to achieve long-term B cells depletion. Patients were closely monitored during 46.5 (2–88) months follow-up with clinical and serological surveillance. They received a RTX cumulative dose of 8 g (2–13).

**Results.** Median serum Ig levels declined continuously – but not gradually – after each RTX re-treatment. The biggest decline in Ig took place after the first RTX round. IgM and IgG levels were below normal in respectively 22 (65%) and 16 (47%) patients – 15 patients (44%) with combined low levels of IgM and IgG – already after the first round.

Eleven patients (29%) had a cumulative CYC dose of 50 g or more and they had lower levels of total Ig after the first 3 RTX rounds and lower levels during RTX maintenance. However the 12 patients (32%) receiving CYC in combination with RTX at induction had bigger overall decline in IgG (3.6 vs 2.2 g/L P = 0.028), IgA (0.78 vs 0.32 g/L P = 0.028), IgM (0.53 vs 0.26 g/L) and total Ig (4.9 vs 2.9 g/L P = 0.030) at last visit compared to those receiving RTX without CYC.

**Conclusion.** Ig decrease the most after the first RTX round under RTX maintenance. While a high cumulative CYC dose (>50 g) decreases Ig levels at all time during RTX maintenance, the combination of CYC-RTX at initiation has a synergistic effect with bigger decline of Ig at last visit.

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**Treatment**

P205

**An international, open label, randomised controlled trial comparing rituximab with azathioprine as maintenance therapy in relapsing ANCA-associated vasculitis (RITAZAREM)**

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**Introduction.** ANCA associated vasculitis (AAV), includes granulomatosis with polyangiitis (GPA, Wegener’s), microscopic polyangiitis (MPA), and their organ-limited variants. Prior to the availability of effective therapy, AAV had a mortality of 93% within 2 years. The introduction of glucocorticoids (GC) and cyclophosphamide transformed survival, with 5 year survival rates nearing 80%. AAV has become a chronic relapsing disorder. Cumulative exposure to GC and immunosuppressive drugs contributes to toxicity and organ damage and is of concern to the 50% of patients who relapse within 5 years of initial remission, and the 10% demonstrating a refractory disease course. Novel therapeutic strategies are required for these patients and the 10% of patients intolerant to current treatments.

**Methods.** RITAZAREM (EudraCT 2012-001102-14; ClinicalTrials.gov NCT01697267) is a parallel, open randomized trial evaluating the efficacy of rituximab (RTX) or azathioprine (AZA) maintenance therapy regimens in patients with relapsing AAV. 190 patients with relapsing AAV will be enrolled at centres across Europe, N America, and Australasia to receive RTX (4 x 375 mg/m²), and GC induction therapy. Patients with stable disease at month 4 will be randomised 1:1 to receive repeat RTX or AZA maintenance therapy. All patients will receive GC concomitant with their maintenance regimen. The primary objective is to demonstrate whether or not fixed interval, repeat RTX is superior to AZA in the prevention of disease flare in AAV patients with relapsing disease. The primary endpoint is the time to disease relapse (either minor or major relapse) from randomisation.

**Results.** RITAZAREM will inform the future standard of care for patients with AAV, and provide data describing long term safety of RTX therapy in AAV patients (Supplementary data).

**Discussion.** RITAZAREM is a joint venture of the European Vasculitis Study Group and the Vasculitis Clinical Research Consortium. RTX is supplied free of charge by Roche/Genentech.

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**P206**

**C5aR inhibitor on leukocytes exploratory ANCA associated renal vasculitis (CLEAR) clinical trial with orally administered CCX168**

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**Introduction.** In ANCA vasculitis, the anaphylatoxin C5a amplifies neutrophil influx and activation through C5aR, leading to renal disease. CCX168, an oral specific C5aR antagonist blocked C5a-induced neutrophil chemotaxis and CD11b expression in human blood samples in Ph1. CCX168 profoundly reduced glomerular crescent formation and necrosis in transgenic hC5aR mice with anti-MPO-induced glomerulonephritis.

**Methods.** This is a Ph 2 clinical trial at 40 study centers. Patients have GPA, MPA, or renal limited vasculitis, are anti-PR3+ or anti-MPO+, and have renal vasculitis. Patients are randomized 1:2, placebo: 30 mg CCX168 b.i.d. for 12 weeks, with 12-wk follow-up. Primary objectives: safety and tolerability. Secondary objectives: feasibility of reducing or eliminating corticosteroids (CS), and effect of CCX168 on renal function and ANCA disease.

All pts received cyclophosphamide IV induction treatment (15 mg/kg up to 1.2 g). CCX168 pts in Step 1 of the trial started at 20 mg/d prednisone, and placebo pts at 60 mg/d. If Step 1 were successful, Step 2 would commence, where CCX168 pts received no oral CS, and placebo pts a full CS dose. Target enrollment was 12 pts per step.