Rheumatoid arthritis - non biologic treatment and small molecules

POS0663 THE USE OF EXPOSURE-ADJUSTED EVENT RATES VERSUS EXPOSURE-ADJUSTED INCIDENCE RATES IN ADVERSE EVENT REPORTING: INSIGHTS FROM FILGOTINIB INTEGRATED SAFETY DATA IN RHEUMATOID ARTHRITIS

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Background: Reporting of treatment-emergent adverse events (TEAEs) in rheumatoid arthritis (RA) clinical trials can be summarized as exposure-adjusted incidence rates (EAIRs) or exposure-adjusted event rates (EAERs). Censored EAIR (EAIR), weighing exposure up to a patient's first event, is commonly reported; uncensored EAIR (EAIRu), using total exposure time for all patients, can also be used. For EAIR, exposure time can vary by event. In contrast to EAIR(u), the total number of events are used to calculate EAER. The three methods account for different exposures and/or multiple events, which can impact the outcome evaluation. Studies of filgotinib (FIL) in RA[1] report safety data as EAIR/100 patient-years of exposure (PYE) for TEAEs, which is uncensored.

Objectives: To describe the outcome of long-term FIL integrated safety data in RA by applying different statistical methodologies: EAER, EAIRu and EAIR.

Methods: Integrated FIL safety data from seven clinical trials were assessed[1]. Predefined adverse events of special interest (AESI) included serious infections (any), herpes zoster (HZ), major adverse cardiac events (MACE), malignancies (excluding nonmelanoma skin cancer [NMSC]), NMSC and venous thromboembolism (VTE). The number of patients with an event, number of events, EAER, EAIRu and EAIR were summarized. The data extraction date was January 2021 for the DARWIN 3 (NCT02065700) long-term extension (LTE) and November 2020 for the FINCH 4 (NCT03025308) LTE.

Results: In total, 3691 patients received ≥1 FIL dose for 8085 PYE. In this population, 176 serious infections were reported in 137 patients, 125 HZ events were reported in 112 patients, 39 MACE were reported in 33 patients, 20 cases of VTE were reported in 15 patients, 60 malignancies excluding NMSC were reported in 49 patients and 21 cases of NMSC were reported in 20 patients. Within each treatment arm (FIL 200 mg [FIL200], FIL 100 mg [FIL100] or combined FIL), rates for most AESI were similar when reported as EAER, EAIRu or EAIR (Table 1). For serious infections, EAER was higher than EAIRu or EAIR. The total exposure time to first event (censored PYE) was high and comparable to total exposure (PYE) (>2700 years and >5100 years for the total populations in the FIL100 and FIL200 groups, respectively).

Table 1. Exposure-adjusted event and incidence rates for AESI

		FIL200	FIL100	FIL combined
Number of patients/PYE		2267/5302.5	1647/2782.6	3691/8085.1
Serious infections	**EAER**	1.9 (1.5, 2.4)	3.2 (2.2, 4.5)	2.0 (1.7, 2.4)
	EAIRu	1.5 (1.1, 1.9)	2.7 (1.9, 3.9)	1.6 (1.3, 2.0)
	EAIR	1.5 (1.2, 1.9)	2.8 (1.9, 4.0)	1.7 (1.4, 2.0)
HZ	**EAER**	1.6 (1.3, 2.1)	1.3 (0.9, 1.8)	1.5 (1.2, 1.8)
	EAIRu	1.5 (1.2, 2.0)	1.1 (0.8, 1.5)	1.4 (1.1, 1.7)
	EAIR	1.6 (1.2, 2.0)	1.1 (0.8, 1.6)	1.4 (1.1, 1.7)
MACE	**EAER**	0.3 (0.2, 0.5)	0.6 (0.4, 1.0)	0.4 (0.3, 0.6)
	EAIRu	0.3 (0.2, 0.5)	0.5 (0.3, 0.8)	0.4 (0.2, 0.6)
	EAIR	0.3 (0.2, 0.5)	0.5 (0.3, 0.9)	0.4 (0.2, 0.6)
VTE	**EAER**	0.3 (0.2, 0.5)	0.1 (0.1, 0.4)	0.2 (0.2, 0.4)
	EAIRu	0.2 (0.1, 0.4)	0.1 (0.1, 0.4)	0.2 (0.1, 0.3)
	EAIR	0.2 (0.1, 0.4)	0.1 (0.1, 0.4)	0.2 (0.1, 0.3)
Malignancies excluding NMSC	**EAER**	0.8 (0.5, 1.1)	0.8 (0.5, 1.2)	0.7 (0.2, 2.8)
	EAIRu	0.6 (0.4, 0.9)	0.6 (0.4, 1.0)	0.6 (0.4, 0.8)
	EAIR	0.6 (0.4, 0.9)	0.6 (0.4, 1.0)	0.6 (0.4, 0.8)
NMSC	**EAER**	0.3 (0.2, 0.5)	0.2 (0.1, 0.5)	0.3 (0.2, 0.4)
	EAIRu	0.3 (0.2, 0.5)	0.2 (0.1, 0.4)	0.2 (0.2, 0.4)
	EAIR	0.3 (0.2, 0.5)	0.2 (0.1, 0.4)	0.2 (0.2, 0.4)

Data are rate (95% CI) unless otherwise stated.

Conclusion: These data confirm that using different methods to analyze FIL safety data (EAER, EAIRu, EAIR) does not result in different safety outcomes, reinforcing the previously reported FIL safety profile in patients with RA. As the AESI reported in the long-term safety database with FIL are rare, patients commonly have long exposure times before experiencing an event, which are often associated with end of treatment. As such, EAIRu, EAIR and EAER are similar.

REFERENCES:

[1] Winthrop KL et al. Ann Rheum Dis 2021, doi: 10.1136/annrheumdis-2021-221051.

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POS0664 RADIOGRAPHIC CHANGE IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ESTIMATED BASELINE YEARLY PROGRESSION ≥5 OR <5: POST HOC ANALYSIS OF TWO PHASE 3 TRIALS OF FILGOTINIB

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Background: In some patients (pts) with rheumatoid arthritis (RA), especially those with joint damage early in the disease, first-line methotrexate (MTX) treatment may not suffice to prevent further rapid radiographic progression (RRP).[1] In FINCH 1 (NCT02889796), filgotinib 200 mg (FIL200) and 100 mg (FIL100) reduced change in modified total Sharp score (mTSS) vs placebo (PBO) in pts with RA and inadequate response to MTX (MTX-IR).[2] In FINCH 3 (NCT02886728), FIL200 and FIL100 reduced change in mTSS vs MTX monotherapy (MTX mono) in MTX-naïve pts.[3]

Objectives: To evaluate, via post hoc analysis of 2 trials, filgotinib's effects on radiographic progression vs MTX mono in pts with estimated baseline (BL) yearly progression ≥5 or <5 mTSS units/year.

Methods: The double-blind 52-week (W) FINCH 1 study randomised MTX-IR pts with moderate–severe active RA to FIL200 or FIL100, subcutaneous adalimumab (ADA) 40 mg, or PBO; at W24, PBO pts were rerandomised blinded to FIL200 or FIL100; all took stable background MTX.[2] In FINCH 3, MTX-naïve pts were randomised, blinded, to FIL200 + MTX, FIL100 + MTX, FIL200 alone, or MTX mono for up to W52.[3] This analysis examined subgroups by estimated BL yearly progression (BL mTSS/duration in years of RA diagnosis), based on ≥5 or <5 mTSS units/year,[4] a threshold commonly used to define RRP. We assessed effects of filgotinib vs ADA or PBO in mTSS change from BL (CFB) at W24/W52 (using a mixed model for repeated measures) and percentages with no W24 progression (mTSS change ≤0, ≤0.5, ≤smallest detectable change [SDC], using Fisher's exact test).

Results: At BL, 558/1755 MTX-IR and 787/1249 MTX-naïve pts had BL estimated yearly progression ≥5. Median mTSS in pts with BL yearly progression ≥5 and <5 was 53.25 vs 5.00 respectively in the MTX-IR trial and 6.00 vs 2.50 in the MTX-naïve trial. At W24, the mTSS CFB in pts with BL yearly progression ≥5 and <5 was 0.84 and 0.22 in MTX-IR pts taking PBO + MTX, and 0.67 and 0.25 in MTX-naïve pts taking MTX mono. At W52, in pts with BL yearly progression ≥5, FIL200 + MTX reduced mTSS change vs PBO + MTX in the MTX-IR trial and vs MTX mono in the MTX-naïve trial (Figure 1). At W24, among pts with estimated BL yearly progression ≥5, FIL200 + MTX increased odds of no