Abstract AB0482 – Table 1

	Week 0	Week 12	Week 24	Week 36	Week 48	Week 60	*p	**P	***p
Patients with response data, (n)	118	39	41	31	32	28			
Disease activity level, n (%)									
Remission		7 (6)	17 (47)	10 (32)	16 (59)	12 (43)	17 (63)		
Moderate		64 (59)	14 (39)	12 (39)	7 (26)	10 (36)	8 (30)		
High		29 (27)	1 (3)	1 (3)	1 (4)	2 (7)	2 (7)		
DAS28, Median (Q1-Q3)	4.4 (3.7–5.1)	2.8 (2–3.5)	3 (2.4–3.6)	2.2 (1.9–3.3)	3.1 (1.9–4.2)	2.1 (1.9–4.1)	<0.001	<0.001	<0.001
Swollen joint (0–28); Median(Q1-Q3)	2 (0–4.3)	0	0	0	0	0	<0.001	<0.001	<0.001
Tender joint (0–28); Median (Q1-Q3)	4 (2–10)	0 (0–1.3)	0 (0–2)	0 (0–0)	0 (0–2)	0 (0–0)	<0.001	<0.001	<0.001
CRP (mg/L); Median (Q1-Q3)	13 (4.7–29)	4.8 (3–12.8)	4.3 (3–10.3)	4 (3–9)	6 (3–12)	9 (3–17.5)	0.005	0.015	0.110
Patient global score (0–100); Median	62.5 (42–80)	44 (12–60)	30 (20–50)	27(12–31)	30.5 (15–69)	27.5 (13–46)	<0.001	0.001	<0.001
HAQ score; Median	1 (0.8–1.5)	0.5 (0–1.3)	0.6 (0.1–1.3)	0.5 (0.3–0.8)	0.6 (0.2–1.2)	0.6 (0–1)	0.003	0.008	0.001

Abstract AB0482 – Table 2. Disease activity parameters baseline and weeks 12, 24, 36, 48 and 60

First biological tofacitinib n:105	Response data:n	58	18	15
	DAS28, Median	4.5 (3.7–5.2)	2.4 (1.6–3.6)	3 (2.4–3.6)
	(Das 28<3.1) n	11 (19%)	11 (61%)	8 (53%)
Using other biological drugs before TOFA n:75	response data, n	50	18	16
	DAS28, Median	4.4 (3.7–5)	2.9 (2.4–3.5)	3 (2.3–3.7)
	Das28<3.1 n (%)	4 (8%)	10 (56%)	10 (63%)
	#p	0.577	0.516	0.921
	##p	0.173	1.000	0.879

*p for week 0 vs 12; **p for week 0 vs 48,***p for week 0 vs 60 #p das28median for TOFA versus other biological ##p das28 <3.1for TOFA versus other biological

with and without previous ≥ 1 biologics at weeks 0,12 and 24 (table 2) Remission rate was(43%)at week 60(derived data) (table 2) A total of 9 adverse events (3infection,3allergic rx,2 rash)were observed during the followup period

Conclusions: Treatment with TOFA may provide good response rates in RA patients refractory previous biologics

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.6391

AB0483 PHYSICIANS' AWARENESS ON THE USE OF METHOTREXATE BY RHEUMATOID ARTHRITIS PATIENTS

B.N. Coskun¹, B. Yagiz², Y. Pehlivan², E. Dalkilic². ¹Rheumatology, Ilker Celikcan Physical Therapy and Rehabilitation; ²Rheumatology, Uludag University, Bursa, Turkey

Background: Methotrexate (MTX) is an anchor drug used in the treatment of rheumatoid arthritis (RA). It is notable that although MTX has severe potential side effects, most of these side effects could be prevented. Patients should be informed very well regarding MTX and prescriptions should be prepared carefully.

Objectives: In this research, we sought to investigate patients with RA and also physicians, awareness regarding use of MTX, which is under-researched.

Methods: Following Fayet et al., the data were collected from rheumatoid arthritis patients (n=98) and physicians (n=82) through a questionnaire that included questions regarding the effects of MTX, MTX administration, drug interaction, side effects, the frequency of patient follow-up and changes regarding daily life. The questionnaire was filled by the patients in the hospital and physicians filled the on-line questionnaire.

Results: 23% patients responded correctly about that MTX is drug modifying anti-rheumatic drugs (DMARD). 88% of the patients stated that they used MTX weekly, only 16% of the patients were able to explain the reason why they used folic acid was reducing the toxicity of MTX and only 5% reported that folic acid did not increase the efficacy of MTX. 95% did not know that trimethoprim should not be combined with MTX. 11% were familiar with haematologic risks. 7% were aware of hypersensitivity pneumonitis. 42% had information regarding laboratory tests. 20% were conscious concerning the need for contraception. 33% noted that alcohol consumption must be limited. The striking findings physicians responded wrongly was that according to 51% physicians, MTX leads to cancer. Surprisingly, approximately 30% physicians responded wrongly concerning surgery protocol.

Abstract AB0483 – Table 1

	Right answer (%)		Wrong answer (%)		Unknown (%)	
	Patient	Physician	Patient	Physician	Patient	Physician
Mechanism of action						
Methotrexate is a disease-modifying drug	23	93	17	7	60	0
Time when MTX becomes effective	12	83	20	12	68	5
Should not be stopped on the disappearance of symptoms	13	98	16	0	71	2
Dosage should not be adjusted to the pain	40	76	15	19	45	5
Maximum dosage allowed	12	82	7	13	81	5
Once weekly administration	88	100	4	0	8	0
Folic acid reduces toxicity of MTX	16	94	5	5	79	1
Decreases efficacy at high doses	3	61	11	28	86	11
Does not increase efficacy of MTX	5	93	10	6	85	1
Should not be combined with trimethoprim	5	71	4	11	91	18
Nonapplicable interactions with analgesics	23	94	16	5	61	1
NSAIDs	22	93	13	3	65	4
Corticosteroids	23	98	13	2	64	0
DMARDs	23	94	12	6	65	0
Nonapplicable interactions with antibiotics	11	88	11	5	78	7

Conclusions: The findings showed that patients with RA, who used MTX frequently, had insufficient information regarding MTX. Notably, patients are lack of information about the side effects of MTX, drug interactions and the need for contraception. Hence, we recommend that patients' knowledge should be increased regarding MTX. Physicians should be provided with training to raise awareness proper use of MTX.

REFERENCE:

- [1] Fayet F, Savel C, Rodere M, et al. The development of a questionnaire to evaluate rheumatoid arthritis patient's knowledge about methotrexate. *J Clin Nurs*. 2016 Mar;25(5-6):682-9.

Acknowledgements: We thank Jean-Jacques Dubost medical rheumatologist France for sharing the questionnaire that we used in this research.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.7095

AB0484

MONOTHERAPY WITH FILGOTINIB, A JAK1-SELECTIVE INHIBITOR, REDUCES DISEASE SEVERITY AND ALTERS IMMUNE CELL SUBSETS IN THE NZB/W F1 MURINE MODEL OF LUPUS

C. Pohlmeier, Z.-H. Cui, P. Han, A.S. Clarke, R.M. Jones, N. Mollova, I. Mikaelian, S. Zaboli, A. Shauf, J.A. Di Paolo. *Gilead Sciences, Inc, Foster City, USA*

Background: Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease characterised by immune system hyperactivation leading to the production of autoantibodies and immune attack on multiple organs including the skin and kidneys. High levels of type I interferons (IFN α /b) alter the activation state of immune cell populations and have been identified as a risk factor for SLE. Antibody blockade of the interferon alpha receptor (IFNAR) has demonstrated clinical efficacy in a Phase 2b study in SLE, and validates targeting this pathway in SLE¹. Janus kinase 1 (JAK1) is critical for mediating downstream signalling of type I IFNs. Inhibition of JAK1, therefore, is anticipated to reduce IFN signalling, activation of immune cell subsets, and SLE disease activity. The JAK1 selective inhibitor filgotinib (FIL) is currently being evaluated in three proof-of-concept Phase 2 studies in SLE-like diseases.

Objectives: To characterise the efficacy and mechanism-of-action of FIL in the NZB/W F1 spontaneous mouse model of lupus in a therapeutic setting.

Methods: FIL was tested in the NZB/W F1 model of lupus at two concentrations (0.05% and 0.1%) formulated in chow and administered *ad libitum* from weeks 28–40. Cyclophosphamide (CP) was used as a positive control at 5 mg/kg, once daily, i.p. Efficacy was determined by changes in proteinuria, renal histopathology, and survival. Splenic cell populations were analysed by flow cytometry at study termination at week 40 to measure changes in immune cell subsets in diseased versus non-diseased mice and following FIL treatment. An *in vitro* murine whole blood pSTAT1 assay and PK exposure data were used to assess target coverage in the model.

Results: In the NZB/W model, FIL showed a dose-dependent decrease in proteinuria with a concomitant reduction in BUN levels, renal inflammation, improved glomerular morphology, and increased survival (table 1). Diseased mouse spleens had decreased frequencies of naive T cells, increased frequencies of CD11⁺dendritic cells (DCs), and an increased ratio of memory:naive T cells versus non-diseased mice. FIL treatment showed a dose-responsive reversal of these populations toward non-diseased levels. FIL inhibited *in vitro* IFN α -stimulated pSTAT1 signalling in T cells. Calculated JAK target coverage of pSTAT1 inhibition was similar to that observed in human studies at clinical doses.

Abstract AB0484 – Table 1. Efficacy scores in the NZB/W F1 model

	Placebo	FIL (0.05%)	FIL (0.1%)	CP (5 mg/kg)
Proteinuria ^a	30.72	29.03 (-5%)	23.40 (-24%)*	17.47* (-43%)
Survival	55%	73%	93%*	100%*
Glomerular diameter	3.66	2.10 (-43%)	0.83 (-77%)*	0.75*
Summed renal histology ^b	14.71	6.81 (-54%)	3.20 (-78%)*	0.37 (-90%)*
Glomerular myeloperoxidase	3%	2% (-52%)	1.1% (-101%)*	1.6% (-73%)*

^aUrine score AUC (week 28–40)

^bIncludes: glomerular diameter, protein casts, interstitial inflammation, and vasculitis p-values comparing % changes between treatment and placebo groups: *p<0.05

Conclusions: FIL demonstrated efficacy in the NZB/W F1 murine model of lupus with an alteration of splenic immune cell subsets affected by type I IFNs toward non-diseased levels. This data provides the basis for the evaluation of FIL as monotherapy in the currently ongoing Phase 2 studies in lupus-related diseases.

REFERENCE:

- [1] Furie R, et al. *Arthritis Rheumatol* 2017;69:376–386.

Disclosure of Interest: C. Pohlmeier Shareholder of: Gilead Sciences, Inc, Employee of: Gilead Sciences, Inc, Z.-H. Cui Shareholder of: Gilead Sciences, Inc, Employee of: Gilead Sciences, Inc, P. Han Shareholder of: Gilead Sciences, Inc, Employee of: Gilead Sciences, Inc, A. Clarke Shareholder of: Gilead Sciences, Inc, Employee of: Gilead Sciences, Inc, R. Jones Shareholder of: Gilead Sciences, Inc, Employee of: Gilead Sciences, Inc, N. Mollova Shareholder of: Gilead Sciences, Inc, Employee of: Gilead Sciences, Inc, I. Mikaelian Shareholder of: Gilead Sciences, Inc, Employee of: Gilead Sciences, Inc, S. Zaboli Shareholder of: Gilead Sciences, Inc, Employee of: Gilead Sciences, Inc, A. Shauf Shareholder of: Gilead Sciences, Inc, Employee of: Gilead Sciences, Inc, J. Di Paolo Shareholder of: Gilead Sciences, Inc, Employee of: Gilead Sciences, Inc

DOI: 10.1136/annrheumdis-2018-eular.3367

AB0485

COMPARATIVE EFFICACY OF TOFACITINIB AND BIOLOGIC DMARDS IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH INSUFFICIENT RESPONSE TO SUBCUTANEOUS METHOTREXATE IN CLINICAL PRACTICE

E.L. Luchikhina¹, D. Karateev¹, G. Loukina², M. Borisova³, N. Demidova³, E. Nasonov³. ¹1st Department of internal medicine, Moscow Regional Research and Clinical Institute (MONIKI); ²Department of rheumatology, Moscow Clinical scientific center; ³V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation

Background: Tofacitinib (TOFA) – the first registered member of the group of Janus-kinase inhibitors – actively entered into practice. Some clinical trials show efficacy similar to biological DMARDs, but we still do not have enough data from the practice of post-marketing use.

Objectives: To evaluate the comparative effectiveness of TOFA and biological DMARDs in clinical practice.

Methods: Patients with RA (according to the ACR/EULAR 2010 criteria) having active disease despite treatment by subcutaneous (SC) methotrexate (MTX) were included in post-marketing observational study (REMARCA trial). The patients received a combination of MTX and biologics or TOFA. The follow-up period was 12 months. Patients received biologics in clinical practice according to national standards of care. We used SDAI as a main parameter of disease activity.

Results: In total 163 patients were included (81,6% females, 80,4% anti-CCP positive, 79,8 RF-positive, 74,9% with erosive disease, mean age 50,65±12,54, disease duration 30,45±41,9, BMI 27,1±5,78). All patients received SC MTX in the mean dose 22,17±3,92 mg per week, but the most of them had high activity at baseline (SDAI=32,42±14,59). After switching to a combination treatment regimen 88 patients received TNF inhibitors (70 patients – adalimumab, 18 patients – certolizumab pegol), 34 patients – abatacept (ABA), 41 patients – TOFA. Patients in the groups were comparable according to age and the main characteristics of disease severity. We found significant decrease of disease activity in every group (see table 1). In the group receiving TOFA results at 12 months were comparable with patients on anti-TNFs and significantly better than in patients on ABA. Remission (SDAI <3,3) has been achieved in 35,7% of patients on TOFA, in 28,4% – on anti-TNFs and in 14,7% on ABA (p=0055 in comparison with TOFA). No significant differences in safety parameters were found.

Abstract AB0485 – Table 1. Changes in disease activity in RA patients during follow-up period.

Group	SDAI at baseline	SDAI at 12 months
Biologics (total), n=122	33,22±15,18	11,05±9,94
Anti-TNFs, n=88	33,98±14,49	9,79±9,22
Abatacept, n=34	31,11±17,05	14,32±11,09*
Tofacitinib, n=41	30,20±12,24	7,59±8,37*

*) p<0,05 between the groups

Conclusions: Tofacitinib demonstrated similar efficacy in comparison to TNF inhibitors and was slightly better than abatacept in clinical practice in RA patients who did not respond to SC methotrexate.

Disclosure of Interest: E. Luchikhina Grant/research support from: Biocad, Speakers bureau: Abbvie, Pfizer, Biocad, D. Karateev Consultant for: Pfizer, Biocad, Egis, Novartis, Speakers bureau: Abbvie, Bristol Myers Squibb, Pfizer, Roche, Biocad, Novartis, Egis, MSD, UCB, G. Loukina: None declared, M. Borisova: None declared, N. Demidova: None declared, E. Nasonov: None declared

DOI: 10.1136/annrheumdis-2018-eular.7306