Letters to the Editor

Efficacy of rituximab in patients with rheumatoid arthritis refractory or with contra-indication to anti-tumor necrosis factor-alpha drugs in daily practice: an open label observational study

Sirs,

Rheumatoid arthritis (RA) is a chronic disease that leads to inflammation and joint damage. Despite the efficacy of disease-modifying antirheumatic drugs (DMARDs) such as methotrexate and biologic DMARDs agents, 30% of patients have no response or unsustained response (1). While the exact pathogenesis of RA has not been fully established, evidence suggest the importance of B lymphocytes in RA (2). Therefore, randomised controlled trials indicated that selective depletion of B cells led to sustained clinical improvements for patients with active RA despite methotrexate (3, 4) or anti-tumor necrosis factor (TNF)-alpha agents (5). Our aim was to determine, in routine care, the safety and efficacy of rituximab treatment in patients who had experienced an inadequate response to treatment with anti-TNF-alpha agents or had a contra-indication to these drugs and to compare the effects in these 2 groups.

Twenty-one patients with active, seropositive RA (American College of Rheumatology (ACR) revised criteria) (6) were included but the complete follow-up was available for 18 patients (3 had moved up). The mean age was 55 ± 11 years and mean disease duration 12 ± 7 years. Nine patients had a contra-indication to anti-TNF drugs (past of recurrent infections (n = 4), tuberculosis under anti TNF drugs (n = 1), personal familial past of multiple sclerosis (n = 2), cardiac heart failure (n = 1), vasculitis under etanercept (n = 1) and 9 had an inadequate response to anti-TNF (7 with failure of the 3 available anti-TNF drugs). Concomitant therapy consisted in methotrexate (12.5-20 mg/w). The patients had highly active disease as shown by the baseline values in Table I. Rituximab was administered as a 1000-mg intravenous infusion on days 1 and 15 with corticosteroids to attenuate the effects in these 2 groups.

Median [range] value; *p<0.05

<table>
<thead>
<tr>
<th></th>
<th>DAS28 week 0</th>
<th>DAS28 week 24</th>
<th>CRP(mg/L) week 0</th>
<th>CRP(mg/L) week 24</th>
<th>EULAR response</th>
<th>EULAR good response</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients (n = 18)</td>
<td>5.75 (4.2-8.6)</td>
<td>4.2 (1.8-10.6)*</td>
<td>26 (6-292)</td>
<td>10 (1-99)*</td>
<td>13/18</td>
<td>3/18</td>
</tr>
<tr>
<td>Refractory to anti-TNF; (n = 9)</td>
<td>6.5 (5.2-8.6)*</td>
<td>4.8 (3.4-6.5)*</td>
<td>30 (6-292)*</td>
<td>14 (1-99)*</td>
<td>5/9</td>
<td>0/9</td>
</tr>
<tr>
<td>Contra-indication to anti-TNF; (n = 9)</td>
<td>4.9 (4.2-6.7)*</td>
<td>3.5 (1.8-10.6)*</td>
<td>24 (8-67)*</td>
<td>10 (2-82)*</td>
<td>8/9</td>
<td>3/9</td>
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Among the unanswered questions about rituximab, the requirement for subsequent infusions is emerging. In our study, among the 13 responders, another infusion was performed at week 24 in 7/13 patients and was delayed by the clinician because of sustained effectiveness in 6/13 patients. The follow-up is ongoing but this suggests that some patients may have sustained improvement without the need of re-infusion which is clinically and economically interesting but further data are required to investigate which patients may have this benefit. One infusion-related reaction occurred in the group of patients with failure of anti TNF drugs and one pulmonary infection occurred in the group of patients with contra-indication to anti-TNF drugs without other side-effects confirming the good tolerance observed in randomised trials (3-5) or open labelled studies (8, 9). Thus, in this study of daily practice, a single course of two infusions of rituximab, in combination with continued methotrexate, provided significant improvement in disease activity at week 24.

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Conflict of interest:
Y. Allonore has received speaking honoraria from Roche; M. Dougados has received speaking and consulting honoraria, research grants and has been reimbursed for conference expenses by Roche.

References
5. COHEN SB, EMERY P, GREENWALD MW et al.: Rituximab for rheumatoid arthritis: an open label observational study of daily practice, a single course of rituximab will have to be determined by further investigations with larger sample size.