was lower than that seen following a single RTX course for relapsing GPA, and relapses were rapidly controlled by further RTX. A switch from ANCA negativity to positivity was a relapse predictor but ANCA was negative in one half of the relapses.

http://dx.doi.org/10.1016/j.lpm.2013.02.294

P224
Re-treatment with rituximab in ANCA-associated vasculitis only in the presence of clinical relapse: A single centre experience
G. Jeannin1, C. Salviani2, S. Possenti1, A. Regazzoli3, F. Allegri4, G. Cancarini1, G.A. Gregorini1
1. Spedali Civili di Brescia, UO Nefrologia e Dialisi, Brescia, Italy
2. Policlinico Umberto I di Roma, UO Nefrologia e Dialisi A, Roma, Italy
3. Spedali Civili di Brescia, Laboratorio di Analisi Chimiche e Cliniche, Brescia, Italy
4. Spedali Civili di Brescia, UO Immunologia Clinica, Brescia, Italy

Introduction. – How to use Rituximab (RTX) after RTX induced remission is still a matter of debate. Two main strategies, both preemptive, have been proposed so far:
– re-treatment at fixed intervals (at different times);
– re-treatment after the reconstitution of B lymphocytes.
We report on our experience based on:
– maintaining pts under low-dose steroids and MTX or AZA after RTX-induced remission;
– re-treating pts with RTX only in the presence of clinical relapse.

Methods. – We included all pts with ANCA-associated vasculitis (AAV) treated with RTX at the onset of disease or at a clinical relapse from Jan 2006 to Jan 2013. RTX was initially administered with 4 weekly intravenous (i.v.) infusions, each at a dose of 375 mg/m² of BSA; more recently, a regimen with 2 i.v. doses of 1 g each, administered 2 weeks apart, was adopted.

Results. – Over a 7-year period, 56 pts with AAV were treated with RTX. Thirty-eight pts were affected by granulomatosis with polyangiitis (GPA), 16 by microscopic polyangiitis (MPA) and 2 by Churg-Strauss syndrome (CSS).
ANCA were positive in 56/58 pts (37 anti-PR3 and 17 anti-MPO). Seventeen pts were treated at the onset of disease (11 MPA, 5 GPA, 1 CSS), while 39 pts (33 GPA, 5 MPA, 1 CSS) were treated at relapse. All pts obtained remission. After a mean follow-up of 30.1 months (SD 21.4, range: 6–84), 39 pts (69.6%) didn’t relapse: 15 of 17 pts treated at the onset of AAV, 24 of 39 pts treated at relapse. Only 17 pts relapsed (13 GPA, 4 MPA), after a mean follow-up time of 21.9 months (SD 11.3, range 12–60): 2 of 17 pts treated at the onset, 15 of 39 pts treated at relapse.

Conclusion. – So far, the majority of pts did not relapse after the first RTX treatment. In pts who had relapses, the mean time to relapse was much longer than the times reported in the literature. Our results could depend on the effect of low-dose steroid/immunosuppressive maintenance therapy in prolonging the RTX action.

http://dx.doi.org/10.1016/j.lpm.2013.02.295

P225
Gestational rituximab exposure in women with vasculitis
W. Pendergraft1, M. McGrath2, A. Murphy1, P. Murphy1, K. Laliberte3, J. Niles1
1. Massachusetts General Hospital, Department of Medicine, Division of Nephrology, Boston, USA
2. Brigham and Women’s Hospital, Department of Medicine, Division of Nephrology, Boston, USA

Introduction. – Historically, cyclophosphamide (CYC) has been the mainstay of therapy for ANCA vasculitis. Rituximab (RTX) has proven to be an effective alternative to CYC in women of child-bearing age, but little is known about fetal effects of RTX exposure during pregnancy.

Methods. – While being treated with RTX, women were counselled to avoid or plan pregnancy. Urine hCG was checked before each dose. Among pregnancies, patients and fetuses were monitored for recurrent disease and complications associated with RTX and immunosuppression. Where possible, maternal and fetal cord blood was tested for ANCA negativity to positivity. Six women achieved eight pregnancies (table I), four planned and four unplanned. Patient 3a had progressive airway disease despite absence of B cells, ANCA and other features of active vasculitis. Patient 2b had a miscarriage at 15 wks. Remaining pregnancies were uneventful. Maternal CD20+ B cells were absent at delivery in most patients; however, B cells were at normal levels in fetal cord blood.

Discussion. – Most women were able to achieve and complete pregnancy after RTX treatment, and fetal CD20+ B cells do not appear to be affected.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yrs)</th>
<th>DX</th>
<th>Medications at delivery</th>
<th>Antenatal RTX exposure (months)</th>
<th>Weeks gestation</th>
<th>Child sex</th>
<th>APGAR</th>
<th>Child’s weight (g)</th>
<th>Maternal B cells (%) at delivery</th>
<th>Fetal B cells (%)</th>
<th>APGAR at delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>31</td>
<td>PAN</td>
<td>Azathioprine, prednisone</td>
<td>8</td>
<td>31</td>
<td>M/F</td>
<td>8/9</td>
<td>1625</td>
<td>&lt;0.01%</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>2a</td>
<td>25</td>
<td>GPA</td>
<td>None</td>
<td>6.5</td>
<td>41</td>
<td>F/9.9</td>
<td>3790</td>
<td>2.79</td>
<td>NR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2b</td>
<td>27</td>
<td>GPA</td>
<td>None</td>
<td>7.5</td>
<td>15</td>
<td>N/A</td>
<td>N/A</td>
<td>&lt;0.01%</td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3a</td>
<td>20</td>
<td>GPA</td>
<td>Prednisone</td>
<td>0.25</td>
<td>40</td>
<td>M</td>
<td>2945</td>
<td>&lt;0.01%</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3b</td>
<td>22</td>
<td>GPA</td>
<td>Prednisone</td>
<td>0.5</td>
<td>41</td>
<td>F/9.9</td>
<td>3500</td>
<td>0.54</td>
<td>NR</td>
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<td></td>
</tr>
<tr>
<td>4</td>
<td>29</td>
<td>GPA</td>
<td>Prednisone</td>
<td>13.5</td>
<td>38</td>
<td>F/8.9</td>
<td>3270</td>
<td>&lt;0.01%</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>39</td>
<td>MPA</td>
<td>None</td>
<td>0.25</td>
<td>38</td>
<td>M/10</td>
<td>3515</td>
<td>&lt;0.01%</td>
<td>NR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>32</td>
<td>GPA</td>
<td>None</td>
<td>2.8</td>
<td>40</td>
<td>M/9.9</td>
<td>2693</td>
<td>&lt;0.01%</td>
<td>7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DX: diagnosis; RTX: rituximab; g: grams; NR: not recorded at time of delivery; N/A: not applicable; M: male; F: female; PAN: polyarteritis nodosa; GPA: granulomatosis with polyangiitis (formerly Wegener’s); MPA: microscopic polyangiitis.

Table I
Characteristics of women with autoimmune vasculitis exposed to rituximab and their offspring

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Conclusion.− Further study is needed to determine perinatal safety of RTX, especially as it is replacing CYC as the mainstay of therapy.

http://dx.doi.org/10.1016/j.lpm.2013.02.296

P226 Use of rituximab in Hispanic patients with severe ANCA associated vasculitis: A 6 years experience in a tertiary centre in Chile

F. Silva, L. Massardo, M. Mimica, P. Pastenes, M. Cisternas, F. Radigan, M. Gutierrez
Departamento de Inmunología Clínica y Reumatología. Pontificia Universidad Católica de Chile, Santiago, Chile

Introduction.− ANCA associated vasculitis (AAV) affect small/medium sized vessels in multiple organs, with high morbimortality in the short term and the need for potent immunosuppressant therapy. The chimeric anti-CD20 monoclonal antibody Rituximab (RTX) has shown to be an effective and safe therapy for severe AAV in large studies, which include mostly white non-hispanic populations. Less evidence exists about its efficacy and safety in Hispanics from developing countries. Objective.− To evaluate the safety and efficacy of RTX in a small group of patients with severe AAV in a single center in Santiago, Chile.

Methods.− Retrospective study of consecutive AAV cases (ACR and Chapel Hill criteria), treated with RTX between 2006 and 2012. Baseline demographic and ethnic data, protocol of RTX use and clinical information, including activity (BVASv3 and BVAS/WG scores) and damage (VDI and CDA) every 3 months were obtained. Remission was defined as BVASv3–BVAS/WG scores = 0 for at least 1 month. Adverse events were registered.

Results.− Thirteen cases, 10 male; 47 (19–82) years, eight with Granulomatosis with Polyangiitis and five with Microscopic Polyangiitis. RTX was administered in cycles of 1 to 2 g in two infusions separated by 15 days; four patients received repeated courses. In 8 cases concomitant immunosuppressive was provided (5 MMF; 2 MTX; 3 AZA). Remission post RTX was achieved in ten patients (77%) within 6 m. Reduction of activity was obtained in all cases, and was significant since the third month: BVAS-3 (0 m = 13, 3 m = 3; P = 0.005); BVAS-WG (0 m = 5, 3 m = 1; P = 0.005). Five patients presented disease relapse, the first at 9 m after RTX use. Severe adverse events were observed in two cases (15%; both with grade 3 infections: Pneumocystis jiroveci pneumonia and respiratory syncytial virus infection). Three years after RTX one patient died due to vasculitis reactivation.

Conclusion.− The observed efficacy and safety profile in this small group of Hispanic AAV patients is concordant with the reported in larger studies.

http://dx.doi.org/10.1016/j.lpm.2013.02.297

P227 Long-term efficacy and safety of pre-emptive maintenance therapy with rituximab in Granulomatosis with Polyangiitis: Results from a single centre

E. Besada1, W. Koldingsnes2, J. Nossent3
1. University of Troms, Troms, Norway
2. University hospital North Norway, Troms, Norway
3. Royal Darwin Hospital, Darwin, Australia

Introduction.− Rituximab (RTX) is an anti-CD20 antibody used successfully in Granulomatosis with Polyangiitis (GPA) for induction and maintenance of remission. Our study aims to evaluate the long-term efficacy and safety of chronic pre-emptive RTX therapy in GPA.

Methods.− Retrospective study of 35 GPA patients treated with RTX between April 2004 and September 2011 for active disease and maintenance. RTX was initiated as two 1-g infusions 2 weeks apart and thereafter 2 g RTX was re-administered annually. Patients were followed for 47 (2–88) months. They received a median RTX dose of 8 g (2–13) dealt in five (1–10) rounds.

Results.− All patients had a clinical response, but nine relapses were recorded (flare rate of 6.6/100 patient-years). At last visit, 22 patients were still treated with RTX as 13 patients (37%) had discontinued RTX mainly due to hypogammaglobulinemia (62%). Nine patients (26%) had severe infections (infection rate of 6.6/100 patient-years) and ten patients (29%) had chronic infections. Risks factors for severe infections are older age, renal involvement, high cumulative dose of cyclophosphamide, high prednisolone dose at last visit, low CD4/CD8 ratio and a significant drop in total immunoglobulins after the first RTX round and under maintenance. Risks factors for chronic infections are low total immunoglobulins under maintenance, low B cells at baseline and possibly a high RTX cumulative dose.

Conclusion.− Long term pre-emptive RTX maintenance was efficacious in reducing the risk for relapse but was discontinued in a third of the patients. The patients’ net state of immunodeficiency under RTX changes over time as low level of total immunoglobulins increased the risk for infections.

http://dx.doi.org/10.1016/j.lpm.2013.02.298

P228 Use of an empirically derived cyclophosphamide dosing nomogram for treatment of vasculitis

A. Salama1a, M.D. Gabrel1a, A. Koteci1a, L. Harper2a, D. Jayne3a, D. Nitsch1a, R. Daniel1a, E. Naylor1a, M. Little2b
1. UCL, London, United Kingdom
2. University of Birmingham, Birmingham, United Kingdom
3. University of Cambridge, Cambridge, United Kingdom
4. London School of Hygiene and Tropical Medicine, London, United Kingdom
5. Trinity College Dublin, Dublin, Ireland

Introduction.− Cyclophosphamide (CYC) dose in the CYCLOPS trial was reduced for advanced age and poor kidney function, with reductions for creatinine > 300 µM, and age > 60 and 70 years. This regimen results in relative overdosing of patients between 30 and 60 years of age and creatinine 150–300 µM, which was mirrored by an increase in adverse events. Therefore, using adverse event data from the EUVAS trials, we modelled the optimum dose for age and kidney function. The best-fit line was described by a hyperbolic curve (Y = Bmax \times X/Kd + X), which was used to develop a nomogram in which dose changed continuously for both age and eGFR. We report use of this nomogram in a series of patients with systemic vasculitis.

Methods.− We analysed 22 consecutive patients treated on two sites using the revised CYC nomogram and compared adverse events over the first year with the pulsed IV cyclophosphamide arm of the CYCLOPS trial (n = 76).