicine, Centre of Excellence for Biomedical Research, University of Genoa, Genoa, Italy

Background: Severe acute respiratory syndrome (SARS) coronavirus 2 (SARS-CoV-2) is causing a global pandemic and affecting global health and the world economy. Virus RNA might be detectable in nasopharyngeal swabs (NPS) by reverse transcription PCR (RT-PCR), and RT-PCR has been indicated as the first choice in the diagnosis of SARS-CoV-2. Multiple diagnostic kits, as well as different platforms were used to test COVID-19 infection according to the Ct values for different viral genes detection. We used two one-step RT-PCR assays to detect three different genes (RdRp, ORF1b and N) of the viral genome. We produced qualitative results according to the manufacturers of the different assays. Moreover, we tried to upgrade the assay with a semi-quantitative analysis to provide the results of SARS-CoV-2 RNA as copies per 10^6 cells.

Material and Methods: Nucleic acids from NPS were extracted using Total RNA Purification Kit (Norgen). SARS-CoV-2 RNA was amplified using two commercially available CE IVD kit for the detection of RdRp, N and ORF1b targets according to the manufacturer's specifications. To estimate the cells present in each PCR reaction the single copy human Rpp40 gene was used as a normalization factor.

Results: Eight NPS were selected to obtain the PCR amplification efficiencies of all targets of interest and to determine the optimal amount of sample with no inhibitory effects in qPCR (i.e. undiluted and dilutions). The mean ±SD efficiencies were from 93±7% to 99±8% for the viral genes and 100±12% for the Rpp40 gene. For 4 out of 8 samples only the undiluted sample gave a positive amplification signal for the viral targets (Ct 35.15-41.42). For this reason, the undiluted quantity was chosen for the subsequent quantitative analyses of all the other samples and for Rpp40 amplification. A total of 84 NPS were tested and target copy no./PCR, cells/PCR and target copy no./10^6 cells are shown in Table 1. The copy number was quantified by interpolating the experimentally determined Ct based on standard curves generated using 10-fold serially diluted PCR positive controls provided in each commercial assay. Samples with a similar viral gene copy no./PCR, i.e. those distributed in the range of one log, when normalized for a constant number of cells (one million) were effectively distributed in a range of up to 3 logs (mean±SD 2.21±0.7; range 0.7-3.2), showing differences in viral RNA content up to 1000 times. This was observed for all three genes and for the entire quantitation range.

Conclusions: Qualitative and quantitative measures of viral load in SARS-CoV-2 positive patients provide effective tools for defining the severity of infection and for monitoring the risk of virus transmission and of COVID -19 disease progression. Our results demonstrated that an appropriate reference standard and a normalization factor for viral RNA can be used for viral load quantification to track viral titer kinetics and to compare results between different studies.

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Virology and Pharmacology
Vaccines (other than SARS-CoV-2)

P 116 **PERSISTENCE OF IMMUNE RESPONSES AFTER THE ADMINISTRATION OF THE MENINGOCOCCAL SEROGROUP A, C, W-135 AND Y CRM-197 CONJUGATE VACCINE (MENVEO®) IN HIV-VERTICALLY TRANSMITTED YOUNG PATIENTS**

C. Vanetti[1], C. Fenizia[2], F. Ardizzone[1], I. Saulle[1], M. Stracuzzi[3], F. Da Pozzo[3], L. Paradiso[3], E. Longoni[3], L. Barcellini[4], M. Biasin[1], M. Clerici[2,5], G.V. Zuccotti[3,4], V. Giacomet[3], D. Trabattoni[1]

[1]University of Milan, Department of Biomedical and Clinical Sciences "Luigi Sacco", Milan, [2]University of Milan, Department of Pathophysiology and Transplantation, Milan, [3]Ospedale "Luigi Sacco", University of Milan, Department of Pediatric Infectious Diseases, Milan, [4]University of Milan, Ospedale dei Bambini V. Buzzi, Department of Pediatrics, Milan, [5]IRCCS Fondazione Don Gnocchi, Milan

Background: A higher incidence of meningococcal disease is reported in HIV-infected patients compared with the general population. For this reason, it is recommended that HIV-infected persons aged ≥2 months should routinely receive meningococcal conjugate vaccine. However, HIV-subjects, because of immune abnormalities, may undergo impaired vaccine response. Our study aims to assess humoral and cell-mediated immune responses after the administration of a quadrivalent meningococcal conjugate vaccine Menveo® (MenACWY-CRM, GlaxoSmithKline Vaccines) in HIV-infected young patients.

Material and Methods: We carried out a controlled, non-randomized, observational and prospected study, involving 27 HIV-infected patients aged 9–30 years, reporting vertically-transmitted HIV infection and followed at the Pediatric Infective Disease Clinic of ASST FBF-Sacco, Milan Italy. All patients enrolled were on ART, and 25 out of 27 presented optimal immunological and viral response. Each subject received the vaccine Menveo (0,5 ml i.m.). MenACWY-specific Ab titer, viral load, and CD4+ T cells count were measured at baseline (T0), T3, T6 and T12 months post vaccination. MenACWY-specific cell-mediated immune responses were evaluated at the same time points.

Results: Menveo induced seroconversion in 26 out of 27 subjects. We divided our cohort in different subgroups: Responders (R), reporting seroconversion at T3, Highly-Responders (HR) with a high Ab titer at T0, and Non-Responders (NR). The administration of the vaccine induced MenACWY-specific immunological memory mainly in R and HRs: CD4+ (at T12) and CD8+ (at T3 and T12) T Central Memory. MenACWY-specific TNFα-, IFNγ- CD8+ T cells and IL2-secreting CD4+ T cells were increased in Rs and HRs at T3 and T6. However, at T12, this effect was slightly decreased. In the NR group, terminally-differentiated CD4+ and CD8+ T cells were the only parameters modified.

Conclusions: The administration of Menveo® vaccine induced a valid antibody-mediated protection in both the R and HR subgroups. We observed the development of a stable T cell-mediated immune memory that lasted robustly up to one year since vaccination in most of the subjects analyzed. Furthermore, we observed increased CD8+ CTL functions specifically in Rs and HRs, with significant increases of TNFα and IFNγ secretion.

The lack of Menveo-specific immune response, observed in the NR subject, is associated with a low compliance to the therapy and high viremia. Our data indicate that alternate immunization schedules need to be considered in ART-non-responder patients.

ICAR 2022
Bergamo
14-16 Giugno
2022

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Provider e Segreteria Organizzativa
Effetti srl
Via G.B. Giorgini, 16 - 20151 Milano
Tel. +39 02 3343281- Fax +39 02 38002105
icar2022@effetti.it - @ICARcongress

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