Reviewer’s report

Title: Interventions for renal vasculitis in adults. A systematic review.

Version: 2 Date: 13 December 2009

Reviewer: David Jayne

Reviewer’s report:

This review is of high quality and covers most of the relevant literature in this area, it will be of use to practitioners and clinical researchers. The methodology appears sound. The comments below reflect suggestions which would enhance the manuscript.

1. Renal vasculitis has other presentations such as, cortical infarctions and aneurysms in PAN and renal artery stenosis in Takayasu’s arteritis.

2. Also, renal vasculitis can present without RPGN, such as, asymptomatic urinary abnormality, chronic kidney disease or FSGS.

3. HSP and cryoglobulinemia are causes of renal vasculitis

4. Methodological issues in the MMF and leflunomide trials preclude conclusions.

5. In the results of IV versus daily oral cyclophosphamide trials it is important to add that some trials used no remission maintenance treatment when referring to an increased relapse risk.

6. In the Stegeman study there was no difference in non-respiratory relapse rates, after co-trimaoxazole /placebo. A problem with this study was disentangling the reduction in respiratory tract infections related to the antibiotic and the reduction in respiratory tract relapses.

7. The Hu trial was conducted in China with a majority of MPO-ANCA associated MPA. Any conclusions may not be transferable to populations with higher frequencies of PR3-ANCA disease, Wegener’s. Page 11 “Mycophenolate Mofetil may be equivalent to cyclophosphamide”. Wrong reference quoted – should say 32, i.e. Hu et al, NDT 2008 (not reference 22- Glockner et al ‘88). Short follow-up (only 6 months), also only patients with mild ANCA vasculitis were included so results cannot be extrapolated to those with creat >500 or lung hemorrhage.

8. Could include a note about the ongoing MYCYC trial by the EUVAS group.

9. The leflunomide trial was stopped early by the data monitoring committee. The summary of the trial is misleading as the number of excess SAEs in the leflunomide group exactly matched the number of severe vasculitis flares in the MTX group. Any conclusions must be guarded in view of these observations.
10. The etanercept trial was not able to show a benefit of etanercept on remission induction due to its design, only on remission maintenance.

11. There is of mention of the WEGENT trial (Pagnoux, New Eng J Med 2008) presumably because it was not picked up by the search. Yet the leflunomide trial was picked up. Neither focus on renal vasculitis but both are relevant to the discussion of remission maintenance agents.

12. Although not an aim for the RCTs, plasma exchange is often used for lung hemorrhage, a major vasculitic cause of death. At least, the absence of evidence might be referred to here.

13. As mentioned above the earlier trials of pulse cyclophosphamide did not use remission maintenance therapy and this will have influenced the relapse rates.

14. Definitions of remission and relapse vary between trials which may influence remission and relapse rates.

15. There is no mention of the two rituximab RCTs reported in abstract form (ASN 2008 and ACR 2009).

16. There is no mention of the IMPROVE, MMF vs AZA trial (ASN 2009).

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I have received research grant support and consulting fees from ASPREVA and Roche.