Response to: 'Correspondence on 'Rituximab as therapy to induce remission after relapse in ANCA-associated vasculitis" by Parikh *et al*

We appreciate the thorough and thoughtful review of our work, and the interesting points raised by Drs Parikh, Kumar and Rjasekhar.[1]

We recognise that there were more serious and non-serious infections in the lower dose glucocorticoid group in the induction phase of the RITAZAREM trial, which contrasts with the results of the PEXIVAS trial, where serious infections were less frequent in the reduced dose glucocorticoid group.[2 3] However, in the RITAZAREM trial, the glucocorticoid induction regimen was not randomised. Reflecting the divergence of opinion on glucocorticoid dosing for disease relapse, the protocol permitted investigators to select, at enrolment, either a higher dose (starting at prednisone/prednisolone 1 mg/kg/day, maximum 60 mg) or a lower dose (starting at 0.5 mg/kg/day, maximum dose 30 mg) glucocorticoid induction regimen. Therefore, the selection of glucocorticoid dose is susceptible to bias. Trial participants with a perceived greater risk of infection (such as those with pre-existing comorbidities, older age, or greater prior burden of immunosuppression) may have been enrolled into the lower dose group. Per our prespecified statistical analysis plan, we reported the data but did not perform formal statistical analysis since the study was not powered to detect a difference between high-dose and low-dose glucocorticoids on rates of infection. Further analyses on the effects of glucocorticoid dose on both efficacy and safety parameters across all phases of the trial are planned.

Serious adverse events which could be attributed to active disease were observed. However, induction of remission is not an immediate event, and, therefore, it is not unexpected that some patients were readmitted to hospital during the first few weeks of treatment. By 4 months, 90% of patients met the remission definition for this trial (BVAS/WG≤1, and prednisone/prednisolone dose ≤10 mg daily). Venous thromboembolic events occur in >10% of patients with anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis with active disease.[4 5] It is likely that these events reflect active disease, but are not recorded on the BVAS/WG disease assessment tool. In addition, it is particularly difficult to evaluate some clinical features such as laryngeal stenosis, and to distinguish active disease from damage. These points highlight the limitations of current disease activity assessment tools in ANCA-associated vasculitis and the challenges of defining disease remission.

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Competing interests RMS reports grants from Roche during the conduct of the study. PM reports personal fees from AbbVie, grants and personal fees from AstraZeneca, personal fees from Biogen, grants and personal fees from Bristol-Myers Squibb, grants and personal fees from Boeringher-Ingelheim, grants and personal fees from Celgene, grants and personal fees from ChemoCentryx, CSL Behring, grants and personal fees from Genentech/Roche, grants and personal fees from Genzyme/Sanofi, grants and personal fees from GlaxoSmithKline, grants and personal fees from InflaRx, personal fees from Insmed, personal fees from Jannsen, personal fees from Kiniksa, grants from Kypha, personal fees from Sparrow, grants from TerumoBCT outside the submitted work. DJ reports grants from Roche/Genentech, during the conduct of the study; grants from Sanofi-Genzyme, grants and personal fees from Chemocentryx, grants and personal fees from GSK, grants from Roche/Genentech, personal fees from Takeda, personal fees from Insmed, personal fees from Astra-Zeneca, personal fees from Infla-RX, personal fees from Chugai, personal fees from Boehringer-Ingelheim outside the submitted work.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not required.

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