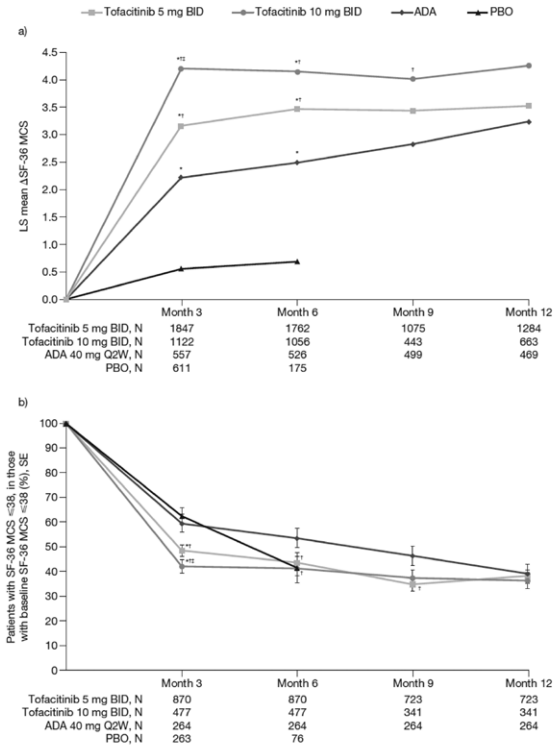
Conclusion: ~40% of RA pts had BL pMDD/pGAD. SF-36 MCS improvements were greater for tofacitinib vs PBO/ADA. With tofacitinib, % of pts with SF-36 MCS ≤38 reduced by ~60% at M12. Tofacitinib efficacy was similar in pts with/without BL pMDD/pGAD. Limitations include using SF-36 MCS to identify probable rather than confirmed MDD or GAD. Future research using gold standard psychiatric interviews to validate use of SF-36 MCS ≤38 is needed.

Figure 1. a) ΔSF-36 MCS at M3/6/9/12; b) percentage of patients with pMDD/pGAD at M3/6/9/12, in those with baseline pMDD/pGAD (SF-36 MCS ≤38)



*p<0.05 vs placebo; †p<0.05 vs ADA; ‡p<0.05 vs tofacitinib 5 mg BID in a) difference in LS mean and b) OR (not shown)
Data pooled from 5 P3 and 1 P3b/4 tofacitinib trials
Δ, change from baseline; ADA, adalimumab; BID, twice daily; LS, least squares; M, month; MCS, Mental Component Summary score; N, number of evaluable patients; OR, odds ratio; PBO, placebo; pGAD, probable generalised anxiety disorder; pMDD, probable major depressive disorder; Q2W, every other week; RA, rheumatoid arthritis; SE, standard error; SF-36, Short Form-36 health survey

Table. M3/6/12 efficacy with tofacitinib 5 mg BID, by BL pMDD/pGAD[a]

	SF-36 MCS ≤38	SF-36 MCS >38	OR (95% CI)	P value
ACR20 (%)[b,c]				
M3	55.1	57.9	0.89 (0.74, 1.08)	0.2330
M6	61.7	62.8	0.96 (0.79, 1.16)	0.6511
M12	58.4	58.6	0.99 (0.80, 1.22)	0.9279
ACR50 (%)[b,c]				
M3	25.9	29.2	0.85 (0.70, 1.03)	0.1022
M6	36.0	38.0	0.92 (0.76, 1.11)	0.3724
M12	33.8	34.3	0.98 (0.80, 1.20)	0.8366
ACR70 (%)[b,c]				
M3	10.1	11.0	0.91 (0.69, 1.18)	0.4704
M6	16.5	16.5	1.00 (0.79, 1.26)	0.9901
M12	18.3	17.5	1.06 (0.83, 1.34)	0.6560
DAS28-4(ESR)<2.6 (%)[b,c]				
M3	5.4	7.4	0.72 (0.49, 1.05)	0.0872
M6	5.9	8.5	0.68 (0.49, 0.94)	0.0199*
M12	8.0	11.9	0.64 (0.47, 0.89)	0.0073**
ΔHAQ-DI, LS mean[c,d]	**SF-36 MCS ≤38**	**SF-36 MCS >38**	**Difference (95% CI)**	**P value**
M3	-0.41	-0.43	0.01 (-0.04, 0.06)	0.6008
M6	-0.49	-0.48	-0.01 (-0.06, 0.04)	0.6617
M12	-0.52	-0.52	-0.01 (-0.06, 0.05)	0.8475

*p<0.05; **p<0.01 Data pooled from 5 P3 and 1 P3b/4 tofacitinib trials [a]BL pMDD/pGAD = SF-36 MCS ≤38; [b]Logistic regression fit; [c]For PBO pts advancing to tofacitinib post-M3, only PBO data were included; [d]Mixed-effects linear model fit

Δ, change from baseline; ACR, American College of Rheumatology; BID, twice daily; BL, baseline; CI, confidence interval; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; HAQ-DI, Health Assessment Questionnaire-Disability Index; LS, least squares; M, month; MCS, Mental Component Summary score; OR, odds ratio; P, Phase; pGAD, probable generalised anxiety disorder; PBO, placebo; pMDD, probable major depressive disorder; pt, patient; RA, rheumatoid arthritis; SF-36, Short Form-36 health survey

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THU0197 SAFETY PROFILE OF UPADACITINIB UP TO 3 YEARS OF EXPOSURE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The safety and efficacy of upadacitinib (UPA), an oral JAK inhibitor, was evaluated in the phase 3 SELECT clinical program, which included 5 randomized, double-blind, controlled trials across a spectrum of rheumatoid arthritis (RA) patients (pts)[1-5].

Objectives: To describe the long-term integrated safety profile of UPA relative to active comparators in pts with RA treated in the SELECT program up to a cut-off date of 30 June 2019.

Methods: Treatment-emergent adverse events (TEAEs: AE onset ≥first dose and ≤30 days after last dose) were summarized for the following: methotrexate (MTX, 1 trial, mean exposure 76 wks); adalimumab (ADA, 1 trial, mean exposure 69 wks); pooled UPA 15 mg (5 trials, mean exposure 90 wks); pooled UPA 30 mg (4 trials, mean exposure 100 wks). TEAEs are reported as exposure-adjusted event rates (EAERs; events/100 patient years [E/100PYs]).

Results: 3833 pts received ≥1 dose of UPA 15 mg [n=2629, 4565.8 PYs] or 30 mg [n=1204, 2309.7 PYs] QD, with no option to switch doses. More than half of pts received UPA for ≥96 wks (median: UPA 15, 101.9 wks; UPA 30: 111.7 wks). The EAERs of overall SAEs and AEs leading to discontinuation on UPA 15 mg were comparable to MTX and ADA; rates on UPA 30 mg were numerically higher than UPA 15 mg (**Table**). The most common AEs (≥5 E/100 PYs) reported with UPA 15 mg were upper respiratory tract infection (URTI), nasopharyngitis, urinary tract infection (UTI), bronchitis, increased CPK, and increased ALT. For UPA 30 mg, the most common AEs reported were URTI, UTI, increased CPK, nasopharyngitis, bacterial bronchitis, and herpes zoster (HZ). Overall rates of serious infections and opportunistic infections were comparable between UPA 15 mg, MTX, and ADA groups but were higher on UPA 30 mg (**Figure**). Rates of HZ were higher in both UPA groups (30 mg higher than 15 mg) vs MTX and ADA. The majority of HZ cases were non-serious (96%) and involved a single dermatome (74%). Rates of VTE were comparable across treatment groups (0.3-0.5/100 PYs), as were rates of adjudicated MACE and malignancies (excluding NMSC). Rates of NMSC in UPA 15 mg and ADA were similar, with numerically higher rates on UPA 30 mg. SMR analysis demonstrated that the number of deaths in pts with RA exposed to UPA was not higher than what would be expected for the general population.

Conclusion: Through long-term follow-up, the integrated safety profile of UPA remained consistent with previous analyses, with no new signals identified.

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[1] Burmester, *et al*. *Lancet* 2018;391:2503-12.
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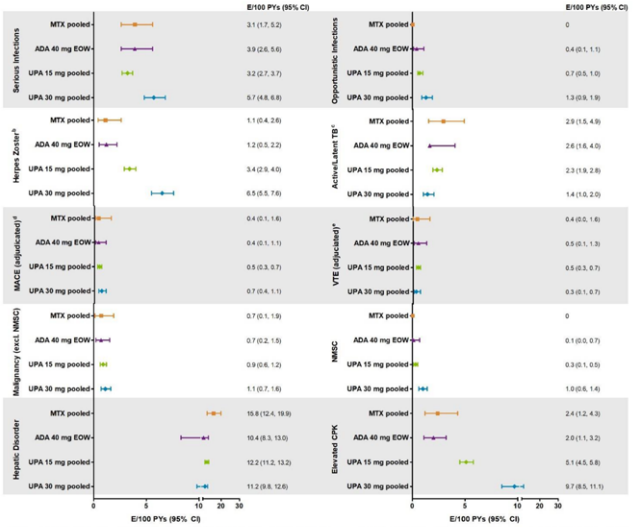
Table. Overall TEAEs for UPA and Active Comparators (E/100 PYs [95% CI])

	MTX n=314 (456.0 PYs)	ADA 40 mg eow n=579 (768.6 PYs)	UPA 15 mg QD n=2629 (4565.8 PYs)	UPA 30 mg QD n=1204 (2309.7 PYs)
Any AE	271.7 (256.8, 287.3)	242.3 (231.4, 253.5)	247.7 (243.2, 252.3)	310.6 (303.5, 317.9)
Any SAE	12.7 (9.7, 16.4)	14.6 (12.0, 17.5)	12.9 (11.9, 14.0)	19.8 (18.0, 21.7)
Any AE leading to discontinuation	7.7 (5.3, 10.7)	8.2 (6.3, 10.5)	6.3 (5.6, 7.1)	10.0 (8.8, 11.4)
Deaths[a]	0.4 (0.1, 1.6)	0.8 (0.3, 1.7)	0.4 (0.2, 0.6)	0.7 (0.4, 1.1)

[a]Deaths included non-treatment emergent deaths: ADA, 1; UPA 15 mg, 3; UPA 30 mg, 3.

Figure. Overall AESIs in Patients Treated with Upadacitinib Compared to Active Controls[a]



MTX pooled: N=314, PYs=456.0; ADA 40 mg EOW: N=579, PYs=768.6; UPA 15 mg pooled: N=2629, PYs=4565.8; UPA 30 mg pooled: N=1204, PYs=2309.7
[a]Patients who switched from PBO, ADA, or MTX to UPA were included in the UPA analysis set from the start of UPA, while those who switched from upadacitinib to ADA were included in the ADA dataset from the start of ADA. There was no switch between UPA doses in any study. MTX monotherapy censored at time of rescue to combination therapy (either UPA + MTX or addition of csDMARD).
[b]Most HZ cases were non-serious (95.9%) and single dermatome (74.4%).
[c]There were 6 cases of active TB on UPA (0.1 E/100 PYs) and 1 on ADA.
[d]MACE was defined as CV death, non-fatal MI, and non-fatal stroke.
[e]VTE was defined as deep vein thrombosis and pulmonary embolism.
ADA, adalimumab; AE, adverse event; CPK, creatine phosphokinase; CV, cardiovascular; E, events; EOW, every other week; MACE, major adverse cardiovascular event; MI, myocardial infarction; MTX, methotrexate; NMSC, non-melanoma skin cancer; PBO, placebo, PYs, patient-years; QD, once daily; TB, tuberculosis; TEAE, treatment-emergent adverse event; UPA, upadacitinib; VTE, venous thromboembolism.

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THU0198

EFFICACY AND SAFETY OF FILGOTINIB FOR PATIENTS WITH RHEUMATOID ARTHRITIS WITH INADEQUATE RESPONSE TO METHOTREXATE: FINCH 1 52-WEEK RESULTS

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Background: Filgotinib (FIL) is an oral, potent, selective JAK1 inhibitor. FINCH 1 (NCT02889796) assessed FIL efficacy and safety in patients (pts) with rheumatoid arthritis (RA) with inadequate response to methotrexate (MTX-IR); primary outcome results at week (W)12 and W24 were previously reported.[1]
Objectives: To present FINCH 1 W52 results.
Methods: This global, phase 3, double-blind, active- and placebo (PBO)-controlled study randomised MTX-IR pts with active RA on a background of stable MTX 3:3:2:3 to oral FIL 200 mg or FIL 100 mg once daily, subcutaneous adalimumab (ADA) 40 mg every 2W, or PBO up to W52; pts receiving PBO at W24 were rerandomised to FIL 100 or 200 mg. Efficacy was assessed from clinical, radiographic, and pt-reported outcomes; W52 comparisons were not adjusted for multiplicity. Safety endpoints included adverse events (AEs) and laboratory abnormalities.
Results: Of 1755 treated pts, 1417 received study drug through W52. The majority (81.8%) were female, mean (standard deviation [SD]) RA duration was 7.8 (7.6) years, and baseline mean (SD) DAS28(CRP) was 5.7 (0.9). FIL efficacy was sustained through W52; 54%, 43%, and 46% of pts receiving FIL 200 and 100 mg and ADA, respectively, had W52 DAS28(CRP) <2.6 (nominal p for FIL 200 vs ADA = 0.024) (Figures 1–2, Table 1). FIL safety profile through W52 was consistent with W24 data. AEs of interest were infrequent and balanced among treatments (Table 2); 82 pts (4.7%) discontinued treatment due to AEs.

Table 1. Efficacy outcomes at week 52

	FIL 200 mg (n = 475)	FIL 100 mg (n = 480)	ADA (n = 325)
ACR20/50/70, %	78/62/44	76/59/38	74/59/39
DAS28(CRP) ≤3.2, %	66^{+}	59	59
mTSS[a]	0.18^{+++}	0.45	0.61
HAQ-DI[b]	−0.93^{+}	−0.85	−0.85
SF-36 PCS[b]	12.0	11.5	12.4
FACIT-F[b]	11.9	12.2	11.7

[a]Least squares mean change from baseline.
[b]Mean change from baseline.
$^{+}$p <0.05, $^{+++}$p <0.001 vs ADA; not adjusted for multiplicity.
ADA, adalimumab; FIL, filgotinib; mTSS, modified van der Heijde TSS.