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**Proceedings Paper:**

Md Yusof, MY [orcid.org/0000-0003-3131-9121](http://orcid.org/0000-0003-3131-9121), Shaw, D, Rawstron, A et al. (2 more authors) (2016) Validation of Highly Sensitive Flow Cytometry as A Biomarker for Rituximab in Sle: A Rationale for More Intensive Treatment To Improve Clinical Outcomes. In: *Annals of the Rheumatic Diseases. Annual European Congress of Rheumatology (EULAR 2016)*, 08-11 Jun 2016, London, UK. BMJ Publishing Group , p. 296.

<https://doi.org/10.1136/annrheumdis-2016-eular.5947>

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## Medical or Research Professionals/Clinicians

Topic area: *Clinical topics by disease*

Topic: 16. SLE, Sjögren's and APS - treatment

EULAR16-5947

### VALIDATION OF HIGHLY SENSITIVE FLOW CYTOMETRY AS A BIOMARKER FOR RITUXIMAB IN SLE: A RATIONALE FOR MORE INTENSIVE TREATMENT TO IMPROVE CLINICAL OUTCOMES

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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 is effective for SLE in open label series however level of clinical response varies and was not superior to standard of care in randomised trials. We previously showed that clinical response was associated with the depth of initial B cell depletion and relapse was associated with early plasmablast repopulation[1].

**Objectives:** To validate B cell depletion as a predictor of response to rituximab in SLE as a basis to develop more effective B cell targeted therapy.

**Methods:** The published discovery cohort included 38 renal and extra-renal lupus patients. A validation cohort of 46 new patients was recruited. All patients received an initial cycle of 2 infusions of 1000mg rituximab, each preceded by 100mg methylprednisolone. Rituximab was repeated on clinical relapse. Concomitant therapy with cyclophosphamide was not used. Oral immunosuppressants were continued if used at baseline. Oral prednisolone doses varied. B cell depletion using a protocol optimized to detect low numbers of B cell subsets and plasmablasts was measured at baseline, after both infusions of rituximab (6 weeks) and at early B cell repopulation (6 months). Complete depletion was defined as total B cell count  $<0.0001 \times 10^9/L$

**Results:** Depletion and response data were available for 84/100 patients. Overall complete depletion rate was 54%.

Cohort	Depletion	Non Response	Response	p
Discovery (n=38)	Incomplete	7/22 (32%)	15/22 (68%)	0.012
	Complete	0/16 (0%)	16/16 (100%)	
Validation (n=46)	Incomplete	6/17 (35%)	11/17 (65%)	0.014
	Complete	2/29 (7%)	27/29 (93%)	
Combined (n=84)	Incomplete	13/39 (33%)	26/39 (67%)	0.001
	Complete	2/45 (4%)	43/45 (96%)	

Incomplete depletion was predicted at baseline by low complement C4 ( $p=0.044$ ) but not baseline BILAG score or immunosuppressant use. In original cohort there was a significant association between plasmablast repopulation ( $>0.0008 \times 10^9/L$ ) and time to relapse  $< 18$  months ( $p=0.024$ ). Follow up for relapse was limited to 22/36 responders in the validation cohort at the time of analysis, with a trend to the same association ( $p=0.119$ ).

**Conclusions:** We have validated depth of B cell depletion as a predictor of response to rituximab in SLE. Clinical trials using more intensive rituximab treatment regimens, or alternative CD20 molecules are likely to increase clinical response rates to B cell depletion in clinical trials. B cell subsets should be monitored in the routine care of SLE patients receiving rituximab and repeat infusions considered if early depletion is incomplete or plasmablast repopulation is detected at 6 months.

**References:** [1] Vital EM et al. A&R 2012.

**Disclosure of Interest:** M. Y. Md Yusof: None declared, D. Shaw: None declared, A. Rawstron: None declared, P. Emery Grant/research support from: Abbott, BMS, Pfizer, MSD and Roche., Consultant for: BMS, Abbott, Pfizer, MSD, Novartis, Roche and UCB, E. M. Vital: None declared