Cyclophosphamide effect on immunoglobulins levels in AAV patients treated with long-term pre-emptive rituximab maintenance.

Besada E ¹, Koldingsnes W ², Nossent JC ¹ ³

1 Bone and joint research group, Institute of Clinical Medicine, University of Tromsø, Tromsø, Norway
2 Department of Rheumatology, University Hospital North Norway, Tromsø, Norway
3 Division of Medicine, Royal Darwin Hospital, Department of Health, NT, Australia

email: emilio.besada@uit.no

Objective:

Rituximab (RTX) is an anti-CD20 antibody used in ANCA-associated vasculitis (AAV) for induction and maintenance of remission.

The objective of this study is to determine the effects of CYC on Ig levels in patients treated with long-term pre-emptive RTX maintenance.

Methods:

Retrospective study of 38 patients (35 with GPA and with 3 with CSS) treated with RTX between April 2004 and September 2011 for active disease. 58% of the patients had renal involvement. The cumulative cyclophosphamide (CYC) dose was 14g (0-250). Twelve patients (32%) were treated with combination CYC-RTX at initiation.

RTX was initiated as two 1g infusion 2 weeks apart (RA protocol) and thereafter 2g RTX was administered annually to achieve long-term B cell depletion. Patients were closely monitored during 46.5 (2-88) months follow-up with clinical and serological surveillance. They received a median of 5 (1-10) rounds of RTX for a cumulative dose of 8g (2-13).

Results:

Median serum Ig levels declined continuously but not in a linear fashion after each RTX re-treatment.

The largest decline in Ig level occurred after the first RTX round.

<table>
<thead>
<tr>
<th>IgG g/L</th>
<th>IgA g/L</th>
<th>IgM g/L</th>
<th>Total Ig g/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.70</td>
<td>0.32</td>
<td>0.25</td>
<td>2.35</td>
</tr>
<tr>
<td>0.20</td>
<td>0.06</td>
<td>0.03</td>
<td>0.27</td>
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<tr>
<td>0.05</td>
<td>0.03</td>
<td>0.03</td>
<td>0.39</td>
</tr>
<tr>
<td>2.80</td>
<td>0.40</td>
<td>0.39</td>
<td>3.46</td>
</tr>
</tbody>
</table>

Patients with cumulative CYC dose > 50g (29%):

Had lower levels of total Ig after the first 3 RTX rounds and had also lower levels during RTX maintenance.

Patients receiving initial RTX in combination with CYC (32%):

Had bigger overall decline from baseline in all Ig classes.

Conclusion:

During RTX maintenance therapy in AAV, the largest Ig decrease occurs after the first infusion round, but Ig levels continue to decrease thereafter albeit at a lower speed.

A high cumulative CYC dose (>50g) as well as combining RTX with CYC at initiation leads to larger decline of Ig during RTX maintenance therapy.