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**Proceedings Paper:**

https://doi.org/10.1136/annrheumdis-2016-eular.6122

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VALIDATION OF B CELL DEPLETION AS A PREDICTOR OF CLINICAL RESPONSE AND EFFICACY OF RETREATMENT OF NON-RESPONSE IN RHEUMATOID ARTHRITIS


Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, NIHR Leeds Musculoskeletal Biomedical Research Unit, Haematological Malignancy Diagnostic Service, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom

Background: Rituximab has been licensed for the treatment of Rheumatoid Arthritis (RA) for over a decade. We previously showed that the initial depth of B cell depletion was associated with clinical response; 96% complete versus 74% incomplete depletion at 6 months (p=0.02)[1] and that retreatment of initial non-responders with incomplete depletion led to 72% response rate in cycle 2 (C2)[2].

Objectives: To validate B cell depletion after the first infusion as a predictor of response to rituximab (Project 1) and assess outcome of retreatment of first cycle non-responders (Project 2) as a basis for B cell monitoring during rituximab treatment.

Methods: The published discovery cohorts included 60 patients in Project 1 and 25 patients in Project 2. For this validation study, we analysed the subsequent consecutive 180 patients with RA treated with rituximab at a single centre. Each cycle of rituximab consisted of 2x1000mg infusions, repeated on clinical relapse. B cell subsets (naïve, memory and plasmablast) were measured at baseline, after first infusion of rituximab (2 weeks) and at early B cell repopulation (6 months) using a flow cytometry protocol optimized to detect low numbers of B cell subsets and plasmablasts. Complete depletion was defined as total B cell count <0.0001 x 10^9/L. First cycle non-responders who had incomplete depletion at C1 were retreated at 6 months.

Results: 180 patients (Female=147(81%), median age at rituximab initiation 62(IQR 51-71) years and median disease duration 10(IQR 5-18) years were studied. 72(40%) patients were biologic-naïve. In C1, 126 (70%) achieved moderate-good EULAR response. The complete depletion rate for C1 was 54%. Complete depletion was associated with response; p=0.027 (Table 1).30 patients who were C1 non-responders and had incomplete depletion were retreated at 6 months. Of these, 20(67%) had complete depletion and 20(67%) responded in C2. Non-responders in C2 had trend to higher plasmablast numbers at retreatment than responders (p=0.14).

Table 1: B cell depletion and response in validation cohort

<table>
<thead>
<tr>
<th>Project A</th>
<th>Depletion</th>
<th>Non Response</th>
<th>Response</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Validation (n=180)</td>
<td>Incomplete</td>
<td>32/82 (39%)</td>
<td>50/82 (61%)</td>
<td>0.036</td>
</tr>
<tr>
<td></td>
<td>Complete</td>
<td>23/98 (23%)</td>
<td>75/98 (77%)</td>
<td></td>
</tr>
<tr>
<td>Combined Discovery + Validation (n=240)</td>
<td>Incomplete</td>
<td>46/117 (39%)</td>
<td>71/117 (61%)</td>
<td>0.003</td>
</tr>
<tr>
<td></td>
<td>Complete</td>
<td>26/123(21%)</td>
<td>97/123 (79%)</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: We have validated that the depth of B cell depletion after the first infusion is a predictor of response to rituximab in RA. A high degree of response in C2 was also confirmed when C1 non-responders who had incomplete depletion were retreated. B cell subsets therefore should be monitored in the routine care of RA patients receiving rituximab and repeat infusions considered if early depletion is incomplete and clinical response poor.

Disclosure of Interest: None declared