

## About mediastinal large B- cell lymphoma and other lymphoma entities

Haematologica 2007; 88:(3):e42

Dear Sirs,

I read with interest the article by Zinzani et al <sup>1</sup> and Lazzarino's comment <sup>2</sup> about the treatment of mediastinal large B-cell lymphoma (MLBCL), in December issue of Haematologica. I believe too that CHOP is not the best treatment for MLBCL, since we observed significantly better results with third generation therapies <sup>3</sup>. These preliminary results are confirmed by Zinzani's recent paper.<sup>1</sup> The search for an effective first-line chemotherapy in MLBCL is not trivial, since salvage therapy is almost invariably unsuccessful in MLBCL, leading the patients to death in a few months. This contrasts with other aggressive lymphomas, where margins of rescue exist. A first question is: should CHOP be considered the golden standard for MLBCL? A second open question regards the use of involved field radiotherapy (IF RT) on the mediastinum after the CR achievement. Indeed, most of the retrospective data suggest that CHOP is less adequate than third generation therapies. After the assessment of different entities <sup>4,5</sup> in aggressive lymphomas, we should reconsider our therapeutic approach for these subgroups of aggressive lymphomas. The various entities should probably be regarded as distinct diseases, rather than as a single disease. In recent literature, there are various examples in this direction from non-randomized studies, suggesting that a *specific* approach is worthwhile. Hoelzer's group <sup>6</sup> reported excellent results in PTCL - a well known unfavorable subgroup of aggressive lymphomas- by using the intensive VACPE regimen (vincristine, high dose anthracycline, cytoxan, prednisone, etoposide). The CR rate was 77%. The EFS was 55%, unusually good for PTCL and not different from the EFS of large B-cell lymphoma treated with the same therapy. In mantle cell lymphoma - another entity characterized by a poor outcome - too studies from the MD Anderson group gave substantial contributions to improving the outcome. HyperCVAD, a very intensive regimen successfully employed in small non cleaved cell lymphoma, was first combined with autologous stem cell transplantation <sup>7</sup>; then with rituximab, without SCT <sup>8</sup>. The results were excellent: in patients under 66 years of age treated with rituximab+ HyperCVAD, the CR rate was 90% and the 2-year PFS was 80%. In contrast, CHOP+ rituximab recently produced only marginal results in newly diagnosed mantle cell lymphoma, with a projected 3-year PFS of about 10%, and absence of *plateau*.<sup>9</sup> This suggests that the real difference comes from the type of chemotherapy rather than from the addition of rituximab. The third generation regimens (mainly MACOP-B and VACOP-B) in mediastinal large B-cell lymphoma are a further example

in this direction. We should probably pay more attention to well conducted pilot studies, even if we definitely need the confirmation of large randomized ones, as suggested by Lazzarino.<sup>2</sup> Multicenter randomized studies require large international cooperation and some years to be conducted. Waiting for these necessary randomized studies, for the time being the use of third generation therapies (namely MACOP-B or VACOP-B) + IF RT to the mediastinum is justified.

Giuseppe Todeschini, MD

Dpt of Hematology, Verona University School of Medicine,  
Ospedale Policlinico "G.B. Rossi", Piazzale A. Scuro, 37134  
Verona

FAX 0039-045-501807

## References

- 1 Zinzani PL, Martelli M, Bertini M, Gianni AM, Devizzi L, Federico M, et al. Induction therapy strategies for primary mediastinal large B-cell lymphoma with sclerosis: a retrospective study on 426 previously untreated patients. Haematologica 2002; 87: 1258-64.
- 2 Lazzarino M. Management of primary mediastinal B-cell lymphoma with sclerosis: advances and caveats. Haematologica 2002; 87: 1238-9.
- 3 Todeschini G, Ambrosetti A, Meneghini V, Pizzolo G, Menestrina F, Chilosi M, et al. Mediastinal large B-cell lymphoma with sclerosis: a clinical study of 21 patients. J Clin Oncol 1990; 8: 804-808.
- 4 Harris NL, Jaffe ES, Stein H, Banks PM, Chan JKC, Cleary ML, et al. A Revised European- American Classification of Lymphoid neoplasms: a proposal from the International Lymphoma Study Group. Blood, 1994; 84: 1361-92.
- 5 Harris NL, Jaffe ES, Diebold J, Flandrin G, Muller-Hermelink HK, Vardiman J, et al. World Health Organization Classification of neoplastic diseases of the hemopoietic and lymphoid tissues: report of the Clinical Advisory Committee- Airle House, Virginia, November 1997. J Clin Oncol 1999; 17: 3835-49.
- 6 Karakas T, Bergmann L, Stuttle HJ, Jager E, Knuth A, Weidmann E, et al. Peripheral T-cell lymphomas respond well to vincristine, adriamycin, cyclophosphamide, prednisone, etoposide (VACPE) and have a similar outcome as high-grade B-cell lymphoma. Leuk Lymphoma, 1996;24:121-9.
- 7 Khouri IF, Romaguera J, Kantarjian H, Palmer JL, Pugh WC, Korblin M, et al. HyperCVAD and high dose methotrexate/ cytarabine followed by stem cell transplantation: an active regimen for aggressive mantle cell lymphoma. J Clin Oncol 1998; 16: 3803-9.
- 8 Romaguera J, Cabanillas F, Dang N, Goy A, Fayad L, Hagemeister FB, et al. Mantle cell lymphoma (MCL). Update on results after R- HCVAD without stem cell transplantation (SCT), Ann Oncol 2002, 13 (suppl 2) abstr #24, 8th International Conference on Malignant Lymphoma, Lugano 12-15 June 2002.
- 9 Howard OM, Gribben JG, Neuberger DS, Grossbard M, Poor C, Janicek MJ, et al. Rituximab and CHOP induction therapy for newly diagnosed mantle-cell lymphoma: molecular complete responses are not predictive of progression-free survival. J Clin Oncol 2000; 20: 1288-94.