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Progress in the treatment of diffuse large B-cell lymphomas: a German perspective

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Young good-prognosis patients comprise the low and low-intermediate risk group (risk factor 0 and 1 according to the age-adjusted IPI) while poor-prognosis patients comprise the high-intermediate and high risk group (≥2 risk factors). Optimum treatment responses in young good-prognosis patients have so far been achieved with 6 cycles of a CHOP-like chemotherapy in combination with the anti-CD20 antibody rituximab. Using this therapeutic approach, 3-year event-free survival rates of >90% and overall survival of >97% can be achieved in a *very favorable subgroup* (patients without IPI risk factor and no bulky disease), while further improvement is warranted for the *less favorable subgroup* (IPI=I and/or bulky disease; 3-year event-free survival: 77%).[1] For young poor-prognosis patients, 5-year survival is approximately 50%, and progress has not been convincingly or specifically demonstrated in this patient group. Ongoing studies will show whether dose-dense conventional or high-dose chemotherapy regimens requiring stem cell support in combination with rituximab will result in improvements for young poor-prognosis patients; such improved responses have recently been demonstrated in young patients with good-prognosis aggressive lymphoma. In elderly patients with DLBCL, reduction of the treatment interval from 3 (CHOP-21) to 2 weeks (CHOP-14) improved treatment outcome significantly without increasing toxicity.[2,3] The addition of rituximab to CHOP-21 produced a similar treatment response in this patient population.[3] The RICOVER-60 trial has been undertaken to assess whether combining dose-dense CHOP-14 with rituximab will further improve treatment response in elderly patients. These patients (aged 61-80 years, stages I-IV) were randomised to receive 6 or 8 cycles of CHOP-14 with or without rituximab. A planned interim with 828 patients showed no difference in freedom from treatment failure (FFTF) between 6 (n=414) and 8 (n=413) cycles (p=0.23), although FFTF following R-CHOP-14 (n=414) was significantly better than after CHOP-14 (n=413) alone (p=0.000025). After a median observation time of 26 months, there was a trend for improved FFTF after 8 cycles of CHOP-14 (n=210) compared to 6 cycles (n=203; 58% vs. 53%; p=0.13), but this was neutralized following the addition of rituximab: 70% FFTF for both 6 (n=211) and 8 cycles R-CHOP-14 (n=203).

The advantage of R-CHOP-14 over CHOP-14 with respect to overall survival after 26 months is not yet significant (74% vs.78%; p=0.13). Excluding patients with stage I, the RICOVER-60 population is very similar to the one included in the GELA trial. However, the projected 2.5-year survival rate for elderly stage II-IV patients after 6 x R-CHOP-14 (74%) compare favorably with 8 x R-CHOP-21 in the GELA trial (64%; Feugier *et al*, 2005). The superiority of 6 x R-CHOP-14 over 8 x R-CHOP-21 is mostly due to the enhanced 2.5-year survival of poor-prognosis patients (IPI=3,4,5: 64% in the RICOVER trial vs. 54% in the GELA trial).[4] In conclusion, the results observed with 6 cycles of R-CHOP-14 are the best ever reported in this largest randomised trial of DLBCL performed to date in elderly patients with DLBCL. 6 x R-CHOP-14 should be considered as reference standard in future trials for elderly patients with DLBCL.

References

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