

## Rituximab and autologous stem-cell transplantation for high-risk diffuse large B-cell lymphoma

### Authors' reply

The results from our randomised phase 3 trial<sup>1</sup> showed that young patients, affected by high-risk diffuse large B-cell lymphoma (age-adjusted International Prognostic Index score of 2–3), who received abbreviated rituximab-dose-dense chemotherapy plus high dose therapy and autologous stem-cell transplantation compared with patients who received full course rituximab-dose-dense chemotherapy had an improvement in failure-free survival, but not in overall survival.

Tetsuya Tanimoto and colleagues commented that the presence of more than one extranodal site of disease might affect the prognosis in young patients with untreated high-risk diffuse large B-cell lymphoma and treated in the rituximab-era.<sup>2</sup>

In our study,<sup>1</sup> involving 399 patients younger than 60 years, 127 (32%) patients had a number of extranodal sites that were more than one at diagnosis, equally distributed into the four randomisation arms (32% in each group). At the end of the treatment, 208 (76%) of 272 patients with no or one extranodal site of disease achieved a complete response compared with 87 (69%) of 127 with more than one extranodal localisation.

In our analysis, patients with more than one extranodal site of disease showed reduced failure-free survival and overall survival compared with those with no or one extranodal site during the first year of observation, but differences disappeared progressively over time (appendix). The failure-free survival at 2 years was 66% (95% CI 60–72) for those with more than one extranodal site compared with 66% (57–74) for those with no or one extranodal site

(log-rank test  $p=0.87$ ). The overall survival at 5 years was 76% (95% CI 67–82) for those with more than one extranodal site compared with 78% (72–83) for those with no or one extranodal site (log-rank test  $p=0.42$ ).

In conclusion, in our randomised phase 3 trial, the number of extranodal sites of disease did not influence the outcome of young patients with high-risk diffuse large B-cell lymphoma with poor prognosis.

AC is on the advisory board of Celgene; and has received lecture fees from Amgen, Celgene, Janssen, Nanostring, Pfizer, Roche, and Teva. MM is on the advisory board of Roche, Janssen, Celgene, Mundipharma, and Teva; and has received lecture fees from Roche, Celgene, and Janssen. UV is on the advisory board of Roche, Janssen, and Celgene; and has received lecture fees from Roche, Celgene, Janssen, Gilead, and Takeda. AE declares no competing interests.

\***Annalisa Chiappella, Maurizio Martelli, Andrea Evangelista, Umberto Vitolo**  
**achiappella@cittadellasalute.to.it**

Department of Haematology, Azienda Ospedaliero Universitaria Città della Salute e della Scienza di Torino, 10126 Turin, Italy (AC, UV); Department of Cellular Biotechnologies and Haematology, Sapienza University, Rome, Italy (MM); and Unit of Clinical Epidemiology, CPO, Azienda Ospedaliero Universitaria Città della Salute e della Scienza di Torino, Turin, Italy (AE)

- 1 Chiappella A, Martelli M, Angelucci E, et al. Rituximab-dose-dense chemotherapy with or without high-dose chemotherapy plus autologous stem-cell transplantation in high-risk diffuse large B-cell lymphoma (DLCL04): final results of a multicentre, open-label, randomised, controlled, phase 3 study. *Lancet Oncol* 2017; **18**: 1076–88.
- 2 Glesson M, Cunningham D, Linch D. The role of myeloablation for lymphoma. *N Engl J Med* 2014; **370**: 575.



See Online for appendix