undermined by their immunogenicity and the development of anti-drug antibodies (ADA) associated with treatment failure and hypersensitivity reactions². Methotrexate (MTX) has been shown to reduce the generation of an ADA response³. 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 types⁶. 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 immunogenicity 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 biologics⁷.

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.

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

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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±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.

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

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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 profile¹.

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.

filgotinib also reduced the B- and T-cell development cytokine IL-7. In contrast, IL-8 was not affected by filgotinib. Reductions in MIP1 α , MIP1 β and GM-CSF are in line with a down modulation of innate immune activity.

Conclusions: Treatment of RA patients with filgotinib monotherapy resulted in significant reduction in the levels of a broad range of cytokines related to T_H1, T_H2, T_H17 and potentially B cells, as well as innate immunity. This observed anti-inflammatory activity of filgotinib is consistent with its efficacy in RA patients.

References:

[1] Kavanaugh A et al. Ann Rheum Dis 2016;0:1–11.doi:10.1136/annrheumdis-2016-210105.

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THU0183 IMPROVED ADHERENCE TO NEWLY PRESCRIBED DMARDS WITH CO-PRESCRIPTION WITH LOW DOSE STEROIDS IN RHEUMATOID ARTHRITIS PATIENTS ATTENDING CLINIC AT A DISTRICT GENERAL HOSPITAL IN THE UK

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Background: Non-adherence to DMARDs is associated with disease flares and increased disability. Adherence rates to prescribed medicine regimes in people with Rheumatoid Arthritis vary from 30–80% in different studies. Improving adherence to therapy leads to better disease outcome and reduced costs associated with management of RA.

Objectives: This study was carried out as a pilot study to look at the effect of co-prescription of steroids on the adherence and side effects to newly prescribed DMARDs in patients with rheumatoid arthritis.

Methods: This is a prospective, observational cohort study, for the duration of three months per participant. Patients were selected sequentially from those attending outpatient clinic at Basildon Hospitals with a confirmed diagnosis of rheumatoid arthritis (ACR/EULAR criteria), and had been planned to start on a new DMARD by the treating physician. Baseline data included demographics, disease characteristics and data regarding steroid co- prescription including route, dose and duration. Patients were reviewed at three months to look at DMARD adherence defined by continuation of the DMARD. We looked at the side effect profile as possible contributing factor to non-adherence. The effect of co-prescription with steroids and other demographic data on treatment duration was investigated using Kaplan-Meier survival plots. Logistic regression analysis was used to investigate the effect of co- prescription of steroids on continuation of medication.

Results: Fifty one patients were recruited to the study. Median age at the time of enrolment was 61 years (IQR 46–71), 73% were females and 92% were caucasians. seventy percent of the patients were seropositive and DMARD naïve with a mean DAS CRP at recruitment of 4.13 (1.21). Seventeen (33%) patients were co-prescribed with steroids at the initiation of DMARDs. Out of these 59% (n=10) were DMARD naïve. Thirteen patients received a tapering dose of oral prednisolone with a mean starting dose of 13.8mg daily (range 3mg - 20 mg) for a mean duration of 10.8 weeks. Two patients received oral prednisolone 5mg daily for 12 week. The mean cumulative dose of oral prednisolone prescribed was 632.2mg. The two remaining patients received 120 mg of depomedrone IM. The non adherence rate for our cohort was 35%, 6% for patients co-prescribed with steroids versus 50% for patients who were not co-prescribed with steroids. The odds ratio for likelihood of discontinuation for patients who were not co-prescribed with steroids versus patients who were, was 16 (1.94–134.5, p=0.011).

At the end of three months 25% of the whole cohort, 12% of the patients who were co-prescribed with steroids versus 32% of the patients who were not co-prescribed with steroids reported side effects to the DMARD initiated, the odds ratio for reporting side effects with steroid co-prescription was 0.28 (0.054–1.438, p=0.12).

Conclusions: Co-prescription of low dose steroids with initiation of DMARDs increases the chances of adherence and possibly reduces the side-effect profile

References:

[1] van den Bemt BJ, Zwikker HE, van den Ende CH. Medication adherence in patients with rheumatoid arthritis: a critical appraisal of the existing literature. Expert Rev Clin Immunol. 2012;8(4):337–351.

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THU0184 ADHERENCE PROFILES TO METHOTREXATE OF PATIENTS WITH RHEUMATOID ARTHRITIS (RA) ELIGIBLE FOR BIOLOGICS: TYPOLOGIES FROM FORGET, A CROSS-SECTIONAL SURVEY OF 244 PATIENTS

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Background: Adherence to Methotrexate (MTX) is not optimal in RA patients [1]. Conflicting determinants of adherence have been identified in literature. Our hypothesis was that the discordant results were related to different typologies of patients.

Objectives: Determine the Methotrexate adherence profiles of patients with RA eligible for biologics.

Methods: The FORGET survey carried out in 2016 was aimed to assess the MTX adherence rate of RA patients, insufficient responders to MTX, biologic-naïve, when an initiation of biologics was being considered. Non-adherence was defined as a compliance rate <80% according to the CQR19 (Compliance Questionnaire for Rheumatology) [2]. The factors tested were socio-demographic characteristics, DAS 28, RAID, CQR responses, beliefs, voluntary or involuntary dose skipping, social and medical support.

Results: Of the 244 patients analyzed, the non-adherence rate was 34%. The rather weak correlation between adherence (CQR) and the disease impact (RAID) tended to confirm the hypothesis of different profiles. Four typologies of patients were determined. Groups G1 and G2 were non-adherent patients with high (G1) or lower (G2) impact. Groups G3 and G4 were patients with good adherence with high (G3) or lower impact (G4). Significant adherence factors were found for these 4 groups (p<0.01) (table).

	Non-adherent patients		Adherent patients	
	G1	G2	G3	G4
%	14	19	33	34
CQR 19 (%)	21	40	78	88
RAID (0–10) mean	6,7	4,6	6,3	3,7
Skipped doses (%)	66	55	15	11
Skipped doses without doctor's recommendation (%)	38	41	3	3
I comorbidity or more (%)	62	68	57	45
Depression (%)	31	14	12	3
Anxiety	16	9	9	1
Good information received (%)	69	83	81	93
I find constraints to take my treatment (% yes)	59	61	21	6
I tolerate my treatment badly (% yes)	47	18	16	18
I think every day about my arthritis (% yes)	83	63	88	53
I find it hard to keep my professional obligations because of my arthritis (% yes)	79	38	65	32
I feel well informed about my arthritis (% yes)	69	83	81	93
I had support from my relatives (% yes)	55	55	82	96
My treatment is doing me more harm than good (% no agreement at all)	0	22,7	36,8	71
The most important reason to take my treatment is that I can still do what I want to do (% complete agreement)	6,3	11,4	17,2	60,5
I do not expect miracles from my treatment (% no agreement at all)	0	0	10,3	23

Conclusions: Four adherence profiles to Methotrexate have been identified. Among the non-adherent patients, 2 topologies are opposed: 1- patients in state of suffering, with low support from relatives, negative beliefs and significant professional impact. 2-patients with less disease impact, who perceived their treatment with constraints although well tolerated. Detection of patients' profiles may allow targeted strategies to improve or maintain adherence.

References:

[1] DiBenedetti D Rheumatol Ther 2015.

[2] de Klerk E et al, J Rheumatol 1999.

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THU0185 COMPARISON OF TOFACITINIB SAFETY AND EFFICACY IN RHEUMATOID ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE TO CONVENTIONAL SYNTHETIC DMARDS, OR TO ONE OR MORE BIOLOGICAL DMARDS

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Background: Tofacitinib is an oral JAK inhibitor for the treatment (tx) of rheumatoid arthritis (RA). Studies have shown diminishing response to tx in RA patients (pts) when cycling through TNF inhibitors. Prior analyses assessed tofacitinib in csDMARD-inadequate response (IR) pts vs overall bDMARD-IR pts.