HemaSphere
Powered by EHA

EHA EUROPEAN HEMATOLOGY ASSOCIATION

Comment
OPEN ACCESS

# Hodgkin Lymphoma: Comments on ESMO Clinical Practice Guidelines

Igor Aurer[1], Natalia Zing[2,3], Massimo Federico[3]

**Correspondence:** Massimo Federico (e-mail: massimo.federico@unimore.it).

EHA and ESMO recently agreed to collaborate in the production of European Guidelines for different hematological malignancies. As a first step, a number of completed guidelines have been reviewed by the corresponding EHA Scientific Working Groups in a standardized review process.

The ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up for Hodgkin lymphoma (HL) released in the mid of 2018 in accordance with the ESMO standard operating procedures for Clinical Practice Guidelines development,[1] represents an example of this collaboration and have been recently endorsed by the EHA Lymphoma Group (LyG).[2]

HL is a highly curable disease by current treatment modalities with a reported 5-year survival of 90% in 2015 in the United States.[3] However, if we consider that in HL survivorship starts with initial treatment selection, the availability of recommendations prepared by experts in the field represent a relevant support for decision making in the daily practice.

The ESMO for HL guidelines were based on results of studies whose results were available in 2018 and provided robust recommendations regarding treatment strategies designed on PET based staging and early response assessment.[4] In the past 2 years, some new data emerged which we will discuss in this editorial.

When deciding on optimal treatment it is important to allocate patients in the appropriate risk group according to the EORTC/LISA or the GHSG criteria.

For patients with limited or intermediate-stage disease, combined modality treatment consisting of a brief chemotherapy (ChT) followed by radiation therapy (RT) is still the standard approach, also in case of PET guided approach.[5,6]

Advanced-stage HL is usually treated with systemic treatment, additional RT is confined to approximately 10% of patients with residual disease after systemic treatment.[7,8]

Patients $\leq$ 60 years may be successfully treated with either ABVD (6 cycles) (adriamycin, bleomycin, vinblastine, dacarbazine) or escBEACOPP (4– 6 cycles) (escalated bleomycin, etoposide, Adriamycin, cyclophosphamide, Oncovin, procarbazine, prednisone). New data indicate that 6 cycles of AVD + brentuximab vedotin (BV) (with obligatory G-CSF support) represent a third opportunity with efficacy and toxicity intermediate between ABVD and eBEACOPP.[9] ABVD represents the standard of care for older HL patients who are fit enough for doxorubicin containing regimens, but patients older than 65 to 75 should not receive more than 2 cycles of bleomycin due to increased severe lung toxicity.[10] Concomitant administration of AVD+BV is too toxic in this patient population, but interesting results can be achieved with sequential administration.[11]

High dose chemotherapy (HDCT) followed by autologous stem cell transplantation (ASCT) represents the treatment of choice for fit patients with refractory/relapsed HL,[12] with BV and antiPD-1 antibodies proposed as options in patients failing ASCT.[13,14] Recently, published phase 2 studies suggest that addition of BV to HDCT is feasible, possibly resulting in ≈15% more PET negative remissions and 2 to 3 year event-free survival, than chemotherapy alone.[15]

Hopefully some of the many recent trials exploring new regimens like antiPD-1 antibodies plus AVD in first line,[16] as well as better tools for response-adapted treatment or new molecular prognostic markers able to more precisely identify the high risk population, will further improve the efficacy and safety of treatment of HL.

## References

1. ESMO Guidelines Methodology. https://www.esmo.org/guidelines/esmo-guidelines-methodology. Accessed 18 May 2020.
2. EHA Lymphoma Group (EHA LyG) 2020. https://www.ehalyg.org/. Accessed 18 May 2020.
3. National Cancer Institute, Surveillance, Epidemiology, and End Results Program 2020. https://seer.cancer.gov/statfacts/html/hodg.html. Accessed 18 May 2020.
4. Eichenauer DA, Aleman BMP, André M, et al. Hodgkin lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2018;29(Suppl 4):iv19–iv29.
5. Engert A, Plütschow A, Eich HT, et al. Reduced treatment intensity in patients with early-stage Hodgkin's lymphoma. *N Engl J Med.* 2010;363:640–652.

[1]*Division of Hematology, Department of Internal Medicine, University Hospital Centre Zagreb and Medical School, University of Zagreb, Zagreb, Croatia*
[2]*Departament of Onco-Hematology, Beneficência Portuguesa Hospital, São Paulo, Brazil*
[3]*Medical Oncology, CHIMOMO Department, University of Modena and Reggio Emilia, Modena, Italy.*
*IA: Employment/Consultation with Takeda. Grants from Takeda. Royalties of payments for lectures/manuscript preparations/etc from Takeda.*
*NZ: Employment with Prevent Senior; Beneficência Portuguesa de São Paulo. Grants from AstraZeneca.*
*MF: Nothing to disclose.*

*HemaSphere (2020) 4:4(e458). http://dx.doi.org/10.1097/HS9.0000000000000458.*
*Received: 18 May 2020 / Accepted: 23 June 2020*

6. André MP, Girinsky T, Federico M, et al. Early positron emission tomography response-adapted treatment in stage I and II Hodgkin lymphoma: final results of the randomized EORTC/LYSA/FIL H10 trial. *J Clin Oncol.* 2017;35:1786–1794.
7. Borchmann P, Goergen H, Kobe C, et al. PET-guided treatment in patients with advanced-stage Hodgkin's lymphoma (HD18): final results of an open-label, international, randomised phase 3 trial by the German Hodgkin Study Group. *Lancet.* 2018;390:2790–2802.
8. Johnson P, Federico M, Kirkwood A, et al. Adapted treatment guided by interim PET-CT scan in advanced Hodgkin's lymphoma. *N Engl J Med.* 2016;374:292419.
9. Connors JM, Jurczak W, Straus DJ, et al. Brentuximab vedotin with chemotherapy for Stage III or IV Hodgkin's Lymphoma. *N Engl J Med.* 2018;378:331–344.
10. Böll B, Goergen H, Behringer K, et al. Bleomycin in older early-stage favorable Hodgkin lymphoma patients: analysis of the German Hodgkin Study Group (GHSG) HD10 and HD13 trials. *Blood.* 2016;127:2189–2192.
11. Evens AM, Advani RH, Helenowski IB, et al. Multicenter phase II study of sequential brentuximab vedotin and doxorubicin, vinblastine, and dacarbazine chemotherapy for older patients with untreated classical hodgkin lymphoma. *J Clin Oncol.* 2018;36:3015–3022.
12. Rancea M, Monsef I, von Tresckow B, Engert A, Skoetz N. High-dose chemotherapy followed by autologous stem cell transplantation for patients with relapsed/refractory Hodgkin lymphoma. *Cochrane Database Syst Rev.* 2013:CD009411.
13. Younes A, Santoro A, Shipp M, et al. Nivolumab for classical Hodgkin's lymphoma after failure of both autologous stem-cell transplantation and brentuximab vedotin: a multicentre, multicohort, single-arm phase 2 trial. *Lancet Oncol.* 2016;17:1283–1294.
14. Younes A, Gopal AK, Smith SE, et al. Results of a pivotal phase II study of brentuximab vedotin for patients with relapsed or refractory Hodgkin's lymphoma. *J Clin Oncol.* 2012;30:2183–2189.
15. Moskowitz AJ, Herrera AF, Beaven AW. Relapsed and refractory classical hodgkin lymphoma: keeping pace with novel agents and new options for salvage therapy. *Am Soc Clin Oncol Educ Book.* 2019;39:477–486.
16. Bröckelmann PJ, Goergen H, Keller U, et al. Nivolumab and AVD for early-stage unfavorable hodgkin lymphoma (NIVAHL). *Blood.* 2019;134 (Supplement_1):236.