comes did not differ significantly; serious adverse events MMF 32/70 (46%) vs. CYC 27/70 (39%) (RD 7%, 95%CI –9 to 23%), serious infections MMF 18/70 (26%) vs. CYC 11/70 (16%) (RD 10%, 95%CI –3 to 23%), dialysis MMF 2/70 (3%) vs. CYC 3/70 (4%) (RD –1%, 95%CI –8 to 5%), death MMF 5/70 (7%) vs. CYC 4/70 (6%) (RD 1%, 95%CI –7 to 10%).

Conclusion.– In the primary analysis we were unable to demonstrate that MMF is non-inferior to IV CYC for remission induction at six months in newly diagnosed AAV. How, glucocorticoid treatment affects remission induction with MMF requires further study. Longer term safety outcomes and relapse data are required to fully understand the role of MMF as induction therapy for severe AAV.

http://dx.doi.org/10.1016/j.lpm.2013.02.067

A66

Rituximab versus azathioprine for maintenance in ANCA-associated vasculitis. A prospective study in 117 patients


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Introduction.– Once ANCA-associated vasculitis (AAV) remission has been achieved with CS and cyclophosphamide (CYC), maintenance therapy usually relies on azathioprine (AZA) or methotrexate. However, 28-month relapse rate remains of 28%. Although rituximab (RTX) has been demonstrated to be as effective as CYC for induction of complete remission, the remission rate at 2 years is 31% (46%) vs. CYC 27/70 (39%) (RD 7%, 95%CI 1% to 16%), 2 months was superior to AZA to maintain AAV remission. The infection frequencies were comparable in the two arms, and other SAE were infrequent and resolved in most patients.

http://dx.doi.org/10.1016/j.lpm.2013.02.068

A67

Treatment of systemic necrotizing vasculitides in patients ≥ 65 years old: Results of the multicenter randomized CORTAGE trial


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Introduction.– Trial aim was to optimize the therapeutic strategy for patients > 65 yo with SNV (PAN, GPA, MPA or EGPA). Patients.– Multicenter RCT on patients > 65 yo with newly diagnosed SNV to compare conventional therapy (based on FFS: for all, ~ 28 mo of CS alone, combined with 500-mg/m2 CYC IV pulses every 2–3 wk participating in the study (59 in the AZA arm, 58 in the RTX arm): 89 had GPA, 23 MPA and five kidney-limited diseases. The main clinical manifestations at diagnosis or relapse included ENT involvement in 88 (77.2%), lung in 69 (60.5%) and kidney in 82 (71.9%). Creatininemia was 185 ± 184 µmol/L. All patients have completed their follow-up. Major relapses have occurred in 18 (15.7%) patients: three (5.4%) in the RTX arm and 15 (25.4%) in the AZA arm, with two AZA-arm deaths (one sepsis, one pancreatic cancer). Thirty-three experienced SAE: 18 related to AZA, 15 to RTX. In the AZA arm, 12 infections (one fatal) and one skin cancer were observed vs. 11 infections (none fatal) in the RTX arm.

Conclusion.– This study demonstrated that 500 mg of RTX every 6 months was superior to AZA to maintain AAV remission. The infection frequencies were comparable in the two arms, and other SAE were infrequent and resolved in most patients.
until remission for EGPA or PAN with FFS ≥ one and GPA or MPA, then switched to maintenance) and an experimental regimen, with faster CS dose-tapering and systematic but reduced CYC exposure (for all, ~9 mo of CS and 500-mg fixed-dose IV CYC pulse, given every 2–3 wk, switched after a maximum of six pulses to maintenance). Trial follow-up closure was scheduled 3 yr after enrollment of last patient. The judgment criterion was time to 1st severe adverse event (SAE) hypothesizing a 30% reduction in experimental arm.

**Results.**– One hundred and four patients were randomized (eight PAN, 13 EGPA, 37 GPA, 46 MPA; 91 ANCA+): aged 75.2 ± 6.3 yr at diagnosis; FFS = 0 for seven PAN and ten EGPA-patients. Baseline features were evenly distributed (fever, 53%; lung, 64%; ENT, 40%; kidney, 69%; heart, 20%; skin, 35%; PNS, 25%; CNS, 3%); mean serum creatinine was 234 ± 199 µmol/L. Mean follow-up was 28 ± 11 mo. HR for first SAE (primary endpoint) for experimental vs. conventional treatment was 0.61 [95% CI, 0.38–0.97], i.e., 39% SAE-rate reduction (3-yr event-free survival: 37.6% [95% CI, 26.4–53.7] in experimental vs. 19.2% [95% CI, 10.9–34.1] in conventional treatment arms; P = 0.04). Ninety-one (88%) patients achieved remission with their assigned treatment (47 in experimental vs. 44 in conventional arm; P = 0.37); 21 (20%) patients died (eight vs. 13, respectively; P = 0.22); 16 vs. 11 patients suffered ≥ one relapse(s), with comparable 3-yr relapse-free-survival rates (53.2% [CI 95%, 40.7–69.6] vs. 54.2% [95% CI, 41.9–70]).

**Conclusion.**– Treating SNV patients >65 yo with a specific regimen limiting exposure to CS and fixed low-dose IV CYC pulses can become the standard of care.

http://dx.doi.org/10.1016/j.lpm.2013.02.069

### A68

**Randomized clinical trial of extended versus standard azathioprine maintenance therapy in newly diagnosed PR3-ANCA positive vasculitis patients at high-risk for disease relapse**

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**Introduction.**– Earlier, we found an increased relapse rate in PR3-ANCA-associated vasculitis patients (PR3-AAV) who were C-ANCA positive at remission and switch in therapy to azathioprine. We performed a prospective multicenter randomized clinical trial in PR3-AAV patients who were C-ANCA positive at stable remission to study whether extended azathioprine maintenance therapy could reduce the incidence of relapse.

**Patients.**– Patients newly diagnosed with PR3-AAV between 2003 and 2011 at 12 centers, treated with cyclophosphamide induction, were included (n = 126). Those who were C-ANCA positive (titer ≥ 1:40) at stable remission were randomized to standard or extended azathioprine. Standard treatment consisted of tapering azathioprine (1.5–2.0 mg/kg) with 25 mg every 3 months from 1 year after diagnosis. With extended treatment, azathioprine was continued until 4 years after diagnosis and thereafter tapered.

**Results.**– Median follow-up was 48 months, range 11–53. No difference in relapse-free survival was found between C-ANCA-negative (n = 82) and C-ANCA positive (n = 44) patients at time of stable remission (p = 0.81). In randomized C-ANCA positive patients, relapse-free survival did not significantly differ for standard treatment (n = 24) compared to extended azathioprine (n = 20) (P = 0.36). Also relapse-free survival did not differ between all patients on standard therapy compared to C-ANCA positive patients with extended azathioprine (P = 0.40). Cumulative estimated relapse-free survival at 1 year was 94% (C-ANCA neg standard) versus 92% (C-ANCA pos standard) versus 90% (C-ANCA pos extended). At 4 years, it was 60% (ANCA neg standard) versus 52% (C-ANCA pos standard) versus 74% (C-ANCA pos extended) respectively (figure 1).

**Conclusion.**– Extended azathioprine maintenance therapy did not lead to a significant improvement in relapse-free survival. In this study, a positive C-ANCA status at stable remission was not associated with an increased rate of relapse.

http://dx.doi.org/10.1016/j.lpm.2013.02.070