undermined by their immunogenicity and the development of anti-drug antibodies (ADA) associated with treatment failure and hypersensitivity reactions[2]. Methotrexate (MTX) has been shown to reduce the generation of an ADA response[3]. The ability of other conventional synthetic Disease Modifying Anti-Rheumatic Drugs (csDMARDs) to mitigate unwanted immunogenicity, and prolong efficacy in patients who cannot tolerate methotrexate, is less clear.

Objectives: We previously reported that MTX markedly inhibited the production and release of soluble immunoglobulin (sIgG) by human primary B cells co-cultured with PBMC (BT system) in the *in vitro* BioMAP® phenotypic screening panel[4,5]. MTX also had anti-proliferative effects on human primary tissue and immune cell types[6]. We evaluated other csDMARDs to determine if they were broadly active or, were more similar to MTX in selectively blocking sIgG production and therefore would be more likely to reduce ADA associated with biologics.

Methods: A series of csDMARDS (sulfasalazine, hydroxychloroquine, cyclosporine, leflunomide and azathioprine) were profiled at 4 concentrations across the BioMAP Diversity PLUS™ panel to generate phenotypic activity profiles. In addition to assessing sIgG production, effects on a broad scope of disease-relevant readouts related to primary cell activation and proliferation, inflammation, wound healing, tissue/matrix remodeling, and fibrosis were also evaluated.

Results: Similar to MTX, cyclosporine, leflunomide and azathioprine strongly inhibited sIgG production at all tested concentrations. In contrast, treatment with sulfasalazine or hydroxychloroquine did not decrease sIgG indicating these compounds may not mitigate the immunogenicicty of biologics. In contrast to MTX, several csDMARDS were broadly active in many BioMAP systems. Bioinformatics analysis was used to identify distinct mechanistic signatures for these agents in the BioMAP Panel.

Conclusions: These results support application of the BioMAP *in vitro* assay systems, widely utilized for preclinical drug discovery, to determine the suitability of csDMARDS as anti-immunogenic co-treatments to extend the clinical efficacy of biologics. Clinical studies are needed to confirm these results, however, in inflammatory bowel diseases and to a less extent in rheumatoid arthritis, azathioprine has been shown to reduce immunogenicity of biologics[7].

References:

[1] Rosman, Z, et al., (2013) BMC Medicine. April;11:882.
[2] Mok CC., (2013) Clin Rheumatol. Oct;32(10):1429–35.
[3] Jani M, (2014) Rheumatology. Feb;53(2):213–22.
[4] Berg EL, et al., (2015) Int J Mol Sci. Jan 5;16(1):1008–295.
[5] Tan, T, et al., (2013) Arthritis & Rheumatism. 65 Supplement 10:18666.
[6] O'Mahony et al., (2014) Annals of the Rheumatic Diseases. June. 73(Suppl 2):365–365.
[7] Krieckaert CLM et al. (2010) Arthritis Res Ther. May; 12(5): 217.

Acknowledgements: We acknowledge the contributions of BioMAP operations, bio-analytics and support staff to this data. Thanks to the BioMAP Research Biology team for their analysis and interpretation of BioMAP profiling data.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1942

THU0181 CLINICAL CHARACTERISTICS OF RHEUMATOID ARTHRITIS PATIENTS ONGOING METHOTREXATE THERAPY NOT ACHIEVING DAS28 "LOW DISEASES ACTIVITY": A MATCHED CASE-CONTROL ANALYSIS FROM THE MARI STUDY

A. Giusti[1], M. Manara[2], E. Bruschi[3], V. Azzolini[4], N. Belai Beyene[5], S. Corbanese[6], F. De Gennaro[7], L.S. Martin-Martin[8], A.B. Molica Colella[9], M.R. Pozzi[10], N. Romeo[11], T. Rossini[12], A. Severino[13], L. Sinigaglia[2], G. Bianchi[1]. *[1]Rheumatology, "La Colletta" Hospital, Arenzano, Genoa; [2]Rheumatology, A.O. Istituto Ortopedico G. Pini; [3]Rheumatology Unit, ASST Grande Ospedale Metropolitano Niguarda, Milano; [4]Department of Rheumatology, ASL-TO4, Ospedale Ivrea, Ivrea; [5]Department of Internal Medicine, Azienda ICP Milano, P.O. E. Bassini, Milano; [6]Department of Internal Medicine, O.C. di Vittorio Veneto, Vittorio Veneto; [7]Department of Internal Medicine, A.O. Istituti Ospitalieri, Cremona; [8]Department of Internal Medicine, Ospedale Regina Apostolorum, Albano Laziale; [9]Department of Rheumatology, A.O. Ospedali Riuniti Papardo-Piemonte, Messina; [10]Department of Internal Medicine, A.O. San Gerardo, Università Milano-Bicocca, Monza; [11]Rheumatology Unit, ASO Santa Croce e Carle, Cuneo; [12]Department of Internal Medicine, Ospedale Valduce, Como; [13]Department of Allergology and Clinical Immunology, IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy*

Background: Methotrexate (MTX) is the DMARD of first choice in the treatment of rheumatoid arthritis (RA).

Objectives: To investigate the clinical characteristics and describe therapeutic approaches in RA patients ongoing MTX not achieving a DAS28 "low disease activity" score.

Methods: This is a case-control analysis including 186 patients (mean age±SD, 61±12 years, 16% males) who did not achieve a DAS28 "low disease activity" score (defined by a value ≤3.2) and 558 age- and gender-frequency-matched (1:3), randomly selected controls (mean age age±SD, 61±13 years) who achieved a DAS28 "low disease activity" from the original cohort investigated in the MARI study. The MARI study enrolled RA patients on treatment for at least 12-month with MTX. Demographic, clinical, laboratory and pharmacological characteristics of patients recorded at baseline visit were considered for the current analysis. We first compared the characteristics of patients who reached the endpoint with those of subjects who did not by univariate analyses, thereafter, we performed a multivariate model to identify predictors of not achieving the endpoint. We further investigated the therapeutic approaches in patients not achieving the endpoint.

Results: Compared to patients with a DAS28 ≤3.2, subjects not achieving the endpoint presented with a significant higher (mean±SD) weight and BMI (DAS28 ≤3.2: 25±4 versus DAS28 >3.2: 26±5, P=.022), and longer duration of symptoms (months±SD) before the RA diagnosis (11±15 versus 15±20, P=.009). A higher proportion of subjects within the group not achieving the endpoint presented with polyarticular disease (DAS28 ≤3.2: 57% versus DAS28 >3.2: 96%, P<.001), erosive arthritis (49% versus 73%, P<.001), extra-articular symptoms (3% versus 10%, P<.001), positive RF test (63% versus 73%, P=.013), and increased CRP (13% versus 53%, P<.001). The proportion of patients treated with oral MTX was 25% in the subgroup with DAS28 ≤3.2 and 15% in the subgroup with DAS28 >3.2 (P=.004). In the logistic regression analysis, the variables predictive of a DAS28 >3.2 were polyarticular disease (OR 4.0, 95% CI 2.4–6.7, P<.001), erosive arthritis (OR 2.2, 95% CI 1.4–3.4, P<.001), and increased CRP (OR 7.4, 95% CI 4.9–11.4, P<.001). In patients who did not reach the endpoint, the main therapeutic strategies were: a change in the route of administration of MTX (DAS28 >3.2: 13% versus DAS28 ≤3.2: 4%, P<.001) in favor of subcutaneous MTX, an increase of the dose of MTX (13% versus 2%, P<.001), and the prescription of a new biologic (12% versus 1%, P<.001).

Conclusions: Our results identified a number of variables potentially associated the risk of not achieving a DAS28 "low disease activity" score in RA patients ongoing MTX treatment. Longitudinal studies are warranted.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4619

THU0182 MONOTHERAPY WITH THE JAK1-SELECTIVE INHIBITOR FILGOTINIB DISPLAYS AN ANTI-INFLAMMATORY BIOMARKER PROFILE IN RHEUMATOID ARTHRITIS PATIENTS

A. Kavanaugh[1], A. Van der Aa[2], C. Jamoul[2], W. Li[3], L. Goyal[3], Y. Pan[3], P. Harrison[2], C. Tasset[2], J. Tarrant[3], R. Galien[4]. *[1]University of California, la Jolla, United States; [2]Galapagos NV, Mechelen, Belgium; [3]Gilead Sciences, Foster City, United States; [4]Galapagos SASU, Romainville, France*

Background: Janus kinases (JAKs) are key proteins in the signal transduction of many cytokines and growth factors. The selective JAK1 inhibitor filgotinib (GLPG0634, GS-6034) has been evaluated in a 24-week phase 2B study (DARWIN 2) as monotherapy in active rheumatoid arthritis (RA) patients with inadequate response to methotrexate and has shown a good safety and efficacy profile[1].

Objectives: To gain insight into filgotinib mode of action as monotherapy in RA patients by analysing the impact of filgotinib on a broad panel of immune modulators in the serum.

Methods: RA patients received either placebo (PBO), or filgotinib monotherapy at 50mg, 100mg or 200mg once daily (QD). Serum samples were collected at baseline, week 4 and week 12 and analysed using the 18-plex bead-based immunoassay (HSTCMAG-28SK Merck-Millipore) on BioPLEX-200 instrument to measure cytokine concentration. Median % change from baseline for biomarkers are reported for week 4 and 12. Wilcoxon rank-sum test assessed the significance of difference between filgotinib treated groups and PBO.

Results: Following treatment with filgotinib at 100 mg QD and 200mg QD, there were significant reductions in cytokines important in expansion and activity of multiple T cell subsets and innate immunity compared to PBO (see Table). These changes include decreases in proinflammatory cytokines (IL-6, IL-1β, and TNFα), T_H1-related (IL-2, IFN-γ and IL-12), T_H2-related (IL-4, IL-5, and IL-13) and T_H17-related cytokines (IL-1β, IL-6, IL-17A, IL-21 and IL-23). All doses of

Table 1. Median percent change of biomarkers from baseline

	Week 4			Week 12		
	PBO (N=61)	Filgotinib 100mg QD (N=62)	Filgotinib 200mg QD (N=65)	PBO (N=61)	Filgotinib 100mg QD (N=63)	Filgotinib 200mg QD (N=65)
GM-CSF	0	-11***	-9***	6	-11***	-21***
IFN-γ	13	-15***	-13***	6	-21***	-23***
IL-1β	6	-10**	-13***	8	-24***	-16***
IL-2	4	-9**	-13***	10	-22***	-21***
IL-4	10	-8***	-8***	21	-17***	-22***
IL-5	2	-10**	-3*	3	-20***	-14***
IL-6	17	-20**	-35***	-13	-34*	-52***
IL-7	2	-10***	-1^{NS}	0	-22***	-21**
IL-8	1	-1^{NS}	-1^{NS}	-7	-4^{NS}	-8^{NS}
IL-10	6	-12***	-17***	13	-18***	-26***
IL-12	8	-7***	-14***	6	-20***	-23***
IL-13	1	-10**	-13**	13	-8***	-20***
IL-17A	7	-9***	-12***	1	-21***	-16**
IL-21	11	-14***	-10***	4	-26***	-23***
IL-23	3	-12***	-12***	-4	-24***	-31***
MIP-1α	5	-5***	-8***	3	-7***	-6**
MIP-1β	3	-6**	-6*	3	-5^{NS}	3^{NS}
TNF-α	5	-7***	-12***	5	-11**	-14**

P values comparing % changes between filgotinib and PBO groups: NS p>0.05; *p<0.05; **p<0.01; ***p<0.001.