Correspondence on 'Rituximab as therapy to induce remission after relapse in ANCA-associated vasculitis'

We read with great interest the results of the recently published article titled 'Rituximab as therapy to induce remission after relapse in ANCA-associated vasculitis' This article provides information on reinduction with rituximab in a large cohort of relapsing AAV. This paper as the authors state reports only on the induction phase of the RITAZAREM[1] trial, prior to randomisation. The results of the randomised controlled trial (RCT) were discussed elsewhere.[2]

Ninety per cent of the enrolled subjects achieved remission with four weekly doses of rituximab (RTX). Majority (63%) had severe disease at baseline and surprisingly most of them (71%) received the lower regime of glucocorticoids starting at 0.5 mg/kg and tapered. These results provide evidence of short-term efficacy of RTX and help break inhibitions of using a low dose glucocorticoid regimen in severe relapsing AAV with rituximab as a reinduction agent.

The RAVE[3] trial had a subgroup of severe relapses in which the remission rate was 67% and 42% in the RTX and cyclophosphamide groups, respectively. Remission was assessed at 6 months and was defined as Brimingham Vasculitis Activity Score/Wegener granulomatosis (BVAS/WG) of zero and complete glucocorticoid withdrawal. In this study, remission was defined as BVAS/WG of ≤1 and with prednisone dose of ≤10 mg/day by 4 months. Renal and pulmonary involvement was less frequent compared with the RAVE[3] cohort (47% vs 66% and 37% vs 52%, respectively). Hence, the remission rates across the two studies are not directly comparable. The number of patients who received intravenous methyl prednisolone and plasma exchange in this study is also not mentioned and could act as confounders raising caution about interpreting the results.

The authors concluded that response to RTX in relapsing AAV was not influenced by age, ANCA type at enrolment, glucocorticoid induction regimen, presence of ear, nose and throat or renal involvement. However, they hinted that non-severe disease (with an OR of 2.93 and a wide CI) could predict response. The lack of a comparator arm in the induction phase and the extremely small number of non-responders caution us against generalising the results of efficacy of RTX in relapsing AAV.

The lower glucocorticoid (GC) subgroup had only 2/3 of total GC exposure. Contrary to expectations, the total number of serious and non-serious infections in the lower GC group outnumbered the group with the higher GC exposure (5.2% and 35.1% vs 0 and 22.2%, respectively). This is unexplained and in contrast to report from the PEXIVAS[4] study where serious infections were significantly lower in the reduced dose group.

We would also like to bring to attention that certain serious adverse events listed, namely vasculitis, laryngeal stenosis, DVT and pulmonary embolism were in all likelihood manifestations of the primary disease and could actually be reinterpreted as failure of RTX.

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