by its lack of visceral involvement. Although the chronic, relapsing, non-lethal nature of this condition, ulceration and necrosis of the skin occasionally can occur.

**Methods.**— Review of medical history and current literature.

**Results.**— A 36-year-old woman was diagnosed in 2006 with recurrent scleritis, relapsing polyarthritis and cutaneous PN. In November of 2010 presented with a history of ocular pain, arthritis and subcutaneous erythematous nodules on her lower limbs. She had a history of drug intolerance to steroids, azathioprine and infliximab. She had also previously treated with oral methotrexate and subcutaneous adalimumab without response. Treatment with intravenous immunoglobulin (IVIg) 400 mg/kg for 5 days was administered without clinical changes. Three months later cutaneous lesions persisted therefore infusions of cyclophosphamide 500 mg monthly was initiated. After one month, the patient only had received a single pulse of cyclophosphamide and a painful necrotic ulcer appeared on her left leg. Cyclophosphamide was discontinued due to the high risk of infection. Off-label therapeutic alternative with bosentan 62.5 mg twice daily was begun and after 4 weeks the bosentan dosage was increased to 125 mg twice daily. After three months, the therapy was well tolerated, the ulcer healed and cutaneous lesions resolved completely. Nowadays, the patient doesn’t present any recurrence of cutaneous ulcers on follow up.

**Discussion.**— Bosentan is an oral dual antagonist of endothelin that is indicated for the treatment of primary and secondary pulmonary arterial hypertension and in the prevention of digital ulcers in scleroderma. We hypothesize that bosentan could have a vasodilator and anti-inflammatory effect leading to the rapid clinical improvement in our case.

**Conclusion.**— Clinicians should consider treatment with bosentan in cases of refractory ulcers secondary to PN.

**Further readings**

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**P214**
Plasma exchange and glucocorticoid dosing in the treatment of anti-neutrophil cytoplasm antibody associated vasculitis: A randomized controlled trial. PEXIVAS

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**Introduction.**— PEXIVAS is a 500-subject international, multi-center, randomized, controlled trial examining the efficacy of PLEX and GC dosing in AAV.

**Planned.**— Eighty-five centers from 12 countries are already active and half years ago when the first patient was recruited.

**Methods.**— International, multi-center, randomized, controlled trial.

**Results.**— Sixty-four centres from 12 countries are already active and recruiting. Two hundred and nine patients recruited up to end of December 2012.

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**P215**
Fixed-interval repeat dose rituximab improves abnormalities in the periphera B cell compartment and reduces relapse rates in ANCA associated vasculitis

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**Introduction.**— The ANCA associated vasculitides (AAV) are chronic, relapsing autoimmune disorders, with poorly understood pathogenesis. Rituximab is an effective treatment, likely to be mediated by depletion of autoreactive B cells. Following treatment, B cells repopulate after 6–9 months, and in other autoimmune diseases repopulation with B cells displaying a memory phenotype is associated with relapse. We assessed the phenotype of repopulating cells following fixed interval repeat dosing of Rituximab.

**Methods.**— Eighty-one patients who received fixed-interval repeat dose Rituximab were prospectively followed. Lymphocyte subsets were monitored for CD19, CD4 and CD8 counts. In a subset of these patients more detailed immunophenotyping was undertaken.

**Results.**— Repeat dose Rituximab was effective at inducing and maintaining remission in patients with AAV. Lymphocyte analysis showed sustained depletion of B cells over the 2-year course. On stopping treatment, the majority of patients had return of B cells to pre-treatment levels within the subsequent 12 months. More detailed analysis showed that depletion of B cells was not as efficient as suggested by standard analysis. Those who failed to deplete initially had B cells showing a memory phenotype. However, following 2 years of fixed-interval repeat doses of Rituximab, the surface phenotype of recovering cells suggested they were naive.

**Discussion.**— Fixed interval repeat dose Rituximab led to profound and sustained B cell depletion, and a predominately naive surface phenotype in reconstituting B cells. Sustained B cell depletion had no consistent effects on T cell numbers or subsets in this cohort, but numbers were small and the cohorts were heterogeneous.

**Conclusion.**— Fixed-interval repeat dose Rituximab is a safe and effective treatment for patients with AAV. We postulate that this is due to removal of autoantigen specific memory B cells as they circulate from tissue niches and repopulation with a predominately naive subset of cells. This hypothesis warrants further exploration.

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**P216**
Predictors of treatment resistance and relapse in Chinese patients with antineutrophil cytoplasmic antibody-associated disease

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**Introduction.**— The prevalence and significance of treatment resistance and relapse in ANCA patients of China are poorly understood.

**Methods.**— A total of 102 patients with ANCA vasculitis, diagnosed between January 2003 and December 2009 in China-Japan Friendship Hospital and followed up by the physicians of Nephrology and Rheumatology were enrolled in this retrospective study. Predictors of treatment resistance were evaluated using logistic regression models. Cox proportional hazards models were used to evaluate predictors of relapse.

**Results.**— Two patients with EGPA and two patients with dual ANCA specificities were excluded from the analysis. Of these 98 patients, 15 patients (15.3%) were categorized as having cytoplasmic and/or PR3 ANCA and ANCA (84.7%) could recognise perinuclear and/or MPO...
ANCA. After the induction treatment, disease was resistant to therapy in 24 (25%) of the patients. Six of the 24 patients (18%) progressed to ESKD over 10.9 m. A response to initial treatment occurred in 74 patients (75%), remission was achieved in 41 patients (55%), while 33 (45%) experienced a relapse. Nine of the 33 patients (38%) progressed to ESKD over 29.2 m. Female sex was a statistically significant predictor of treatment resistance (OR 2.85 [95%CI 1.06–2.86], \( P = 0.036 \)). Besides, elevated serum creatinine level, with each increment of 150 µmol/L predicted to treatment resistance (\( P = 0.002 \)). Among the remission patients, those with PR3 ANCA were 1.31 times more likely to experience a relapse than patients with MPO ANCA (95%CI 1.01–5.35) (\( P = 0.0001 \)). Lung involvement was associated with an increased risk of relapse (HR 1.87 [95%CI 1.12–3.53], \( P = 0.014 \)). The impact of female sex approached significance (HR 0.72 [95%CI 0.65–6.87], \( P = 0.08 \)). Our findings highlight the important impact of old age, severity of renal disease at presentation as predictors of treatment resistance, and PR3-ANCA, lung involvement as predictors of relapse.

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P217

Induction treatment of ANCA associated vasculitis with a single dose of rituximab

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Introduction.– Rituximab is effective in inducing remission in ANCA-associated vasculitis (AAV), with randomised evidence to support its use as four infusions of 375 mg/m² (the conventional lymphoma dosing schedule) [1,2]. As B-cell depletion (BCD) appears to occur very rapidly after the first dose, we questioned the need for repeat dosing and adopted a standard single-dose protocol of 375 mg/m² for treating AAV.

Methods.– Four consecutive cases with newly diagnosed or relapsing AAV were treated with a single dose of rituximab. The patients were followed for a mean (±SD) period of 27 ± 8 months. During observation time, seven patients had a relapse and seven (37%) were on additional immunosuppression at the time of rituximab treatment. Circulating CD19 B-cells and clinical and serological markers of disease activity were recorded at regular intervals. Complete remission (CR) was defined as absence of clinical features of AAV with prednisolone dose < 10 mg/day.

Results.– Nineteen patients were included, 17 (89%) with generalised disease and 2 (11%) with severe disease (creatinine level > 500 µmol/L). All but 1 (5%) patient achieved satisfactory BCD (< 0.005 cells/µL) after a median of 13 days. 3-month BCD probability was 92% (Supplementary data). Median time to CR following a single dose of Rituximab was 38 days and the three-month probability of CR was 80%. Median time to B-cell repopulation was 9.5 months, and to disease relapse/re-dose was 27 months. Use of this single-dose protocol saved an estimated £ 4500/patient compared to a 4 × 375 mg/m² dosing schedule.

Conclusion.– Our single centre experience suggests that a single dose of Rituximab of 375 mg/m² is a reasonable, and more cost effective, therapy for inducing remission in patients with AAV.

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P218

Therapeutic drug monitoring detects high interpatient variability in response to myophenolic acid treatment in patients with ANCA-associated vasculitis

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Introduction.– Myophenolic acid (MPA) exerts its immunosuppression by inhibiting inosine 5’-monophosphate dehydrogenase (IMPDH), depleting activated lymphocytes of guanine nucleotides and retarding their proliferation. MPA plays an increasing role in the maintenance therapy of ANCA-associated systemic vasculitis (AASV). The purpose of our study was to examine the correlation between clinical outcome and pharmacokinetic-pharmacodynamic relationships of MPA in patients with AASV.

Methods.– We studied 358 Caucasian blood donors without any MPA therapy to examine basal IMPDH activity. Thirty Caucasian patients with AASV underwent therapeutic drug monitoring. MPA and IMPDH concentrations were measured by a validated high performance liquid chromatography method.

Results.– We observed a high interindividual variability in regard of basal IMPDH activity in patients without any MPA treatment, ranging from 0.84 to 34.82 nmol/mg × protein/h. Patients were followed for a mean (±SD) period of 27 ± 8 months. During observation period, seven patients had a relapse with elevated BVAS score (9.2 ± 6). Patients with relapse during observation time have shown threefold increased predose IMPDH activity before receiving first dose of MPA in contrast to stable patients (\( P = 0.0003 \)). Patients with relapse during maintenance therapy had significant higher levels of mean IMPDH AEC (0–12) 84 ± 17 nmol × h/mg protein/h, indicating inadequate IMPDH suppression. Stable patients had markedly lower IMPDH AEC (0–12) 48 ± 22 nmol × h/mg protein/h (\( P = 0.001 \)). The minimal IMPDH activity was threefold higher in relapse versus stable patients (\( P = 0.002 \)). Furthermore, MPA AUC (0–12) was significantly decreased in relapse patients in contrast to stable patients (\( P = 0.04 \)).

Discussion.– Patients with AASV show high variability in response to maintenance therapy with MPA.

References