Internal Medicine, Rheumatology, Hatay, Turkey; [10]*University of Health Sciences Basaksehir Can and Sakura State Hospital, Internal Medicine, Rheumatology, İstanbul, Turkey*

Background: Beyond the joints, rheumatoid arthritis (RA) may affect lungs. Especially the involvement of the paranchyme, RA-associated interstitial lung disease (RA-ILD), is a major cause of mortality and morbidity. Tofacitinib, an oral JAK 1/3 inhibitor, has been used increasingly in the management of rheumatoid arthritis (RA) in recent years. Recently, a couple of animal and human studies reported promising results (1).

Objectives: To assess the real-life efficacy and safety of tofacitinib in patients with RA-ILD in TReasure registry.

Methods: This is a multicenter, observational study included RA patients with ILD diagnosis based on the HRCT images of the lungs, and were followed in 8 different centers participated in the TReasure database. Demographic data and patients' characteristics regarding RA and RA-ILD at the visit in which tofacitinib was initiated and for the last follow-up visit under tofacitinib were recorded. Using the present study cohort, the RA patients with ILD receiving tofacitinib were compared with those without ILD receiving tofacitinib (controls) in terms of the general and disease-related characteristics and data of concomitant DMARD use. To evaluate retention rates of tofacitinib and reasons for discontinuation, data of the patients with RA-ILD in this study cohort were compared with the data of RA patients without ILD who were followed in Hacettepe University (major contributor of the TReasure registry). This research was funded by Pfizer.

Results: A total of 47 RA patients with RA-ILD and a control group of 387 patients without ILD were included. The RA patients with ILD receiving tofacitinib were mostly male, older, and had higher baseline disease activity as compared with those without ILD (Table). The ILD pattern was known in 44 (93.6%) of 47 RA-ILD: 16 (36.3%) had UIP, 24 (54.5%) had NSIP, and 4 (9.1%) had airway disease. While 15 (31.9%) of the patients was asymptomatic, most common initial symptom was shortness of breath (in 14 (29.7%) patients). 18 patients had pre- and post-treatment FVC% and FEV1% values (with a median of 12 (9-19) months). Mean FEV1%; 82.1 vs. 82.8 (pre and post-treatment, respectively, p=0.079), mean FVC%; 79.8 vs. 82.8 (pre and post-treatment, respectively, p=0.014). To evaluate retention rates and reasons for discontinuation, 47 RA-ILD and 239 RA patients without ILD were analyzed. Retention rates were similar (p=0.21, log-rank) (Figure). Most common cause of tofacitinib discontinuation in RA-ILD group was infections (5 (25%) patients). Follow-up durations under tofacitinib were 15 (7-32) and 11 (4-24) months in ILD + and – groups, respectively. The rate of drug discontinuation due to infection in the RA patients with and without ILD was 6.3 per 100 patient-years and 2.4 per 100 patient-years, respectively.

Table 1. Characteristics of the RA patients with and without ILD under tofacitinib

Variables	RA-ILD(+) n=47	RA-ILD(-) n=387	p
Male sex	20 (42.6)	69 (17.8)	<0.001
Age, years	64 (57-69)	56 (46-64)	<0.001
Disease duration for RA, months	128 (78-212)	110 (64-183)	0.171
Smoking status			
Never smoker	26 (55.3)	211 (56.4)	0.259
Current&Ex-smoker	19 (44.7)	163 (43.6)	
RF (+)	36 (78.3)	249 (68.8)	0.187
Anti-CCP (+)	30 (65.2)	196 (61.6)	0.640
RF positive or CCP (+)	41 (87.2)	242 (76.3)	0.094
Presence of comorbidity	33 (70.2)	203 (52.5)	0.021
DAS-28 before tofacitinib	5.4 (4.6-6.22)	4.36 (3.22-5.58)	<0.001
ESR before tofacitinib, mm/h	38 (19-73)	29 (17-45)	0.029
CRP before tofacitinib	6.75 (1.63-24)	9.95 (4.18-25.1)	0.065
Follow-up duration under tofacitinib	15 (7-32)	7 (3-12)	<0.001

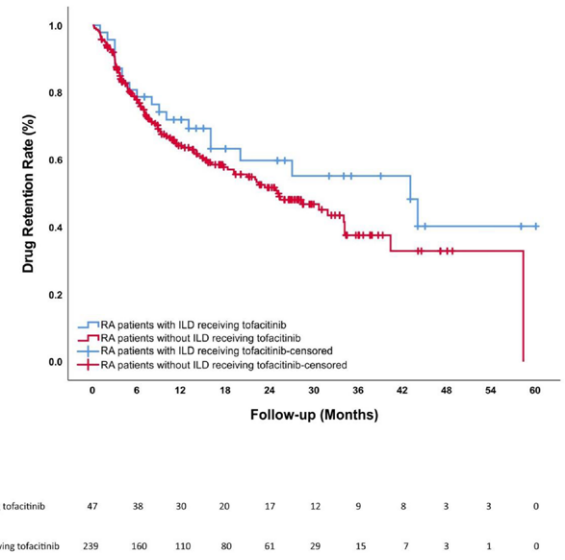

Figure 1. Tofacitinib retention rates in the RA patients with and without ILD

Conclusion: In majority of patients, pulmonary functions remained stable during follow-up. Tofacitinib seems as a promising option for RA-ILD. High rate of discontinuation due infections was observed in RA-ILD patients under tofacitinib; however, it should be kept in mind that RA-ILD patients were older than RA patients without ILD.

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OP0126 INFECTIONS AND SERIOUS INFECTIONS IN THE FILGOTINIB RHEUMATOID ARTHRITIS PROGRAM

J. Galloway[1], M. H. Buch[2], K. Yamaoka[3], C. Leatherwood[4], A. Pechonkina[5], I. Tiamiyu[4], D. Jiang[6], L. Ye[6], R. Besuyen[7], D. Aletaha[8], K. Winthrop[9]. [1]*King's College London, Centre for Rheumatic Diseases, School of Immunology and Microbial Sciences, London, United Kingdom*; [2]*University of Manchester, Division of Musculoskeletal & Dermatological Sciences, Manchester, United Kingdom*; [3]*Kitasato University School of Medicine, Department of Rheumatology and Infectious Diseases, Kanagawa, Japan*; [4]*Gilead Sciences, Inc., Clinical Research, Foster City, United States of America*; [5]*Gilead Sciences, Inc., Inflammation and Respiratory Therapeutic Area, Foster City, United States of America*; [6]*Gilead Sciences, Inc., Biostatistics, Foster City, United States of America*; [7]*Galapagos BV, Clinical Development, Leiden, Netherlands*; [8]*Medical University of Vienna, Division of Rheumatology, Department of Medicine 3, Vienna, Austria*; [9]*Oregon Health and Science University, Division of Infectious Diseases, Portland, United States of America*

Background: The Janus kinase (JAK)-1 preferential inhibitor filgotinib (FIL) improved rheumatoid arthritis (RA) signs and symptoms in 3 phase (P)3 trials.[1–3] Like other RA therapies, JAK inhibition is associated with increased infection rates.[4]

Objectives: To assess long-term safety across the FIL program regarding infections, including serious infections (SI).

Methods: Patients (pts) meeting 2010 ACR/EULAR RA criteria in pooled analysis of P2 DARWIN 1–2 (D1–2), P3 FINCH 1–3 (F1–3), and long-term extension studies (DARWIN 3, FINCH 4) were included. The placebo (PBO)-controlled as-randomised data set included pts receiving FIL 100 mg (FIL100), FIL 200 mg (FIL200), or PBO up to week (W)12 (D1–2, F1–2). The active-controlled as-randomised data set included pts receiving FIL100, FIL200, adalimumab (ADA), or methotrexate (MTX) up to W52 (F1, F3). The long-term as-treated data set included pts in all 7 studies receiving FIL100 or FIL200; data after rerandomisation were included and contributed to treatment received.

Exposure-adjusted incidence rates (EAIRs) per 100 patient-years exposure (PYE) and differences with 95% confidence intervals (CIs) were calculated using Poisson regression; EAIRs for tuberculosis (TB) in active controlled sets were calculated using an Exact Poisson method. Kaplan-Meier (KM) event probabilities with 95% CIs were provided for SI. If pts had multiple events within the same treatment period, only the first event was counted in EAIR calculation; PYE were calculated up to the last follow-up time or day before next treatment, including after first event. For KM analysis, time to event was calculated until the first event.

Results: Of 2267/1647 pts in as-treated set receiving FIL200/FIL100, 1697 had treatment-emergent infection; 118 were SI. Baseline potential risk factors for pts with SI are in Table.

Table 1. Baseline characteristics of pts with/without treatment emergent SI[a]

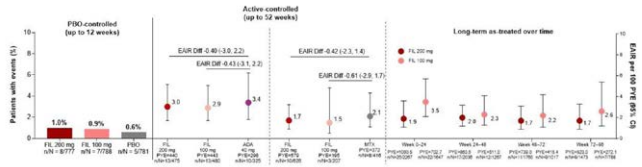
Parameter, n (%)	SI N = 92	No SI N = 2491
Medical history		
Chronic lung disease	13 (14.1)	125 (5.0)
Chronic renal disease	3 (3.3)	23 (0.9)
Infections and infestations	29 (31.5)	499 (20.0)
Baseline body mass index, kg/m^2		
<30	64 (69.6)	1749 (70.2)
≥30	28 (30.4)	742 (29.8)
Age, years		
<65	67 (72.8)	2006 (80.5)
≥65	25 (27.2)	485 (19.5)
Former/current smoker	30 (32.6)	677 (27.2)
Oral corticosteroids, mg		
<7.5	28 (56.0)	731 (66.1)
≥7.5	22 (44.0)	375 (33.9)
Missing data	42	1385

[a]Phase 3 (FINCH 1-4) studies, as randomised.SI, serious infection.

In 12W PBO-controlled period, infection rates were 17.9%/15.6%/13.3% for FIL200/FIL100/PBO. In 52W ADA-controlled period, infection EAIRs (95% CIs)/100 PYE were 46.9 (40.9, 53.7)/43.7 (38.0, 50.4)/43.4 (36.5, 51.5), FIL200/FIL100/ADA; and 38.5 (33.8, 43.9)/39.0 (31.1, 48.8)/42.2 (36.1, 49.3), FIL200/FIL100/MTX in 52W MTX-controlled period; 24.8 (23.1, 26.5)/34.4 (30.4, 38.8), FIL200/FIL100 in long-term analysis. In 12W PBO-controlled period, there was no active TB for FIL200/FIL100/PBO. In 52W ADA-controlled period, active TB EAIRs (95% CIs)/100 PYE were: 0 (0.0, 0.8)/0 (0.0, 0.8)/0.3 (0.0, 1.9), FIL200/FIL100/ADA and 0 (0.0, 0.6)/0 (0.0, 1.9)/0 (0.0, 1.0), FIL200/FIL100/MTX in 52W MTX-controlled period; 0/0.1 (0.0, 0.5), FIL200/FIL100 in long-term analysis.

SI rate or EAIRs are in Figure. Most common infections were upper respiratory tract infection and nasopharyngitis; majority were low grade. Pneumonia was most common SI (<1%). In long-term population, event probability (95% CI) of SI was 2.2% (1.6, 2.9)/2.5% (1.8, 3.4) for FIL200/FIL100 at 52W. In F1–3 (excluding data after rerandomisation), there were no significant changes in mean neutrophil and lymphocyte counts; values remained within normal limits up to W52 for all arms.

Figure. Rate or EAIR of serious infections



ADA, adalimumab; CI, confidence interval; EAIR, exposure-adjusted incidence rate/100 PYE; FIL, filgotinib; MTX, methotrexate; PBO, placebo; PYE, patient-years of exposure.

Conclusion: EAIRs of infections and SI for FIL were similar to PBO, ADA, and MTX. At 52W, incidence rates of SI were comparable for FIL100 and FIL200. Long-term SI EAIR for FIL100 was slightly higher than for FIL200.

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OP0127

CONFOUNDING EFFECTS OF CONTINUED METHOTREXATE IN PLACEBO ARMS (PLC) OF RHEUMATOID ARTHRITIS (RA) CLINICAL TRIALS – A POST-HOC ANALYSIS OF TWO RANDOMIZED CONTROLLED TRIALS (RCTS)

A. Kerschbaumer[1], Z. I. Rivai[1], J. S. Smolen[1], D. Aletaha[1]. [1]*Medical University of Vienna, Department of Medicine III / Division of Rheumatology, Vienna, Austria*

Background: Various hypotheses exist for the explanation of PLC response rates in RA clinical trials. Here we hypothesized that PLC-treated patients who continue to take methotrexate (cMTX) when entering the trial compared to those who have no cMTX would have higher response rates, because of increased adherence to MTX in the trial environment.

Objectives: To compare differences in response rates in PLC treated RA patients receiving MTX background therapy to patients receiving PLC without background conventional synthetic (cs)DMARDs in two RCTs.

Methods: To investigate the hypothesis we conducted a post-hoc analysis of two RCTs that allowed inclusion of patients with and without cMTX - the GO-AFTER and the SIRROUND-T trials, investigating golimumab and sirukumab, respectively, compared with PLC in patients who had an insufficient response to biological DMARDs.(1,2)

All PLC randomized patients of both trials were pooled and included in the analyses; we did not analyse the active treatment groups. Subsequently we stratified the pooled PLC group into patients receiving PLC on top of cMTX and patients receiving PLC without any csDMARD as background therapy. We compared American College of Rheumatology (ACR) 20/50/70% response rates and Clinical Disease Activity Index (CDAI) low disease activity (LDA, i.e. CDAI≤10) responses between the two groups using Fisher's exact test.

Similar to the primary analyses of the individual studies, non-responder imputation (NRI) for state outcomes (ACR responses, CDAI LDA) was applied in patients who initiated any csDMARD after randomization, had MTX or glucocorticoid doses increased during the study or discontinued the study. NRI was also applied for early escape patients receiving active therapy after failing to achieve a ≥20% decrease in joint counts at week (wk) 16 in GO-AFTER and at wk 18 in SIRROUND-T.