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Radiotherapy in the rituximab era: still a place?

Background

The RICOVER60 trial has shown that 6 cycles of CHOP-14 with 8 applications of rituximab (6xR-CHOP-14) was superior to 8xR-CHOP-14, 6xCHOP-14 and 8xCHOP-14 in elderly patients with CD20-positive aggressive lymphoma. In that trial 117/306 (36%) of the patients in the 6xR-CHOP-14 arm were assigned to receive additional radiotherapy (Rx) to bulky disease (Pfreundschuh *et al.*, Lancet Oncol 2008). To study the relevance of additional Rx to bulky disease we subsequently initiated a prospective study in which no Rx was planned after 6 x R-CHOP-14.

Methods

166 elderly patients - subjected to the same inclusion and exclusion criteria as in the RICOVER-60 (R-CHOP-Rx) trial - were recruited for this study to receive 6xR-CHOP-14 without any radiotherapy (R-CHOP-noRx). The outcome of these patients was compared with the 306 patients assigned to receive 6xR-CHOP-14 and radiotherapy to bulky disease (≥7.5 cm) in the R-CHOP-Rx trial.

Results

164/166 R-CHOP-noRx patients are evaluable with a median observation time of 17 months. Patients from both studies were well balanced for many known prognostic factors, but patients in R-CHOP-noRx were older (71 *vs.* 69 years; p=0.018), more frequently in advanced stages (60% *vs.* 50%; p=0.037), and with extranodal involvement (63% *vs.* 53%; p=0.024), while bulky disease was more frequent in the R-CHOP-Rx study (38% *vs.* 29%; p=0.038). Adherence to the immunochemotherapy protocol was excellent in both studies with median relative rituximab and cytotoxic drug doses of 99%. Overall response to therapy was similar in the two studies: CR/CRu: 76% *vs.* 78%; progressions 5.5% *vs.* 6.5%; relapses after CR/CRu 8% *vs.*10%; therapy-associated deaths 7% *vs.* 6% in R-CHOP-noRx and R-CHOP-Rx, respectively. Similarly, there were no significant differences between the two studies with respect to EFS, PFS and OS. This also holds in multivariate models adjusting for the prognostic imbalances between the cohorts. However, the patients with bulky disease in the R-CHOP-Rx trial assigned to receive additional radiotherapy to bulky disease

had a 25% better 18-month EFS (68% [95%-CI: 59-76] *vs.* 43% [29-58]; p=0.002), a 10% better PFS (77% [70-85] *vs.* 67% [52-82]; p=0.123), and a 4% better OS (80% [72-87] *vs.* 76% [63-90]; p=0.509) compared with R-CHOP-noRx. The lower EFS rate in the R-CHOP-noRx study was due to patients with bulky disease not achieving CR or CRu after 6xR-CHOP, while patients with bulky disease in CR or CRu after 6xR-CHOP-14 fared equally well with and without additional radiotherapy (18-month-EFS: 84% *vs.* 86%; p=0.512).

Conclusion

In the rituximab era additional radiotherapy to bulky disease has no role for elderly patients in CR/CRu after completion of 6xR-CHOP-14 immunochemotherapy, but (unlike 2 additional chemotherapy cycles in the 8xR-CHOP-14 arm of R-CHOP-Rx) appears to be beneficial for patients with bulky disease achieving a PR.

Supported by Deutsche Krebshilfe.