THU0202

INTEGRATED SAFETY ANALYSIS OF FILGOTINIB TREATMENT FOR RHEUMATOID ARTHRITIS FROM 7 CLINICAL TRIALS

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Background: Filgotinib (FIL), an oral, potent, selective JAK-1 inhibitor, provided statistically significant and clinically meaningful improvement in rheumatoid arthritis (RA) signs and symptoms, physical function, radiographic progression, and quality of life in a comprehensive clinical program of 4 phase 3 (FINCH 1–4; NCT02889796, NCT02873936, NCT02886728, NCT03025308) and 3 phase 2 (DARWIN 1–3; NCT01668641, NCT01894516, NCT02065700) trials in patients (pts) with early and biologic-refractory RA.^{1–3}

Objectives: To assess long-term safety of FIL.

Methods: Treatment-emergent adverse events (TEAEs) from the FIL clinical program were integrated and presented for pts receiving FIL 200 mg or FIL 100 mg QD (including pts who transitioned to FIL from placebo [PBO], methotrexate [MTX], adalimumab [ADA], or another dose of FIL) as well as pts receiving PBO, MTX, and ADA across all 7 studies. Exposure-adjusted incidence rates (EAIRs) per 100 patient-years (PY) were calculated for adverse events (AEs) of interest per treatment. Incidence was total number of pts with events, and PY exposure was time between first and last doses. Major adverse cardiovascular events (MACE) and venous thromboembolism (VTE) were centrally adjudicated by an independent committee.

Results: Across the 7 trials, 4057 pts with RA (2227 pts FIL 200 mg; 1600 pts FIL 100 mg) received >1 dose of treatment for 5493 total PY of exposure (3079.2 PY FIL 200 mg; 1465.3 PY FIL 100 mg) (Table). EAIRs of serious AEs and TEAEs leading to death in pts receiving FIL were comparable to those for PBO, ADA, or MTX, with no dose-dependent effect (Figure 1). EAIR for herpes zoster (HZ), serious, and opportunistic infections are shown in Figure 2. EAIR for HZ were low overall, but numerically slightly higher for FIL relative to PBO, ADA, and similar to MTX. Serious infection EAIRs were comparable between pts receiving FIL 100 mg and ADA, and numerically slightly lower for FIL 200 mg and MTX. Rates of opportunistic infections (including active tuberculosis) were low overall; EAIR for FIL doses were comparable to placebo and numerically lower than ADA or MTX. Rates of MACE and VTE were numerically lower for FIL relative to PBO (Figure 1). Malignancies, including non-melanoma skin cancer, were rare overall, and rates were low in pts receiving FIL (Figure 1).

Table. Total exposure to study treatments pooled from 7 studies

	Number of patients	Patient-years of exposure
FIL 200 mg	2227	3079.2
FIL 100 mg	1600	1465.3
ADA	325	290.1
MTX	416	356.2
PBO	781	302.4

Patients could contribute to >1 treatment group.

ADA, adalimumab; FIL, filgotinib; MTX, methotrexate; PBO, placebo.

Conclusion: In this integrated analysis, FIL was well-tolerated, and no new safety concerns were identified. No clinically meaningful dose-dependent safety effects were observed. MACE and VTE were uncommon. Serious infections rates were low; HZ reactivation was infrequent. Safety results were consistent with selective JAK-1 inhibition and highlight the favourable safety and tolerability of FIL in patients with RA.

References:

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Figure 1. Rates of TE-AEs, deaths, malignancies, VTE, and MACE by treatment group per 100 patient-years

ADA, adalimumab; CI, confidence interval; EAIR, exposure-adjusted incidence rate; FIL, filgotinib; MACE, major adverse cardiovascular event; MTX, methotrexate; NMSC, non-melanoma skin cancer; PBO, placebo; TEAE, treatment emergent adverse event; TE-AE, treatment-emergent severe adverse event; VTE, venous thromboembolism.

Figure 2. Rates of infections by treatment group per 100 patient-years

ADA, adalimumab; CI, confidence interval; EAIR, exposure-adjusted incidence rate; FIL, filgotinib; MTX, methotrexate; PBO, placebo.

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REAL WORLD EFFECTIVENESS OF BARICITINIB IN THE SWISS RHEUMATOID ARTHRITIS REGISTER (SCQM-RA)

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Background: Patients with rheumatoid arthritis (RA) intolerant or not responding adequately to conventional synthetic DMARD (csDMARD) usually receive biological DMARDs (bDMARDs) or targeted synthetic DMARDs (tsDMARDs) as 2nd line. Baricitinib (BARI), a once-daily oral selective Janus kinase inhibitor, is efficient in randomised controlled trials but still lacks evidence for effectiveness in real world settings.

Objectives: To characterise patients initiating treatment with BARI or other alternative bDMARDs, and to perform an analysis of drug maintenance.

Methods: This is an observational, prospective, cohort study, within the Swiss Clinical Quality Management (SCQM) register.

All treatment courses (TC) initiated between 2017-09-01 and 2019-10-01 were considered, comparing TC with BARI (BARI group) to TC with alternative bDMARDs, either TNF inhibitors (TNFi group) or other mode of action bDMARDs (OMA group), excluding rituximab.

Baseline characteristics were compared using ANOVA or χ^2 tests. The crude drug maintenance was assessed by survival analysis (Kaplan-Meier). To correct for potential confounding factors, a Cox proportional hazard model was used. Missing values were imputed using multiple imputation with chained equations.

Results: During the study period, 979 TC were initiated (240 in BARI group, 461 in TNFi group and 278 in OMA group). BARI was prescribed to significantly older patients, with longer disease durations and more previous treatment failures (Table 1). Unadjusted drug maintenance was significantly shorter in the TNFi compared to the BARI group (log rank $p = 0.019$). After adjustment for potential confounding factors, the hazard of TNFi discontinuation remained higher than for BARI (Hazard Ratio (HR) 1.48 (95% CI = [1.05 – 2.09]; $p = 0.02$)). A similar trend was observed when comparing the OMA drugs to BARI, with a HR for discontinuation of 1.42 (95% CI = [0.98 – 2.05]; $p = 0.06$) (Figure 2). Covariates significantly associated with decreased drug maintenance were concomitant csDMARD and concomitant glucocorticoids (Figure 2).

Conclusion: In this preliminary analysis, baricitinib was prescribed to older patients, with longer disease durations, and more previous treatment failures

compared to alternative bDMARDs. Baricitinib demonstrated a significantly higher drug maintenance than TNFi, while similar trend was observed in comparison to OMA drugs.

Conflict of interest: This analysis has been made possible by financial support of Eli Lilly (Suisse) SA to the Geneva University Hospitals (HUG).

Table 1. Baseline characteristics of studied population

Variable	Categories	Baricitinib (TC = 240; 240 patients) Mean (SD) Otherwise: n %	TNFi (TC = 461; 397 patients) Mean (SD) Otherwise: n %	OMA bDMARDs (TC = 278; 253 patients) Mean (SD) Otherwise: n %	P values
Concomitant csDMARD at baseline		45 %	54 %	46 %	0.02
Line of Therapy	1 st	20 %	46 %	22 %	<0.01
	2 nd	22 %	25 %	26 %	
	3 rd	14 %	14 %	26 %	
	4 th or later	43 %	16 %	27 %	
Gender (female)		80 %	71 %	74 %	0.05
Age		59 (13)	53 (14)	59 (13)	<0.01
Seropositivity (ACPA and/or RF)		75 %	71 %	79 %	0.04
HAQ-DI Score		0.9 (0.7)	0.7 (0.6)	0.8 (0.6)	0.02
Disease duration (years)		12 (10)	9 (10)	11 (9)	<0.01
CDAI baseline		19 (10)	15 (12)	19 (14)	0.09

Legend

TC = Treatment Courses. SD = Standard Deviation. TNFi = TNF inhibitors. OMA bDMARDs = Other Mode of Action biological DMARDs. csDMARD = conventional synthetic DMARD. ACPA = Anti Citrullinated Peptide Antibodies. RF = Rheumatoid Factor. HAQ-DI = Health Assessment Questionnaire Disability Index. CDAI = Clinical Disease Activity Index.

Figure 1: Multivariable Cox model of drug discontinuation by type of treatment

Adjusted for: age, gender, BMI, concomitant csDMARD, concomitant glucocorticoid, disease activity (CDAI), functional disability (HAQ-DI), disease duration, smoking status, line of therapy, and seropositivity (RF and/or ACPA). A cluster term accounted for patients with multiple TC.

Figure 2: Hazard ratio of drug discontinuation (95% CI)