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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.<sup>1</sup> 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%.<sup>2</sup> Duration of treatment and doses of radiation depend on the presence of some adverse prognostic factors.<sup>3</sup> 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%.<sup>4,5</sup> 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.<sup>6–8</sup> Defining which patients really do benefit from more intensive regimens is still a challenge.<sup>9</sup> 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.<sup>10</sup>

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.<sup>11,12</sup> In this issue of the *Revista Brasileira de Hematologia e Hemoterapia*, Jaime-Pérez et al.<sup>13</sup> 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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data has recently been published by the Brazilian Prospective Hodgkin's Lymphoma Registry,<sup>14</sup> 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.<sup>11,12,15,16</sup> 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.<sup>17</sup> Indeed, lower economic status has been associated with more aggressive disease and worse outcomes in HL.<sup>18</sup>

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

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