Letters to the Editors

Comment on: New therapeutics for ANCA-associated vasculitis: 10 years devoted to lessen toxicity

by Rossi *et al*.

Sirs,

We read with interest the review of Rossi *et al*. on ANCA-associated vasculitis (AAV) therapy, in a recent issue of *Clinical and Experimental Rheumatology* (1). We agree with the Authors on the need of more effective and safer treatments. The phenotypic spectrum of AAV is very large, ranging from lung granulomatosis, non-severe AAV, severe PR3-AAV, severe MPO-AAV, small-vessel vasculitis with progressive increased mortality. Severe AAV are a clinical challenge, both for remission induction and remission maintenance, especially in the setting of renal involvement leading increase of mortality risk. According to PEXIVAS, over 25% of patients with nephritis and GFR <50 ml/m develop End Stage Renal Disease (ESRD) (2). The RAVE and RITUXIVAS studies have highlighted the non-inferiority of rituximab towards cyclophosphamide for induction in AAV therapy. MAINRITSAN (maintenance therapy of RTX was superior to AZA even after 60 months) has shown the efficacy of the re-treatment with rituximab in preventing relapse. So, according current guidelines, rituximab is alternative to cyclophosphamide for severe AAV with or without renal involvement (3). In our experience, the plasma exchange does not reduce the incidence of death/ESRD and a reduced-dose regimen of glucocorticoids is non-inferior towards a standard-dose regimen regarding to death/ESRD. In the last decade, as remission-induction therapy, we replaced the standard cyclophosphamide-based regimen with methylprednisolone i.v. pulses 0.5 g x 3 and 0.5 mg/kg/day oral prednisone plus Rituximab 375 mg/m2 x 4. Then we prescribe a minimal dose of glucocorticoids as maintenance regimen. The advances in AAV therapeutics have produced impressive increase in overall survival. In the next years, it is of interest the combined use of cyclophosphamide and rituximab in order to perform a less toxic immunosuppressive treatment, reducing cumulative exposure to cyclophosphamide, with the same efficacy of the currently practiced therapeutic regimens. We agree with the Authors on the target of a disease- and patient-tailored therapeutic regimen in order to reduce the toxic side-effects of corticosteroids and cyclophosphamide. However, the toxicity profile of rituximab and relapse rates in AAV patients remain to be assessed in the follow-up research. As in the past decades the clinical studies were finalised to finding the minimal effective doses of cyclophosphamide and glucocorticoids, the next years they could detect the best safety-efficacy profile of a multitarget AAV therapy (4).

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References

1. Rossi GM, Peyronel F, Fenaroli P, Maritati F, Vaglio A: New therapeutics for ANCA-associated vasculitis: 10 years devoted to lessen toxicity. *Clin Exp Rheumatol* 2020; 38 (Suppl. 124): S18-S22.
2. Walsh M, Merkel PA, Peh CA *et al*.: Plasma exchange and glucocorticoids in severe ANCA-associated vasculitis. *N Engl J Med* 2020; 382: 622-31.
3. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerulonephritis Work Group. KDIGO clinical practice guideline for glomerulonephritis. *Kidney Int Suppl* 2012; 2: 139-274.
4. Mcadoo SP, Medjeral-Thomas N, Gopaluni S *et al*.: Long-term follow-up of a combined rituximab and cyclophosphamide regimen in renal anti-neutrophil cytoplasm antibody-associated vasculitis. *Nephrol Dial Transplant* 2019; 34: 63-73.