

Low initial trough concentration of rituximab is associated with unsatisfactory response of first-line R-CHOP treatment in patients with follicular lymphoma with grade 1/2

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Abstract

For follicular lymphoma (FL) with grade 1/2, the complete response (CR) rate of the first-line R-CHOP treatment was significantly low. In this study, we assessed the rationality of the administration of rituximab for FL patients with grade 1/2 based on concentration–response relationship analyses. Thus, we conducted a prospective pharmacokinetic (PK) study in 68 FL patients with grades 1–3 treated with R-CHOP at 21-day intervals. Plasma rituximab concentrations were quantified using ELISA and the population PK modeling was established with Phoenix® NLME™. The first cycle trough concentration ($C_{1\text{-trough}}$) of rituximab was a significant independent risk factor for achieving CR in matched-pair logistic regression analysis, rather than the concentrations in later cycles; the recommendatory minimum optimal $C_{1\text{-trough}}$ was 13.60 $\mu\text{g/mL}$. Patients with grade 1/2 had significantly lower $C_{1\text{-trough}}$ compared with grade 3 (12.21 $\mu\text{g/mL}$ vs. 23.45 $\mu\text{g/mL}$, $P < 0.001$), only 30% patients with grade 1/2 could reach 13.60 $\mu\text{g/mL}$, compared with 91.67% in patients with grade 3, which was in accord with its unsatisfactory CR rates (43.33% vs. 76.32%). The stage indicating the tumor burden (the target) was a crucial influence factor for $C_{1\text{-trough}}$, accounting for 40.70% of its variability, 70% patients with grade 1/2 were stage IV in this study, since the

systemic therapy only started at the disseminated disease stage. The initial dose of 1800 mg was recommended by Monte Carlo simulation for patients with grade 1/2. In summary, low C_{1-}
trough accounted for low-grade FL's unsatisfactory CR rate, designing the first dosage of rituximab should be a very important component of individualized therapy for FL.