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 1.12–4.35], 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.

Conclusions: 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.

References


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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 to treat active AAV.

Methods: We report consecutive cases with newly diagnosed or relapsing AAV for whom conventional immunosuppression was contraindicated or ineffective were enrolled. All were Rituximab naive and 7 (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 μM). 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 x 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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Therapeutic drug monitoring detects high interpatient variability in response to mycophenolic acid treatment in patients with ANCA-associated vasculitis

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Introduction: Mycophenolic 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 under maintenance therapy with MPA 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 x 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 x mg protein/h, indicating inadequate IMPDH suppression. Stable patients had markedly lower IMPDH AEC (0–12) 48 ± 22 nmol/h x 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.