
To study pharmacokinetics, toxicity, and efficacy of prolonged rituximab exposure in elderly patients with diffuse large B-cell lymphoma (DLBCL). In the SMARTE-R-CHOP-14 trial, rituximab 375 mg/m\(^2\) was administered, together with six cycles of rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone on a 14-day schedule (6×R-CHOP-14), on days -4, 0, 10, 29, 57, 99, 155, and 239. Pharmacokinetics and outcome were to be compared with those of patients who had received 6×R-CHOP-14 in combination with eight 2-week applications of rituximab in the RICOVER-60 (Rituximab With CHOP Over Age 60 Years) trial. The complete response (CR)/unconfirmed CR rate was 85% in 189 evaluable patients, 90% for 90 good-prognosis patients (International Prognostic Index [IPI], 1 or 2), and 81% for 99 poor-prognosis patients (IPI, 3 to 5); 3-year event-free survival (EFS) was 71%, 75%, and 67%, respectively; and 3-year overall survival (OS) was 84%, 88%, and 80%, respectively, with no differences between men and women. The
preplanned historical comparison with 306 RICOVER-60 patients (good prognosis, n = 183; poor prognosis, n = 123) revealed no outcome differences for all and good-prognosis patients; however, the longer exposure time in SMARTE-R-CHOP-14 compared with RICOVER-60 was associated with better 3-year EFS (67% v 54%) and OS (80% v 67%) in poor-prognosis patients. Extended rituximab exposure compared with eight 2-week applications in combination with 6×R-CHOP-14 significantly improved outcome of elderly poor-prognosis patients without increasing toxicity. To our knowledge, results obtained with the SMARTE-R-CHOP-14 rituximab schedule are the best reported for elderly patients with DLBCL to date. In the subgroup of poor-prognosis patients treated with extended rituximab exposure, the outcome seemed superior to that of a similar historical cohort of patients treated with 6×R-CHOP-14 plus 2-week rituximab, with similar toxicity. A randomized comparison of the two schedules is warranted.