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.

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.

**Supplementary data associated with this article can be found on the website of La Presse Médicale (http://www.em-consulte.com/revue/lpm).**

References

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 to treat active AAV.

Methods-- We observed a high interindividual variability in regard of patients with relapse during maintenance therapy had significant higher levels of mean IMPDH AEC (0–12) 48 ± 22 nmol × h/mg protein/h compared to 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 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 AAV show high variability in response to maintenance therapy with MPA.

P218
**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, ranged 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 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.
Conclusion.—Pharmacodynamic drug monitoring seems to be a new tool to detect inadequate immunosuppression in AASV patients.

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P219
Time to remission and relapse following rituximab in an inception cohort of antineutrophil cytoplasmic antibody associated vasculitis

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Introduction.—The objective of this study was to evaluate the impact of using rituximab in an inception cohort of patients treated since 2003.

Methods.—One hundred and twenty-two patients diagnosed with AAV treated with at least one dose of rituximab from 3/15/03–8/17/12 were included. Information was collected on why rituximab was administered, time to remission on or off therapy and relapse. Time to remission and relapse were plotted using Kaplan-Meier Curves.

Results.—Eighty-four percent of the included patients had biopsy proven AAV. Median age of patients at the time of first rituximab treatment was 53 years IQR (38,62), with 53% female, 82% Caucasian, 46% categorized as GPA, and 53% PR3 positive. 13% of the patients were ANCA negative by ELISA and 4% of the patients were ANCA negative by immunofluorescence. Mean total follow up time of the cohort was 7.0 ± 5.5 years and mean follow up after first rituximab infusion was 4.5 ± 4.5 years.

Thirty-eight (19%) of the courses of rituximab were given for new diagnosis of AAV. One hundred and thirty-three (66%) of the courses were given for relapse and 22 (11%) of the courses were for remission maintenance. Following the first course of rituximab 23 (19%) of patients achieved remission off all therapy in 12 ± 11 months and 65% achieved remission on therapy in 4 ± 4 months. Time to relapse or date of last follow up was 20 ± 19 months following first course of rituximab. Rituximab courses were given without cyclophosphamide (CYC) in 18%, with distant prior history of exposure to CYC in 49% and concurrently with CYC in 33%. Time to relapse was shorter for patients not exposed to CYC either concurrently or historically (100% relapsed by 12 months compared to 25%) (P = < 0.0001). At 12 months 75% of ELISA negative patients had relapsed while 25% of PR3 ANCA positive and 25% of MPO ANCA positive patients had relapsed (P = 0.027).

Conclusion.—Time to relapse was shorter for patients never exposed to cyclophosphamide and those who were ANCA negative.

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P220
Rituximab use in patients with ANCA-associated vasculitis: Clinical efficacy and impact on immunological parameters

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Introduction.—Rituximab (RTX) has been reported as an effective therapeutic agent in (refractory) ANCA-associated vasculitis (AAV). We aimed to evaluate clinical efficacy of RTX in AAV along with its impact on humoral and cellular immunological parameters.

Methods.—Eighteen RTX-treated patients with AAV (M/F 11/7; median age 37.5; 15× PR3-ANCA, 3× MPO-ANCA; 16× refractory disease, 2× first-line therapy) were enrolled. Clinical response, ANCA, IgG levels and cellular immunity parameters were examined regularly after RTX administration.

Results.—The patients were followed-up for a median of 26 months (range 3–82), 15 had follow-up ≥ 6 months. All patients achieved B cell depletion that lasted 3–24 months but no significant increase was noted in T cell or NK cell subpopulations. At 6 months, partial remission was achieved in 5/15 patients, and complete remission in eight patients. The median prednisone dose and ANCA levels decreased by 6 months. Other immunosuppressives were withdrawn in all but four patients. RTX retreatment was used in nine patients (7× preemptive, 2× relapse). Six patients relapsed during follow-up, but none in the preemptively treated group. Three patients died of infectious complications. Despite B cell depletion, markers of T cell activity (higher percentage of HLA-DR + CD3+ cells and lower percentage of CD4 + CD45RA+ naive T cells) persisted during the follow-up. IFN-γ production increased at 6 months compared to baseline and no significant change was noted in the intracellular IL-10 and IL-12 production. IgG levels at 3 months decreased below normal range in most patients but this was well tolerated.

Conclusion.—RTX is an effective induction and also maintenance therapy for AAV that helps to lower the glucocorticosteroids dose and withdraw cytotoxic drugs in most patients. Hypogammaglobulinaemia was common but well tolerated. Peripheral circulating T cells remained activated despite B cell depletion. Our results suggest a favourable effect of RTX on immune system regulatory potential (e.g. IL-10 production).

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P221
Maintenance therapy using rituximab-induced continuous B cell depletion for ANCA vasculitis

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Introduction.—Remission in the majority of ANCA vasculitis patients is not sustained after a single course of rituximab. Long-term risk of relapse warrants development of a successful strategy to maintain remission.

Methods.—Remission maintenance therapy with rituximab was initiated after achieving remission or by converting from other prior maintenance therapy. Rituximab (1000 mg) was administered every 4 months. Rituximab courses were given without cyclophosphamide and those who were ANCA negative. Retreatment was used in nine patients (7× preemptive, 2× relapse). Six patients relapsed during follow-up, but none in the preemptively treated group. Three patients died of infectious complications. Despite B cell depletion, markers of T cell activity (higher percentage of HLA-DR + CD3+ cells and lower percentage of CD4 + CD45RA+ naive T cells) persisted during the follow-up. IFN-γ production increased at 6 months compared to baseline and no significant change was noted in the intracellular IL-10 and IL-12 production. IgG levels at 3 months decreased below normal range in most patients but this was well tolerated.

Conclusion.—RTX is an effective induction and also maintenance therapy for AAV that helps to lower the glucocorticosteroids dose and withdraw cytotoxic drugs in most patients. Hypogammaglobulinaemia was common but well tolerated. Peripheral circulating T cells remained activated despite B cell depletion. Our results suggest a favourable effect of RTX on immune system regulatory potential (e.g. IL-10 production).

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