Long-Term Safety of Filgotinib in Patients with Psoriatic Arthritis: Week 52 Safety Data from a Phase 2 Open-Label Extension Study

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Background

- **Filgotinib (FIL)** is an oral, selective **Janus kinase 1 inhibitor** under clinical investigation in a number of inflammatory diseases, including **psoriatic arthritis (PsA)**[1–5]
- The phase 2 **EQUATOR** study, a 16-week, double-blind, randomized controlled trial involving patients with active PsA, demonstrated that **FIL significantly improved multiple disease domains** vs placebo (PBO) and was **well tolerated** in this patient population[5]
- **EQUATOR2** is an ongoing, **open-label, long-term extension** study to assess the long-term **safety and efficacy** of FIL for up to an additional 148 weeks of treatment[6]

Objective

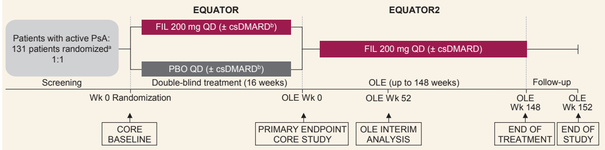
- To evaluate interim safety and efficacy of FIL 200 mg in patients participating in EQUATOR2, at 52 weeks' treatment

Methods

Study Design and Patients

- EQUATOR2 (NCT03320876) is a 148-week, open-label extension (OLE) of EQUATOR (NCT03101670) (**Figure 1**)
- Patients with active PsA were randomized 1:1 to oral FIL 200 mg or PBO once daily for 16 weeks in EQUATOR; those completing the core study were eligible to enter EQUATOR2
- In EQUATOR2, patients receive open-label oral FIL 200 mg once daily for up to 148 weeks
- Key inclusion criteria for the core EQUATOR study were:[5]
  - Adults (aged ≥18 years) with PsA as defined by Classification for Psoriatic Arthritis criteria
  - PsA diagnosed ≥12 weeks before screening
  - Active moderate-to-severe PsA (≥5 swollen joints and ≥5 tender joints)
  - Active, or history of, plaque psoriasis
  - Insufficient response or intolerance to ≥1 conventional synthetic disease-modifying antirheumatic drug (csDMARD); previous use of one tumor necrosis factor (TNF) inhibitor was allowed
- Key exclusion criteria for the EQUATOR2 OLE study are:
  - Patients not deemed to be benefiting from FIL, based on worsening symptoms
  - Persistent abnormal laboratory values potentially associated with the use of FIL, according to investigators' judgment

Figure 1. Study Design



[a]Randomization was stratified by current use of csDMARD and previous use of antitumor necrosis factor; [b]Patients continued csDMARD if they had received treatment for ≥12 weeks before screening and were on a stable dose for ≥4 weeks before baseline
csDMARD, conventional synthetic disease-modifying anti rheumatic drug; FIL, filgotinib; OLE, open-label extension; PBO, placebo; PsA, psoriatic arthritis; QD, once daily; Wk, week

Interim Analysis at OLE Week 52

- For the safety analysis, all data were included up to the data cutoff of April 18, 2019
  - Analysis was according to the study treatment received in the core study and/or OLE
  - Safety analysis included the evaluation of adverse events (AEs) and clinical laboratory data
- For the efficacy analysis, all data until the OLE week 52 visit (for each patient) were included
  - Efficacy analysis included 20/50/70% improvement in the American College of Rheumatology response criteria (ACR20/50/70) and the proportion of patients achieving minimal disease activity

Statistical Analysis

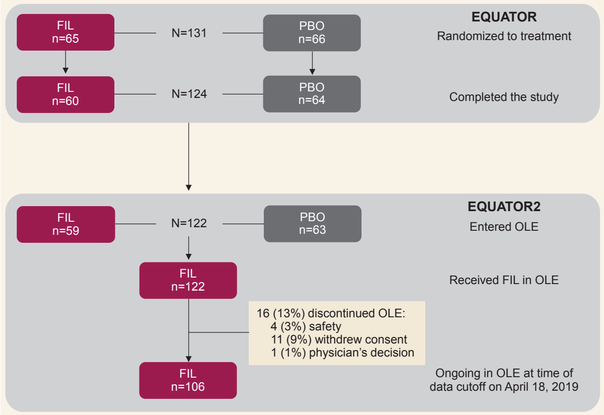
- All analyses were based on observed cases (i.e. no imputation of missing data)
- All analyses were descriptive in nature; no statistical analyses of potential treatment group differences were conducted
- For AEs, the rate of the number of treatment-emergent AEs (TEAEs) per 100 patient-years of exposure (PYE) was calculated

Results

Patient Disposition

- Of the 131 patients randomized to receive FIL or PBO in EQUATOR, 124 (95%) completed the study and 122 (93%) enrolled in the EQUATOR2 OLE. At this week 52 interim analysis, 106/122 (87%) remained in the OLE (**Figure 2**)

Figure 2. Patient Disposition



FIL, filgotinib; OLE, open-label extension; PBO, placebo

Baseline Characteristics

- Baseline patient demographics and disease characteristics have been described previously for EQUATOR[5]
  - Overall, 50% of patients were female, mean age was 50 years and mean duration of PsA was 7 years
  - 15% of patients had received prior anti-TNF therapy; 74% of patients received concurrent csDMARD therapy at baseline and during the core study
  - In the FIL and PBO groups, respectively, median (interquartile range) Psoriasis Area and Severity Index score (of patients with a baseline body surface area of psoriasis of ≥3%) was 6.5 (2.6–15.0) and 6.9 (3.8–18.6), mean (standard deviation [SD]) PsA Disease Activity score was 6.1 (0.8) and 6.2 (1.0), and mean (SD) Disease Activity Index for PsA score was 44.0 (14.3) and 47.8 (19.8)

Exposure and Safety Results

- At the interim analysis, total FIL exposure was 160 patient-years (PY); median time on FIL was 66 weeks
- Total PBO exposure during the core EQUATOR study was 20 PY; median time on PBO was 16 weeks
- Key safety endpoints and TEAEs of special interest in EQUATOR and EQUATOR2 are summarized in **Table 1** and **Table 2**, respectively
  - TEAEs were mostly mild or moderate in severity
  - One patient reported a serious, non-fatal, drug-related TEAE (tick-borne viral encephalitis) with FIL during the EQUATOR2 OLE study (leading to treatment discontinuation) and one patient treated with FIL died on Day 106 of the core EQUATOR study (due to a serious drug-related TEAE of pneumonia)
  - The incidence of TEAEs was generally low, except for respiratory tract infection, which occurred at a rate of 46.2 per 100 PYE
- Key treatment-emergent laboratory abnormalities are shown in **Table 3**
  - The most notable abnormal changes (Grade ≥2 event) in laboratory parameters with FIL treatment were decreased lymphocyte and neutrophil counts

Table 1. Summary of Key Safety Endpoints in Core EQUATOR Randomized Controlled Trial[5]

	Incidence of TEAEs, number of patients (%)	
	FIL 200 mg (n=65)	PBO (n=66)
TEAEs		
All	37 (57)	39 (59)
Drug-related	11 (17)	9 (14)
Serious	1 (2)[a]	1 (2)
Drug-related serious	1 (2)[a]	0
Grade 3 or worse	1 (2)[a]	5 (8)
Led to permanent discontinuation of study drug[b]	1 (2)[a]	0
TEAEs of special interest		
Infections	14 (22)	14 (21)
All serious infections	1 (2)[a]	0
Opportunistic infections	0	0
Herpes zoster	1 (2)	0
Active tuberculosis	0	0
Urinary tract infections	1 (2)	3 (5)
Respiratory tract infections	10 (15)[a]	10 (15)
Malignancies	0	0
Deep vein thrombosis	0	0
Pulmonary embolism	0	0
Major cardiac events (adjudicated)	0	0
Deaths	1 (2)[a]	0

[a]One patient died following the onset of pneumonia; [b]Not including deaths
FIL, filgotinib; PBO, placebo; TEAE, treatment-emergent adverse event

Table 2. Summary of Key Safety Endpoints in Core EQUATOR Randomized Controlled Trial and EQUATOR2 OLE

	Incidence, number of patients (%)	Rate per 100 PYE (number of events)
	FIL 200 mg (n=128)	FIL 200 mg (PYE=160)
TEAEs		
All	85 (66)	213.9 (342)
Drug-related	29 (23)	31.9 (51)
Serious	9 (7)	5.6 (9)
Drug-related serious	2 (2)	1.3 (2)
Grade 3 or worse	12 (9)	10.0 (16)
Led to permanent discontinuation of study drug[a]	5 (4)	3.1 (5)
TEAEs of special interest		
Infections	53 (41)	62.5 (100)
All serious infections	3 (2)	1.9 (3)
Opportunistic infections	0	0
Herpes zoster	1 (1)	0.6 (1)
Active tuberculosis	0	0
Urinary tract infections	5 (4)	3.8 (6)
Respiratory tract infections[b]	45 (35)	46.2 (74)
Malignancies	1 (1)	0.6 (1)
Deep vein thrombosis	0	0
Pulmonary embolism	0	0
Major cardiac events (adjudicated)	1 (1)	0.6 (1)
Deaths	1 (1)	0.6 (1)

[a]Not including deaths; [b]Includes upper respiratory tract infection, lower respiratory tract and lung infection, and latent tuberculosis (10 cases of latent tuberculosis were detected during annual, routine, protocol-specified testing for latent tuberculosis infection)
FIL, filgotinib; OLE, open-label extension; PYE, patient-years of exposure; TEAE, treatment-emergent adverse event

Table 3. Summary of Key Treatment-Emergent Laboratory Abnormalities in EQUATOR2 OLE

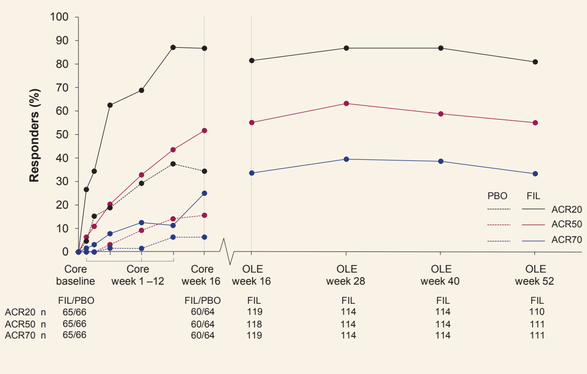
	Incidence, number of patients (%)
	FIL 200 mg (n=128)
Grade ≥2 treatment-emergent laboratory abnormalities	
Lymphocytes	
Grade 2	11 (9)
Grade 3/4	0
Neutrophils	
Grade 2	6 (5)
Grade 3/4	1 (1)
Platelets	0
Hemoglobin	0
Alanine aminotransferase	
Grade 2	2 (2)
Grade 3/4	0
Creatinine	
Grade 2	1 (1)
Grade 3/4	0

FIL, filgotinib; OLE, open-label extension

Efficacy Results

- At OLE week 52, 81%, 55%, and 33% of patients achieved ACR20/50/70 responses, respectively (**Figure 3**)
  - ACR20/50/70 response rates were maintained over time from OLE week 16 to week 52 (**Figure 3**)
- At OLE week 52, 34% of patients fulfilled criteria for minimal disease activity (data not shown)
  - Rates of minimal disease activity were maintained over time from OLE week 16 to week 52 (data not shown)

Figure 3. ACR20/50/70 Response Rates up to OLE Week 52



FIL, filgotinib; OLE, open-label extension; PBO, placebo

Conclusions

- The safety profile of oral FIL 200 mg once daily in patients with PsA is consistent with findings from rheumatoid arthritis studies,[1,2,4] with **no new or unexpected safety signals**
- In EQUATOR2, FIL is generally well tolerated and associated with mostly mild or moderate AEs
- In EQUATOR2, FIL showed **sustained efficacy up to OLE week 52**, as demonstrated by maintained ACR20/50/70 responses and sustained low disease activity

References

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3. Vermeire S, et al. *Lancet* 2017;389:266–275. 4. Genovese MC, et al. *JAMA* 2019;322:315–325. 5. Mease P, et al. *Lancet* 2018;392:2367–2377. 6. ClinicalTrials.gov identifier: NCT03320876. Available at: https://clinicaltrials.gov/ct2/show/NCT03320876. Accessed October 24, 2019.

Disclosures

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