Dermatology Practical & Conceptual

Real Life Comparative Effectiveness of IL-23 Inhibitors in the Treatment of Moderate to Severe Psoriasis: A Multicenter Experience

Alessandro Borghi[1], Giulia Odorici[1], Federico Bardazzi[2], Federica Filippi[2], Laura Bigi[3], Claudia Lasagni[3], Marco Manfredini[3], Vito Di Lernia[4], Francesca Peccerillo[4], Andrea Conti[5], Rossana Tiberio[5], Francesca Satolli[6], Carolina Fantini[6], Miriam Rovesti[7], Massimo Gasperini[7], Michela Tabanelli[8], Simone D'Adamio[8], Maria Elena Flacco[9], Monica Corazza[1]

1 Section of Dermatology and Infectious Diseases, Department of Medical Sciences, University of Ferrara, Ferrara, Italy
2 Dermatology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Policlinico S. Orsola-Malpighi, Bologna, Italy
3 Dermatology Unit, Department of Surgical, Medical, Dental and Morphological Sciences Related to Transplant, Oncology and Regenerative Medicine, University of Modena and Reggio Emilia, Modena, Italy
4 Dermatology Unit, Arcispedale Santa Maria Nuova, Azienda Usl-IRCCS di Reggio Emilia, Reggio Emilia, Italy
5 Dermatology Unit, Infermi Hospital, Rimini, AUSL Romagna, Italy
6 Section of Dermatology, Department of Medicine and Surgery, University of Parma, Parma, Italy
7 Dermatologic Unit, Ospedale "Guglielmo da Saliceto" di Piacenza PC, Italy
8 UOC Dermatology of Ravenna, Lugo and Faenza, Italy
9 Department of Environmental and Prevention Sciences, University of Ferrara, Ferrara, Italy

Key words: Psoriasis, IL23 inhibitors, therapy, effectiveness, retention rate, real life

Citation: Borghi A, Odorici G, Bardazzi F, et al. Real Life Comparative Effectiveness of IL-23 Inhibitors in the Treatment of Moderate to Severe Psoriasis: A Multicenter Experience. *Dermatol Pract Concept*. 2024;14(3):e2024179. DOI: https://doi.org/10.5826/dpc.1403a179

Accepted: March 25, 2024; **Published:** July 2024

Funding: None.

Competing Interests: None.

Authorship: All authors have contributed significantly to this publication. Alessandro Borghi and Giulia Odorici contributed equally and share first authorship. Maria Elena Flacco and Monica Corazza contributed equally and share co-senior authorship.

Corresponding Author: Dr. Giulia Odorici, UO Dermatologia, Dipartimento Ospedaliero Oncologico- Medico specialistico, Azienda Ospedaliero - Universitaria Arcispedale Sant'Anna, Via Aldo Moro 8, Cona (FE), Italy. Tel: (+39) 0532/239684, Fax: 0039 0532/206791. E-mail: giulai87@hotmail.com

Introduction

With the aim of assessing and comparing IL23 inhibitors' effectiveness, safety and drug survival in a real life setting, we performed a retrospective study involving all psoriasis centers of Emilia Romagna, northern Italy.

Case Presentation

All 427 patients affected with moderate-to-severe psoriasis who consecutively underwent treatment with anti IL23 drugs from December 2018 to June 2022 were included. Among them, 201 received guselkumab, 116 risankizumab and 110 tildrakizumab (Table 1).

Table 1. Selected baseline demographic and clinical characteristic of the sample, overall and by type of anti-IL23.

Variables	Overall sample (n=427)	Guselkumab (n=201)	Risankizumab (n=116)	Tildrakizumab (n=110)	p*
Mean age in years (SD)	54.3 (14.7)	52.8 (14.6)	56.0 (13.6)	55.2 (15.7)	
Male gender, %	63.2	60.7	62.9	68.2	
Mean BMI (SD)	27.9 (5.2)	27.8 (5.4)	27.9 (5.0)	28.2 (5.0)	
Current smoker, %	58.4	49.4	68.5	63.6	a, b
Comorbidities, %					
None	36.1	36.3	31.9	40.0	
One	43.3	38.8	50.9	43.6	a
Two	17.3	19.4	15.5	15.5	
Three or more	3.3	5.5	1.7	0.9	b, c
Mean length of disease in years (SD)	20.6 (12.4)	20.1 (12.5)	21.7 (12.2)	20.2 (12.6)	
Mean age at onset (SD)	33.3 (16.0)	32.3 (16.2)	33.7 (14.4)	34.8 (17.2)	
Concomitant arthritis, %	27.3	30.8	28.7	19.3	b
Psoriasis type, %					
Vulgaris	84.0	84.6	80.9	86.4	
Inverse	3.1	2.5	0.8	6.4	a, b, c
Others[A]	4.9	3.4	7.0	5.4	
Composite[B]	8.0	9.5	11.3	1.8	b
Psoriasis site, %					
Typical	58.8	58.7	44.8	73.6	a, b, c
Folds	27.2	28.8	35.3	15.5	b, c
Hands and feet	11.7	10.0	16.4	10.0	
Others (nails, scalp, genital)	2.3	2.5	3.5	0.9	
Number of previous traditional treatments, %					
None	4.2	4.0	1.7	7.3	
One	31.6	28.9	29.3	39.1	
Two	34.2	33.3	33.6	36.4	
Three or more	30.0	33.8	35.3	17.3	
Number of previous biologic treatments, %	(N=395)	(N=189)	(N=111)	(N=95)	
None	24.8	23.8	26.1	25.3	
One	29.9	23.3	24.3	49.5	
Two	21.3	22.2	25.2	14.7	b
Three or more	24.0	30.7	24.3	10.5	b
Median duration of previous biologic treatments in months (IQR)	29.0 (69.5)	35.0 (69.0)	40.0 (60.0)	14.5 (24.0)	
Mean PASI at baseline (SD)	12.9 (7.3)	13.5 (7.6)	11.9 (7.1)	12.9 (6.8)	

SD: Standard deviation; IQR: Interquartile range. PASI: Psoriasis area severity index.

[A]Guttate, pustular, or erythrodermic psoriasis; [B]More than one type of psoriasis concomitantly reported.

*Chi-squared test for categorical variables; one-way ANOVA with Sidak corrections for continuous ones. a: $p<0.05$ for the comparison between patients treated with Guselkumab and patients treated with Risankizumab; b: $p<0.05$ for the comparison between patients treated with Guselkumab and patients treated with Tildrakizumab; c: $p<0.05$ for the comparison between patients treated with Risankizumab and patients treated with Tildrakizumab. All p-values that are not indicated were ≥0.05.

Overall, 63.9% of the patients had at least one comorbidity, including infectious, cardiometabolic and autoimmune diseases or cancer-positive history; 27.3% had concomitant psoriatic arthritis.

At baseline, the mean PASI was 12.9 ±7.3, without differences among treatment groups.

With reference to previous systemic treatments for psoriasis, 95.8% of patients had previously been treated with at least one traditional drug and 75.2% were biologic-experienced.

After 12 weeks of treatment, mean PASI score decreased by almost 80% from baseline in the entire study population and nearly half of the subjects achieved PASI90 (Table 2). A complete clearance was reached by more than one third of the study patients at this time point.

It should be noted that in the early stages of treatment, a difference was observed among the three molecules. In fact, risankizumab was significantly more effective than the other two molecules after a 12-week treatment duration and guselkumab was more effective than tildrakizumab.

After 28 weeks, clinical improvement was further increased, with a mean PASI reduction of 86% compared with the baseline. Mean PASI was 1.5 ±3.3 in the study population considered as a whole. Nearly 60% of patients achieved complete clearance. Unlike the first weeks of treatment, no significant differences were found with respect to the performance of the three molecules at the 28-week control.

Gender, age, BMI, disease duration, concomitant psoriatic arthritis, involvement of particular anatomical districts, number of previous traditional treatments and duration of previous biologic treatments did not correlate with psoriasis improvement. Therefore, involvement of critical and/or difficult-to-treat skin areas, including face, palms, soles, scalp and genitals, which are characterized by a high impact on sufferers' quality of life and functionality, overweight or obesity, which are common among psoriatic patients, or

Table 2. Selected clinical characteristic of the sample, and outcomes, overall and by type of anti-IL23.

Variables	Overall sample (n=427)	Guselkumab (n=201)	Risankizumab (n=116)	Tildrakizumab (n=110)	p *
Mean duration of anti-IL 23 treatment in months (SD)[A]	18.9 (10.8)	22.2 (11.7)	15.9 (7.5)	15.8 (10.4)	a, b
Drug survival, %	94.6	95.0	96.6	91.7	
Mean PASI at baseline (SD)	12.9 (7.3)	13.5 (7.6)	11.9 (7.1)	12.9 (6.8)	
Mean PASI at week 12 (SD)	2.8 (3.4)	2.2 (2.1)	1.5 (2.7)	4.1 (4.5)	
Mean PASI % reduction between baseline and week 12, (SD)	77.8 (25.9)	82.2 (18.7)	89.8 (20.5)	67.4 (31.4)	b, c
Baseline-week 12 PASI reduction ≥75%, %	63.3	67.3	86.1	48.8	a, b, c
Baseline-week 12 PASI reduction ≥90%, %	45.0	45.8	72.2	32.6	a, c
Baseline-week 12 PASI 100% decrease, %	34.1	30.8	69.4	23.3	a, b, c
Mean PASI at week 16 (SD)	1.8 (3.0)	1.6 (2.4)	1.2 (2.5)	4.4 (5.1)	b, c
Mean PASI % reduction between baseline and week 16, (SD)	81.9 (39.5)	82.6 (41.3)	86.6 (30.4)	64.5 (51.0)	
Baseline-week 16 PASI 90% decrease, %	64.7	64.9	75.0	33.3	b, c
Baseline-week 16 PASI 100% decrease, %	47.4	39.2	68.2	26.7	a, c
Mean PASI at week 28 (SD)	1.5 (3.3)	1.2 (2.9)	1.5 (2.8)	1.9 (4.0)	
Mean PASI % reduction between baseline and week 28, (SD)	86.0 (33.3)	86.3 (40.3)	83.1 (32.5)	87.4 (19.3)	
Baseline-week 28 PASI reduction ≥75%, %	83.9	87.9	78.3	81.4	
Baseline-week 28 PASI 90% decrease, %	73.2	76.9	69.6	70.0	
Baseline-week 28 PASI 100% decrease, %	57.1	61.1	60.9	48.6	

SD: Standard deviation; PASI: Psoriasis area severity index.

[A]Patients not withdrawn from anti-IL 23 treatment only.

*Chi-squared test for categorical variables; one-way ANOVA with Sidak corrections for continuous ones. a: p<0.05 for the comparison between patients treated with Guselkumab and patients treated with Risankizumab; b: p<0.05 for the comparison between patients treated with Guselkumab and patients treated with Tildrakizumab; c: p<0.05 for the comparison between patients treated with Risankizumab and patients treated with Tildrakizumab. All p-values that are not indicated were ≥0.05.

advanced age do not represent either selection or exclusion criteria for this class of drugs.

IL23 inhibitors showed no significant safety findings and no relevant clinical or laboratory side-effects were recorded. The incident events that led to treatment suspension, namely a diagnosis of melanoma, concurrent urticaria and worsening of the arthritis, had no correlation with their administration. These drugs did not impact on concomitant critical infectious conditions or on cancer history.

IL23 inhibitors' favorable safety profile accounts for the very high drug survival found in the study, which was close to 95%. (1,2,3)

Conclusion

The study findings show that these drugs are very effective, rapid, well tolerated, also in comorbid subjects. Apart from initial differences in rapidity, risankizumab being more rapid than guselkumab and even more than tildrakizumab in the early treatment stages, the three drugs do not differ either in effectiveness or in safety.(4,5)

The overall very high drug survival of IL23 inhibitors observed, allows us to consider them optimal therapeutic options in clinical practice. (6)

References

1. Mastorino L, Dapavo P, Susca S, et al. Drug survival and clinical effectiveness of secukinumab, ixekizumab, brodalumab, guselkumab, risankizumab, tildrakizumab for psoriasis treatment. *J Dtsch Dermatol Ges*. 2023 Nov
2. Megna M, Tommasino N, Potestio L, et al. Real-world practice indirect comparison between guselkumab, risankizumab, and tildrakizumab: results from an Italian 28-week retrospective study. *J Dermatolog Treat*. 2022;33:2813-2820
3. Reich K, Gordon KB, Strober B, et al. Super-response to guselkumab treatment in patients with moderate-to-severe psoriasis: age, body weight, baseline Psoriasis Area and Severity Index, and baseline Investigator's Global Assessment scores predict complete skin clearance. *J Eur Acad Dermatol Venereol*. 2022; 36:2393-2400.
4. Elgaard CDB, Iversen L, Hjuler KF. Guselkumab, Tildrakizumab and Risankizumab in Real-World Setting: Drug Survival and Effectiveness in the Treatment of Psoriasis and Psoriatic Arthritis. *J Dermatolog Treat*. 2022 6:1-24.
5. Ruggiero A, Fabbrocini G, Cinelli E, et al. Real world practice indirect comparison between guselkumab and risankizumab: Results from an Italian retrospective study. *Dermatol Ther*. 2022;35:e15214.
6. Gisondi P, Fargnoli MC, Amerio P, et al. Italian adaptation of EuroGuiDerm guideline on the systemic treatment of chronic plaque psoriasis. *Ital J Dermatol Venerol*. 2022;157(Suppl. 1 to No. 1):1-78.