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Scientific Comment

Hodgkin's lymphoma in developing countries: can we go further?☆

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Hodgkin's lymphoma (HL) is a B cell malignancy that affects approximately 8000 new patients in the United States annually.¹ This is the most common lymphoma affecting the young population with a higher incidence at ages 15 to 35 years. Because of its particular histological features and biological behavior, HL is highly responsive to chemotherapy and radiation, and therefore is considered a model of successful cancer treatment. In fact, in the last decades, important advances were made regarding HL treatment resulting in unprecedented high cure rates. Elegantly designed clinical trials conducted by important cooperative groups in Europe and North America have set the basis for treatment and established the guidelines for HL management in the modern era. In early-stage disease, treatment based on the ABVD (Doxorubicin, Bleomycin, Vinblastine, Dacarbazine) regimen remains the standard of care. Short-course chemotherapy (2–4 cycles) followed by radiotherapy (20–30 Gy) has demonstrated high efficacy and acceptable acute and long-term toxicity, with cure rates that exceed 90%.² Duration of treatment and doses of radiation depend on the presence of some adverse prognostic factors.³ In advanced-stage HL, the best treatment choice has been a matter of exhaustive debate. In the United States, 6–8 cycles of ABVD remains the standard of care, resulting in 5-year failure-free survival of 60% and 5-year OS of 73%.^{4,5} In Europe, the German Hodgkin Study Group has developed a more intensive protocol, the escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine,

procarbazine, and prednisone) regimen, which is widely used in many centers. When compared to ABVD, escalated BEACOPP results in better progression-free and overall survival but with more acute and late toxicities.^{6–8} Defining which patients really do benefit from more intensive regimens is still a challenge.⁹ More recently, the concept of response-adapted therapy based on interim positron emission tomography-computed tomography (PET-CT) has proven to be of prognostic importance and seems to improve outcomes by identifying patients who are most likely to benefit from more potent treatment regimens.¹⁰

In developing countries, however, the outcomes of HL treatment are not so exciting. Although data is scarce and mostly comes from small population-based and retrospective studies, the reported progression-free survival and overall survival are significantly lower than those observed in developed countries, especially for advanced-stage disease.^{11,12} In this issue of the *Revista Brasileira de Hematologia e Hemoterapia*, Jaime-Pérez et al.¹³ present the data of 128 HL patients retrospectively studied at a university hospital in Monterrey, Mexico. The authors found a high rate of primary refractory disease (43% of the entire cohort) and poor 5-year progression-free survival (PFS) even for the early-stage population (median: 42.7%; 95% confidence interval: 27.5–57.9). Noteworthy, the majority of patients presented with advanced disease and up to 20% experienced chemotherapy dose reductions due to toxicity or did not complete the planned treatment. Some robust

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☆ See paper by Jaime-Pérez et al. on pages 325–30.

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data has recently been published by the Brazilian Prospective Hodgkin's Lymphoma Registry,¹⁴ similarly showing a high proportion of advanced-stage HL at the moment of diagnosis in Brazil. However, the 3-year PFS and overall survival (OS) were 74% and 90%, respectively, better than those observed in the Mexican study. With small differences, similar findings have been observed in other developing countries.^{11,12,15,16} Altogether, these data suggest that outcomes of HL treatment are very heterogeneous across different regions of the world. One possible explanation is that in many developing countries patients may not have easy access to public healthcare, which could postpone diagnosis and increase the number of more advanced-stage HL. Once diagnosed, patients not always have full access to adequate staging procedures (even computed tomography), resulting in a considerable number of under staged and, therefore, undertreated cases. Additionally, some hospitals not always have appropriate emergency supportive care to deal with chemotherapy complications, thereby increasing morbidity and mortality rates. Finally, differences in the economic and social environment, pattern of Epstein-Barr virus infection and genetic background may also explain some differences in HL behavior at different geographic locations.¹⁷ Indeed, lower economic status has been associated with more aggressive disease and worse outcomes in HL.¹⁸

Although Jaime-Pérez et al. described a single institution experience, their work brings into focus a very important concern about the management of HL in countries with limited resources. All the efforts necessary to improve diagnosis and treatment outcomes are of extreme importance and strongly desirable in the context of a highly curable disease.

Conflicts of interest

The author declares no conflict of interest

REFERENCES

1. National Cancer Institute Surveillance. Epidemiology, and End Results (SEER) Program Populations (1969–2015). DCCPS, Surveillance Research Program, released December, 2016. Available from: www.seer.cancer.gov/popdata
2. Engert A, Plütschow A, Eich HT, Lohri A, Dörken B, Borchmann P, et al. Reduced treatment intensity in patients with early-stage Hodgkin's lymphoma. *N Engl J Med*. 2010;363(7):640–52.
3. Eich HT, Diehl V, Gorgen H, Pabst T, Markova J, Debus J, et al. Intensified chemotherapy and dose-reduced involved-field radiotherapy in patients with early unfavorable Hodgkin's lymphoma: final analysis of the German Hodgkin Study Group HD11 trial. *J Clin Oncol*. 2010;28(27):4199–206.
4. Viviani S, Bonadonna G, Santoro A, Bonfante V, Zanini M, Devizzi L, et al. Alternating versus hybrid MOPP and ABVD combinations in advanced Hodgkin's disease: ten-year results. *J Clin Oncol*. 1996;14(5):1421–30.
5. Duggan DB, Petroni GR, Johnson JL, Glick JH, Fisher RI, Connors JM, et al. Randomized comparison of ABVD and MOPP/ABV hybrid for the treatment of advanced Hodgkin's disease: report of an intergroup trial. *J Clin Oncol*. 2003;21(4):607–14.
6. Engert A, Diehl V, Franklin J, Lohri A, Dörken B, Ludwig W-D, et al. Escalated-dose BEACOPP in the treatment of patients with advanced-stage Hodgkin's lymphoma: 10 years of follow-up of the GHSG HD9 study. *J Clin Oncol*. 2009;27(27):4548–54.
7. Engert A, Haverkamp H, Kobe C, Markova J, Renner C, Ho A, et al. Reduced-intensity chemotherapy and PET-guided radiotherapy in patients with advanced stage Hodgkin's lymphoma (HD15 trial): a randomised, open-label, phase 3 non-inferiority trial. *Lancet*. 2012;379(9828):1791–9.
8. Skoetz N, Will A, Monsef I, Brillant C, Engert A, von Tresckow B. Comparison of first-line chemotherapy including escalated BEACOPP versus chemotherapy including ABVD for people with early unfavourable or advanced stage Hodgkin lymphoma. In: The Cochrane Collaboration, editor. *Cochrane Database of Systematic Reviews* [Internet]. John Wiley & Sons, Ltd.; 2017. Available from: <http://doi.wiley.com/10.1002/14651858.CD007941.pub3> [cited 27.8.17].
9. Vassilakopoulos TP, Johnson PW. Treatment of advanced-stage Hodgkin lymphoma. *Semin Hematol*. 2016;53(3):171–9.
10. Moghbel MC, Mittra E, Gallamini A, Niederkohr R, Chen DL, Zukotynski K, et al. Response assessment criteria and their applications in lymphoma: Part 2. *J Nucl Med*. 2017;58(1):13–22.
11. Maddi RN, Linga VG, Iyer KK, Chowdary JS, Gundeti S, Digumarti R, et al. Clinical profile and outcome of adult Hodgkin lymphoma: experience from a tertiary care institution. *Indian J Med Paediatr Oncol*. 2015;36(4):255–60.
12. Chatenoud L, Bertuccio P, Bosetti C, Rodriguez T, Levi F, Negri E, et al. Hodgkin's lymphoma mortality in the Americas, 1997–2008: achievements and persistent inadequacies: Hodgkin's lymphoma mortality in the Americas. *Int J Cancer*. 2013;133(3):687–94.
13. Jaime-Pérez JC, Gamboa-Alonso CM, Padilla-Medina JR, Jiménez-Castillo RA, Olguín-Ramírez LA, Gutiérrez-Aguirre CH, et al. High frequency of primary refractory disease and low progression-free survival rate of Hodgkin lymphoma: a decade of experience in a Latin American center. *Rev Bras Hematol Hemoter*. 2017;39(4):325–30.
14. Biasoli I, Castro N, Delamain M, Silveira T, Farley J, Simões BP, et al. Treatment outcomes for Hodgkin lymphoma: first report from the Brazilian Prospective Registry. *Hematol Oncol*. 2017 (ahead of print).
15. Andjelic B, Antic D, Jakovic L, Todorovic M, Bogdanovic A, Djurasinovic V, et al. A single institution experience on 314 newly diagnosed advanced Hodgkin lymphoma patients: the role of ABVD in daily practice. *Eur J Haematol*. 2014;93(5):392–9.
16. Shafi RG, Al-Mansour MM, Kanfar SS, Al Hashmi H, Alsaeed A, Al-Foheidi M, et al. Hodgkin lymphoma outcome: a retrospective study from 3 tertiary centers in Saudi Arabia. *Oncol Res Treat*. 2017;40(5):288–92.
17. Hoppe RT, Mauch PT, Armitage JO, Diehl V, Weiss LM. *Hodgkin Lymphoma*. 2nd ed. Philadelphia; 1999.
18. Biasoli I, Castro N, Delamain M, Silveira T, Farley J, Simões BP, et al. Lower socioeconomic status is associated with shorter survival in HL patients – an analysis from the Brazilian Hodgkin Lymphoma Registry. Cologne, Germany: Poster presented at: 10th international Symposium on Hodgkin Lymphoma; 2016.