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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

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My abstract has been or will be presented at a scientific meeting during a 12 months period prior to EULAR 2016:

No

Is the first author applying for a travel bursary and/or an award for undergraduate medical students?: No

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 $<0.0001 \times 10^9/L$. 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

| Project A | | | | |
|---|------------|--------------|--------------|-------|
| Cohort | Depletion | Non Response | Response | p |
| Validation (n=180) | Incomplete | 32/82 (39%) | 50/82 (61%) | 0.036 |
| | Complete | 23/98 (23%) | 75/98 (77%) | |
| Combined Discovery + Validation (n=240) | Incomplete | 46/117 (39%) | 71/117 (61%) | 0.003 |
| | Complete | 26/123(21%) | 97/123 (79%) | |

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.

References: [1] Dass S et al. A&R 2008 [2] Vital EM et al. A&R 2010

Disclosure of Interest: None declared