Response to: '"MAINRITSAN2-the future", with some doubts!' by Chattopadhyay *et al*

We would like to thank Chattopadhyay *et al*[1] for their comments regarding our paper.[2]

The MAINtenance of Remission Using RITuximab in Systemic ANCA-associated Vasculitis (MAINRITSAN2) trial was designed in 2011. At that time, the MAINRITSAN trial results were not yet available, which explains why a conservative hypothesis was used to calculate the sample size. Given the low relapse rate (9.9%) observed with rituximab maintenance therapy for antineutrophil cytoplasm antibody (ANCA)-associated vasculitides (AAVs), our study was underpowered to detect an absolute relapse rate difference of 7%. However, a post-hoc power calculation is not necessary to reach this conclusion.[3] The individually tailored group had more relapses (and major relapses), and these differences might have been statistically significant had the sample size been larger and/or follow-up longer.

To overcome this situation, we compared absolute differences of 7% for relapse rates and 3.7% for major relapse rates with the numbers of infusions needed to prevent those relapses. That is to say, the tailored-infusion or fixed-schedule group, respectively, received 248 or 381 infusions, meaning that 133 infusions were needed to prevent 3 major relapses (ie, ~45 infusions to prevent a major relapse at month 28), which would certainly make a difference for the patients. A lighter therapeutic regimen is always better, as has clearly been supported historically for patients with vasculitis. Indeed, the dramatically improved prognoses for AAVs observed over the 30 last years are mainly attributable to the lower cumulative immunosuppressant and glucocorticoid doses administered. Based on our findings, we concluded that it seems possible to reduce patients' rituximab exposure, thereby avoiding overtreatment and meeting one of our goals.

For the MAINRITSAN and MAINRITSAN2 trials, use of a composite outcome (eg, Q-TWIST) was not planned, so the required data are not available, but we do not think these analyses would have made our message clearer. As previously written, relapses were more frequent in the tailored arm, and at 28 months serious adverse events had occurred in 26 (32.1%) tailored-arm vs 31 (38.3%) systematic infusion-arm patients.

In online supplementary table S1, patient 9 had a minor relapse with purpura and, despite escalating the glucocorticoid dose, he developed mononeuritis multiplex with severe right peroneal nerve motor deficit; he was then considered to have had a major relapse by the Adjudication Committee. Patient 3 (online supplementary table S2) experienced only sensory symptoms without motor deficiency, and the mononeuritis multiplex was confirmed by electromyogram and neuromuscular biopsy. We acknowledge that the definition of the severity of these AAV peripheral nerve involvements is difficult, but only the former patient's motor deficit warranted being classified as a major relapse. Considering patient 9 (online supplementary table S1) to be misclassified, as suggested by Chattopadhyay *et al*,[1] would have slightly disadvantaged the individually tailored group.

Finally, when we undertake the medical-economic analysis, all direct and indirect costs will have to be accounted for, that is, hospitalisations (with all related costs), rituximab infusions, laboratory tests and so on.

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