

'MAINRITSAN2-the future', with some doubts!

We read with great interest the article on 'comparison of individually tailored versus fixed-schedule rituximab regimen to maintain ANCA-associated vasculitis remission: results of a multicentre, randomised controlled, phase III trial (MAINRITSAN2)' by Charles and Terrier.¹ They have tried to address a crucial aspect of rituximab dose titration during remission maintenance of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). The key message is that, although AAV relapse rates did not differ significantly among the two groups, the patients in the individually tailored group received fewer rituximab infusions. This outcome has a significant bearing on cost and drug-related side effects. However, certain aspects of this study require further clarification.

First, 'the trial was designed to detect a 20% absolute between-arm difference of relapse, with a 5% alpha risk and 80% power in a two-sided test, with 35% relapses in control group'. It is not clear why the arbitrary figure of 35% relapse rate in the control group was considered when the MAINRITSAN² study had shown a rate of major and minor relapse of 5% and 11%, respectively. The same was evident in the present study where the relapse rate in the control group was only 9.9%. It would be interesting to know the post-hoc power analysis of the present study given the difference between the presumed and observed relapse rates (35% vs 9.9%).

Second, both the total number of relapses and major relapses were higher in the tailored-infusion group compared with the fixed-schedule group. Though these were not statistically significant in the present study, these might become significant on long-term follow-up of a larger cohort. It is interesting to know that half of the patients with total relapses were always negative for CD19+B cells. There might be two reasons for this. First may be the disturbance of b-cell activating factor (BAFF) homeostasis,³ and analysis of BAFF levels in both these groups can provide that answer if it has been carried out or the samples have been preserved. Second, it may be due to the persistence of tissue B cells, despite depletion of the circulatory CD19+ B cell.⁴ If a biopsy was done in any of the patients with relapse then the presence of tissue B cells can be looked at in the biopsy specimens.

Third, it would be good to have the comparison of a composite outcome measure like Q-TWiST [Q-TWiST = (u TOX x TOX)+TWiST + (uProg x PROG)] in both these groups. This has been reported previously in 'CORTicosteroid and cyclophosphamide-based induction therapy for SNV patients AGED ≥65 years (CORTAGE)' trial by the same group,⁵ and this can give a better idea regarding the time in which the patient experienced ≥1 (TOX) serious adverse event (SAE), the time without disease activity and SAE (TWiST) and time with disease activity (PROG).

Fourth, the definition of major and minor relapses is not clear from the supplementary tables. In table S1,¹ the patient at serial no 9 with mononeuritis was considered to have a major relapse, whereas in table S2,¹ the patient at serial number 3 with mononeuritis was considered to have a minor relapse.

Finally, while doing the cost-benefit analysis of lower rituximab pulses in the tailored arm, the costs of frequent ANCA and CD19+ B levels need to be factored in.

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