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

^aPhase 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)

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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.

Results: Of the 398 pooled PLC patients, 285 continued their MTX and 113 had no MTX (or other background csDMARDs). Baseline characteristics were similar (Table 1).

Table 1. Baseline characteristics

	Placebo without background csDMARD	Placebo + continued MTX
n	113	285
Age (years) *	56 (48-64)	56 (45-64)
Female (%)	95 (84.1%)	236 (82.8%)
Disease duration (years)	8.4±5.2	8.8±7.5
ACPA positive (%)	88 (77.9%)	214 (75.1%)
RF positive (%)	90 (79.6%)	211 (74%)
SJC 66 (0-66)	15.9±9.9	16.2±10.8
TJC 68 (0-68)	29.1±16.8	26.7±15.7
PGA (VAS 0-10)	6.8±2.2	6.5±2.1
EGA (VAS 0-10)	6.4±1.8	6.1±1.9
Pain (VAS 0-10)	7.0±1.9	6.6±2.1
HAQ-DI (0-3)	1.6±0.7	1.6±0.6
CRP (mg/dL) *	1.2 (0.5-3.5)	1.0 (0.4-2.6)
CDAI	39.4±13.5	38.5±12.8
Concomitant GC intake (%)	67 (59.3%)	174 (61.1%)
Concomitant MTX (%)	0 (0%)	285 (100%)
MTX dosage ≥12.5mg (%)	0 (0%)	222 (77.9%)
MTX dosage <12.5mg (%)	0 (0%)	63 (22.1%)

Data is shown as mean (± standard deviation) or n (%) unless stated otherwise* median (IQR)

At wk 16, an ACR20 response was achieved by 72/285 (25.3%) of PLC+c-MTX and 14/113 (12.4%) receiving PLC only patients ($p=0.005$); for ACR50 these numbers were 25/285 (8.4%) vs. 1/113 (0.9%; $p=0.003$); and for ACR70 they were 8/285 (2.8%) vs. 0/113 (0%; $p=0.112$). Also, significantly more PLC+cMTX patients achieved a CDAI LDA at wk 16 (25/285, 8.8%) compared to PLC only treated patients (2/113; 1.8%; $p=0.013$). Results between the two arms were numerically or statistically different already from week 4 (for ACR 20) or week 8 (ACR 50, CDAI LDA) onwards (Figure 1).

Figure 1. ACR 20/50/70 and CDAI LDA responses of PLC patients with continued MTX vs. PLC patients without csDMARD background therapy.

Conclusion: In patients randomized to placebo therapy, continued MTX background therapy increases clinical responses and achievement of good clinical states. These findings imply that pre-existing and putatively insufficient background therapy should be effectively optimized before enrollment into a clinical trial protocol.

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OP0128 INTEGRATED LABORATORY ABNORMALITY PROFILES OF UPADACITINIB WITH UP TO 4.5 YEARS OF EXPOSURE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED IN THE SELECT PHASE 3 PROGRAM

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Background: Upadacitinib (UPA) is an oral Janus kinase inhibitor approved for rheumatoid arthritis (RA). The safety and efficacy of UPA has been evaluated across a spectrum of patients (pts) with RA in the phase 3 SELECT clinical program.^{1,2}

Objectives: To describe long-term laboratory profiles (cutoff date: June 30, 2020) associated with exposure to UPA, adalimumab (ADA), and methotrexate (MTX) in pts with RA treated in the SELECT trials.

Methods: Data were analyzed from 6 randomized controlled UPA RA trials.^{1,2} The proportions of pts experiencing potentially clinically significant laboratory changes at a single time point were summarized for the following groups: pooled UPA 15 mg once daily (QD; UPA15; 6 trials), pooled UPA 30 mg QD (UPA30; 4 trials), ADA 40 mg every other week (EOW; 1 trial), and MTX monotherapy (1 trial). Pts received UPA with/without background conventional synthetic disease-modifying antirheumatic drugs. Treatment-emergent adverse events are reported as exposure-adjusted event rates (events/100 pt-years [E/100 PY]). Toxicity was graded per OMERACT criteria, or NCI CTCAE for creatine phosphokinase (CPK) and creatinine.