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Background: The Janus kinase-1 preferential inhibitor filgotinib (FIL) improved signs and symptoms of rheumatoid arthritis (RA) in the FIL clinical program.¹⁻³

Objectives: To assess FIL safety across regions.

Methods: This was an analysis of patients (pts) meeting 2010 ACR/EULAR RA criteria in pooled phase (P)2 DARWIN 1-2 (D1-2), P3 FINCH 1-3 (F1-3), and long-term extension studies (DARWIN 3, FINCH 4). Data were analyzed by region: North America, South and Central America, Western Europe, Eastern Europe, Asia, South East (SE) Asia, and Other. Week (W)12 placebo (PBO)-controlled analysis included data from pts receiving once-daily FIL 100 mg (FIL100), FIL 200 mg (FIL200), or PBO for ≤ 12 W (D1-2, F1-2); long-term as-treated data included pts from all 7 studies receiving FIL100 or FIL200; data after rerandomization were included and contributed to treatment received. Data presented as exposure-adjusted incidence rates (EAIRs)/100 patient-years of exposure (PYE) of treatment-emergent (TE) adverse events (TEAEs).

Results: Table 1 shows EAIRs of TEAEs in PBO-controlled analysis. EAIRs/100 PYE of all TEAEs in Western Europe, Asia, and Other were higher than in remaining regions and for PBO vs FIL arms; EAIRs for FIL200/FIL100 in North America and SE Asia were higher vs PBO. EAIRs/100 PYE of TE serious AEs were higher in SE Asia for FIL100 and for FIL200/FIL100 in Other, with high PBO EAIRs in Western Europe. EAIRs/100 PYE of TEAEs leading to study discontinuation were higher in FIL arms vs PBO in Western Europe and Other (FIL200); in Asia and SE Asia, EAIRs were higher for PBO vs FIL200/FIL100.

Table 1. EAIR of TEAEs (placebo-controlled)

	North America N = 481	South and Central America N = 350	Western Europe N = 141	Eastern Europe N = 933	Asia N = 236	South East Asia N = 135	Other N = 70
TEAE							
FIL200 ^a	216.9 (162.5, 289.5)	205.6 (155.1, 272.6)	285.0 (188.6, 430.8)	150.3 (119.3, 189.4)	248.9 (180.6, 343.1)	165.1 (104.0, 262.1)	298.4 (150.3, 592.5)
FIL100 ^b	182.2 (136.8, 242.7)	159.2 (117.3, 216.1)	285.7 (183.7, 444.3)	146.4 (115.9, 185.0)	246.9 (180.3, 338.1)	153.7 (94.2, 251.0)	263.5 (113.9, 609.2)
PBO ^c	174.5 (130.3, 233.7)	162.1 (118.8, 221.2)	314.9 (200.7, 493.9)	148.4 (117.6, 187.4)	259.0 (188.0, 356.8)	81.6 (40.8, 163.3)	306.0 (142.8, 655.7)
TE serious AE							
FIL200 ^a	14.3 (6.0, 34.4)	11.4 (3.7, 35.5)	8.3 (1.2, 59.0)	12.2 (5.2, 28.7)	5.5 (0.8, 38.9)	0.0 (0.0, ∞)	49.6 (10.2, 144.9)
FIL100 ^b	10.6 (4.0, 28.3)	7.2 (1.8, 28.7)	19.9 (5.0, 79.7)	15.1 (6.8, 33.7)	16.2 (5.2, 50.2)	28.8 (9.3, 89.4)	20.5 (0.5, 114.0)
PBO ^c	16.1 (7.2, 35.9)	7.5 (1.9, 30.0)	29.6 (9.5, 91.7)	4.6 (1.3, 15.8)	11.4 (2.8, 45.5)	10.2 (1.4, 72.4)	0.0 (0.0, 69.2)
TEAE leading to discontinuation							
FIL200 ^a	8.6 (2.8, 26.6)	3.8 (0.1, 21.2)	16.6 (4.2, 66.5)	12.9 (5.5, 30.5)	0.0 (0.0, 20.2)	9.2 (1.3, 65.1)	16.5 (0.4, 92.1)
FIL100 ^b	10.6 (4.0, 28.3)	7.2 (0.9, 26.0)	19.9 (5.0, 79.7)	1.9 (0.2, 13.8)	5.4 (0.1, 30.1)	9.6 (1.4, 68.2)	0.0 (0.0, 75.5)
PBO ^c	5.4 (1.3, 21.5)	0.0 (0.0, 13.8)	9.9 (1.4, 70.0)	12.9 (5.4, 30.7)	17.1 (3.5, 49.9)	20.4 (5.1, 81.6)	0.0 (0.0, 69.2)

Data presented as EAIR (95% CI)/100 patient-years

^aN = 777, 179.8 PYE ^bN = 788, 181.6 PYE ^cN = 781, 178.4 PYE

A subject may contribute to more than one treatment group if they received more than one treatment of interest.

EAIR and corresponding 95% CI were estimated using Poisson regression model by treatment, including study and treatment with an offset of natural log of exposure time, except when 0 events occurred; Poisson model was not adjusted by study.

AE, adverse event; CI, confidence interval; EAIR, exposure-adjusted incidence rate; FIL, filgotinib; PBO, placebo; PYE, patient-years of exposure; TE, treatment-emergent Figure shows serious infections (SI), venous thromboembolism (VTE) and herpes zoster (HZ) EAIRs.

EAIRs for SI were highest in Other for FIL200 and SE Asia for FIL100. While VTE EAIRs were low, pts in 5/7 regions had VTE. HZ EAIRs were highest in Asia.

Conclusion: Although EAIR of TEAEs varied between regions, no consistent trend was reflected in any particular region.

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POS0658 GEOGRAPHIC VARIATION OF EFFICACY IN THE FILGOTINIB RHEUMATOID ARTHRITIS PROGRAM

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Background: The Janus kinase-1 preferential inhibitor filgotinib (FIL) improved signs and symptoms of rheumatoid arthritis (RA) across the FIL clinical program.¹⁻³

Objectives: To assess FIL efficacy across geographic regions.

Methods: Pooled data from patients (pts) meeting 2010 ACR/EULAR RA criteria randomised to once-daily FIL 200 mg (FIL200), FIL100 mg (FIL100), or placebo (PBO) with background conventional synthetic disease-modifying antirheumatic drugs in DARWIN 1 (P2; up to week [W]12) and FINCH 1-2 (P3; up to W24) studies were evaluated. Data were analysed by region: North America, South and Central America, Western Europe, Eastern Europe, Asia, South East (SE) Asia, and Other. W12 American College of Rheumatology 20% improvement (ACR20) and W24 Disease Activity Score in 28 joints (C-reactive protein) (DAS28[CRP]) <2.6 and ≤ 3.2 response rates were analysed by a logistic regression model. Change from baseline (CFB) in Health Assessment Questionnaire-Disability

Index (HAQ-DI) at W12 was analysed by a mixed-effects model for repeated measures. Analyses were exploratory and not adjusted for multiplicity.

Results: Despite high PBO response rates in Eastern Europe and South and Central America, greater proportions of pts receiving FIL200 or FIL100 vs PBO achieved ACR20 at W12 ($P < 0.05$) in all regions, except Other (with lowest sample size, $n = 69$), where both FIL doses were numerically greater than PBO (Table 1). At W12, least-squares mean CFB in HAQ-DI improved for pts receiving FIL200 or FIL100 vs PBO ($P < 0.05$) in all regions, except SE Asia, where improvement was numeric (Table 1).

Table 1. Proportion of pts achieving ACR20 and LSM change from baseline HAQ-DI at week 1

	ACR20			HAQ-DI		
	FIL200	FIL100	PBO	FIL200	FIL100	PBO
North America	64.8 [†]	58.3 [†]	33.8	-0.63 [†]	-0.58 [†]	-0.34
n = 455	(56.7, 72.9)	(50.3, 66.4)	(26.0, 41.6)	(-0.70, -0.56)	(-0.65, -0.51)	(-0.41, -0.27)
South and Central America	77.2	77.3	57.4	-0.77 [†]	-0.67 [†]	-0.43
n = 283	(68.1, 86.3) [†]	(65.8, 86.2) [†]	(46.9, 68.0)	(-0.85, -0.68)	(-0.75, -0.59)	(-0.52, -0.35)
Western Europe	69.4 [†]	68.3 [†]	24.4	-0.69 [†]	-0.61 [†]	-0.28
n = 135	(55.5, 83.3)	(52.8, 83.8)	(10.8, 38.1)	(-0.80, -0.58)	(-0.73, -0.49)	(-0.40, -0.17)
Eastern Europe	77.1 [†]	69.1 [†]	54.6	-0.62 [†]	-0.51 [†]	-0.34
n = 822	(71.9, 82.3)	(63.5, 74.7)	(48.5, 60.7)	(-0.68, -0.56)	(-0.57, -0.45)	(-0.40, -0.28)
Asia	81.0 [†]	60.0 [†]	37.7	-0.83 [†]	-0.61 [†]	-0.42
n = 236	(71.7, 90.3)	(48.6, 71.4)	(26.2, 49.1)	(-0.92, -0.73)	(-0.70, -0.52)	(-0.52, -0.33)
South East Asia	70.2 [†]	71.1 [†]	39.5	-0.61 [†]	-0.57 [†]	-0.45
n = 135	(56.1, 84.4)	(56.8, 85.5)	(23.8, 55.3)	(-0.73, -0.49)	(-0.69, -0.45)	(-0.58, -0.33)
Other	60.0	52.4	39.1	-0.56 [†]	-0.60 [†]	-0.33
n = 69	(38.8, 81.2)	(28.6, 76.1)	(17.0, 61.2)	(-0.72, -0.41)	(-0.76, -0.43)	(-0.49, -0.17)
Overall	73.4 [†]	66.4 [†]	45.3	-0.71 [†]	-0.61 [†]	-0.40
N = 2135	(70.1, 76.8)	(62.9, 70.0)	(41.5, 49.0)	(-0.76, -0.66)	(-0.66, -0.56)	(-0.45, -0.35)

Includes only patients initially randomised to the treatment groups in each study for the comparison of interest. ACR20 presented as percentage (95% CI); 95% CI was based on normal approximation method with a continuity correction; P values calculated from the logistic regression. HAQ-DI presented as LSM (95% CI); LSM, 95% CI, and P value calculated from a mixed-effects model for repeated measures. * $P < 0.001$, † $P < 0.01$, ‡ $P < 0.05$; not adjusted for multiplicity.

ACR20, American College of Rheumatology 20% improvement; CI, confidence interval; FIL, filgotinib; HAQ-DI, Health Assessment Questionnaire-Disability Index; LSM, least square mean; PBO, placebo.

At W24, DAS28(CRP) < 2.6 and ≤ 3.2 response rates were higher for both doses of FIL vs PBO ($P < 0.05$) in all regions, with the exception of Other, where PBO was higher than FIL100 for DAS28(CRP) < 2.6 (Figure 1).

Conclusion: In exploratory analyses, ACR20, DAS28(CRP) < 2.6 and ≤ 3.2 response rates and HAQ-DI scores varied between regions; however, no stable trend was shown in any particular region. Small pt numbers in some subgroups may confound statistical analysis.

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POS0659 REAL WORD EXPERIENCE WITH TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS: AN INTERIM ANALYSIS FROM A FRENCH PROSPECTIVE OBSERVATIONAL STUDY DeFacTo

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Background: Tofacitinib is an oral JAK inhibitor indicated for moderate to severe active rheumatoid arthritis (RA).

Objectives: To present baseline patients characteristics and effectiveness data at 6 months of DeFacTo real life study ("Identification of Factors predictive of Tofacitinib's survival").

Methods: DeFacTo is an observational, open-label, prospective, multi-center, national study designed to evaluate the predictive factors of tofacitinib's survival in patients with moderate-to-severe active rheumatoid arthritis according to the SmPC^[1]. Here we present the 1st interim results involving a descriptive analysis of the 221 patients included between January 2019 and March 2020 (POP1). Effectiveness results at 6 months of 145 patients having ≥ 6 months follow-up (POP2) are also described.

Results: The baseline characteristics of the POP1 patients ($n = 221$) were: 78.3% women with a mean age ($\pm$ SD) of 60.4 ± 11.1 years, disease duration of 12.0 ± 9.8 years, TJC: 7.3 ± 5.7 and SJC: 5.1 ± 4.7 ; 44.0% of patients had erosions, 79.5% were RF+ and 75.9% were ACPA+. The mean CRP was 15.3 ± 21.8 mg/l, the ESR at one hour was 28.7 ± 23.6 mm, DAS28-4 CRP was 4.6 ± 1.0 , DAS28-4 ESR was 4.9 ± 1.1 and the FACIT-Fatigue score was 27.6 ± 11.3 . A total of 97.3% of patients had been previously treated by ≥ 1 csDMARD (mean number 1.9 ± 1.0) and 66.1% by b/tsDMARDs (mean number 2.9 ± 2.5), tofacitinib was prescribed as monotherapy (without csDMARD) in 49.3% of patients. The characteristics of the POP2 patients were similar to those of POP1. At 6 months in POP2, 29 patients have discontinued their treatment with tofacitinib. The results showed a decrease from baseline in inflammatory markers (CRP from 14.2 ± 17.1 to 4.7 ± 4.2 mg/l), pain (Pain VAS from 58.3 ± 23.4 to 27.6 ± 22.1) and DAS28 activity scores with 23% of patients in DAS28-CRP remission and 36% of patients in DAS28-CRP LDA (figure 1). This interim analysis didn't identify any new safety findings (Table 1).

Conclusion: Preliminary results from this prospective observational study on the use of tofacitinib in patients suffering with RA in France indicate that its effectiveness and safety are similar to those found in the clinical studies^[1-3]. In this study, tofacitinib was prescribed as monotherapy (without csDMARD) in more than 49% of cases.

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