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POS1037

CORRELATION BETWEEN SKIN INVOLVEMENT, JOINT INVOLVEMENT AND ENTHESITIS IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: POST-HOC ANALYSIS OF EQUATOR/EQUATOR2

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Background: Psoriatic arthritis (PsA) is a heterogeneous, inflammatory disease involving multiple clinical domains including arthritis/synovitis, enthesitis, dactylitis, spondylitis and psoriasis. Effects on each domain should be assessed to determine the overall quality of treatment. Filgotinib (FIL) is a novel preferential Janus kinase 1 inhibitor that is in development for inflammatory conditions including PsA. EQUATOR (NCT03101670) was a 16-week, Phase 2, double-blind, randomised, placebo (PBO)-controlled trial of FIL for patients with active PsA.¹ EQUATOR2 (NCT03320876) is an open-label extension (OLE) of the study.

Objectives: This post-hoc analysis of EQUATOR and EQUATOR2 assessed the patient-level correlation between changes over time in the three PsA clinical disease domains of skin, joint and enthesitis in patients treated with FIL.

Methods: In EQUATOR, patients with active moderate-to-severe PsA (≥ 5 swollen joints and ≥ 5 tender joints, fulfilling Classification for PsA criteria) were randomised 1:1 to receive oral FIL 200mg or PBO once daily (QD) for 16 weeks. At Week 16, patients could continue into the 304-week OLE, with all patients receiving FIL 200mg QD regardless of previous treatment in EQUATOR. This post-hoc analysis was limited to patients with skin involvement ($\geq 3\%$ body surface area), joint involvement and enthesitis at baseline, with changes from baseline in the three domains assessed using the Psoriasis Area and Severity Index (PASI), swollen/tender joint count (S/TJC), and the Leeds Enthesitis Index (LEI) and Spondyloarthritis Research Consortium of Canada (SPARCC) index, respectively. Analyses that used LEI as the enthesitis index to assess change from baseline included patients with LEI score ≥ 1 at baseline; those using SPARCC included patients with SPARCC score ≥ 1 at baseline.

Results: The EQUATOR study enrolled 131 patients and 122 patients continued into the EQUATOR2 OLE. Of the 131 patients enrolled in EQUATOR, 49 and 56 patients had PsA involving all three domains at core study baseline when enthesitis was assessed using LEI and SPARCC index, respectively. Pooled data for all patients receiving FIL during the OLE indicate that improvements from baseline in the clinical domains continued with long-term treatment, with 22/42 (52%) and 23/38 (61%) patients having both SJC66 and LEI resolution at Weeks 52 and 100, respectively. For the 22 patients with both SJC and LEI resolution at Week 52, the mean percent change from baseline for PASI was -64%; for the 23 patients with both SJC and LEI resolution at Week 100, the mean percent change from baseline for PASI was -60%. The Figure 1 shows correlation between SJC, LEI and PASI at Week 100. A relationship between the three clinical domains was observed at the individual level; within a single patient, an improvement in one domain was generally followed by improvements in the other two domains. With regard to the sequence in which changes were observed, joints improved first, followed by improvements in the skin and enthesitis. There were no notable differences between changes in LEI and SPARCC enthesitis index in terms of their correlation with improvements in joint and skin involvement. Similarly, there were no notable differences in correlation between the three domains when joints were assessed using TJC rather than SJC.

Conclusion: Patients with improvements in skin, joints or enthesitis following treatment with FIL generally also had improvements in the other clinical domains of PsA. The joints were found to be the first of the three domains to improve.

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Figure: Correlation between SJC, LEI and PASI at Week 100 of the OLE

Plot shows observed cases. Number of plotted patients: 38 out of 49 patients with involvement in all three clinical domains at baseline. Resolved: -100% percent change from baseline; Improved: -100% < percent change from baseline < 0%; Unimproved: 0% ≤ percent change from baseline. Patients were on placebo or filgotinib (200 mg) during the core study (initial 16 weeks). LEI, Leeds Enthesitis Index; OLE, open-label extension; PASI, Psoriasis Area and Severity Index; SJC(66), (66-)swollen joint count.

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POS1038

THE EFFECT OF FILGOTINIB ON ENTHESITIS: 100-WEEK DATA FROM AN OPEN-LABEL EXTENSION STUDY IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

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Background: Filgotinib (FIL), a novel preferential Janus kinase 1 inhibitor, was assessed in patients with active psoriatic arthritis (PsA) in the 16-week, Phase 2, EQUATOR trial (NCT03101670).¹ EQUATOR2 (NCT03320876) is the open-label extension (OLE). As previously reported, an interim analysis of the OLE showed that the majority of patients had clinical resolution of enthesitis by Week 52.²

Objectives: This post-hoc analysis evaluated the effect of FIL on clinical enthesitis after 100 weeks of treatment in the OLE, as assessed using the Leeds Enthesitis Index (LEI) and Spondyloarthritis Research Consortium of Canada (SPARCC) index, and evaluated the discriminatory capacity of the two indices. In addition, we assessed which of the sites included in LEI and SPARCC were most frequently involved and whether treatment effect was consistent across sites.

Methods: In EQUATOR, patients with active moderate-to-severe PsA (≥ 5 swollen joints and ≥ 5 tender joints, fulfilling Classification for PsA criteria) were randomised 1:1 to receive oral FIL 200mg or placebo (PBO) once daily (QD) for 16 weeks. At Week 16, all patients could continue into the OLE, receiving FIL 200mg QD for up to an additional 304 weeks. We compared changes from core baseline in LEI and SPARCC measures, the effect on enthesitis at sites included in LEI and SPARCC assessments and the discriminatory capacity of both enthesitis indices.

Results: Of 131 patients randomised to EQUATOR, 122 entered the OLE. There was strong agreement between LEI and SPARCC at baseline. While most patients had enthesitis at baseline according to either index (76/131 [58.0%] by LEI; 85/131 [64.9%] by SPARCC), a minority had enthesitis at a large number of sites (6.9% with 5–6 LEI sites; 12.2% with ≥ 9 SPARCC sites). The sites most frequently involved at baseline were the lateral epicondyle humerus and Achilles tendon, sites common to both LEI and SPARCC. There was greater variability in the change from baseline to Week 16 in SPARCC compared with LEI (Table 1). LEI showed a greater discriminatory capacity than SPARCC when change from baseline was compared for FIL vs PBO at Week 16, as shown by higher absolute standardised mean difference: -0.70 (LEI) and -0.30 (SPARCC) (observed cases; Table 1). Subgroup analyses indicated that the treatment effect of FIL vs PBO at Week 16 for all sites was consistent with the overall treatment effect seen for LEI or SPARCC, and indicative of an improvement with FIL vs PBO for nearly all sites. The proportion of patients with enthesitis decreased from baseline up to OLE Week 100 (Figure 1). There were no major differences in long-term effect on enthesitis between sites.

Conclusion: FIL improved enthesitis consistently across sites compared with PBO. Rapid improvement in enthesitis was seen up to Week 16 of the core study and improvements continued up to Week 52, after which responses were generally stable up to Week 100. LEI assesses fewer locations than SPARCC, but reassuringly captured the sites most commonly affected by enthesitis; LEI also had greater discriminatory capacity.

TABLE: Mean change from baseline in enthesitis assessed by LEI and SPARCC

Index	Imputation	n	Filgotinib		Placebo		Pooled SD	Mean difference	Standardised mean difference	Guyatt effect size
			n	Mean (SD) change from baseline at Week 16	n	Mean (SD) change from baseline at Week 16				
SPARCC	OC	34		-2.9 (3.43)	47	-1.9 (3.24)	3.32	-1.0	-0.30	-0.90
SPARCC	LOCF	37		-2.8 (3.29)	47*	-1.9 (3.24)	3.26	-0.9	-0.28	-0.86
LEI	OC	30		-1.7 (1.49)	43	-0.7 (1.37)	1.42	-1.0	-0.70	-1.24
LEI	LOCF	33		-1.8 (1.49)	43	-0.7 (1.37)	1.42	-1.1	-0.77	-1.31

Includes patients with enthesitis at baseline at core study baseline

*One patient with SPARCC enthesitis at baseline had no post-baseline value

LEI, Leeds Enthesitis Index; LOCF, last observation carried forward; OC, observed case; SD, standard deviation; SPARCC, Spondyloarthritis Research Consortium of Canada

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Figure: Proportion of patients with enthesitis over time

Includes patients with enthesitis at baseline. Non-responder imputation.

From core Week 16 to OLE Week 16, patients are presented according to original treatment, but all received filgotinib during this time and for the remainder of the OLE. BL, baseline; FIL, filgotinib; LEI, Leeds Enthesitis Index; OLE, open-label extension; PBO, placebo; SPARCC, Spondyloarthritis Research Consortium of Canada; W, Week.

Figure 1.

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POS1039 PSORIATIC ARTHRITIS AND PHYSICAL ACTIVITY, A SYSTEMATIC REVIEW

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Background: The beneficial effects of physical activity (PA) have been demonstrated in rheumatoid arthritis and ankylosing spondylitis on disease and co-morbidities while they are not clearly established in psoriatic arthritis.

Objectives: Thus, the aim of this study was, on the basis of a systematic review of the literature, (i) to assess the level of physical activity in these patients and (ii) to determine the effects of physical activity on joint and extra articular symptoms and on well-being.

Methods: The research strategy was performed on Pubmed, Cochrane, and PEDro databases using the following keywords: "psoriatic arthritis AND physical activity" without restriction. Articles published in English before October 2019 were identified and selected according to the PRISMA methodology by two independent investigators. In case of disagreement, a third investigator was interviewed. To be included in the qualitative synthesis, the studies had to meet the PICOS criteria.

Results: Among the 259 studies identified, 13 were finally included. 241 were excluded because they did not address the topic or were not in English and 5 were duplicated. Two epidemiological studies revealed that 17 and 68 % of patients comply with WHO recommendations for the general population in terms of physical activity. The main explanations expressed by patients are: a lack of promotion of physical activity by the rheumatologist and the fear of pain during the movement also called "kinesiophobia". Among the three prospective randomized clinical trials, one of them showed a significant 20% reduction in the BASDAI (Bath Ankylosing Spondylitis Disease) and a 25% reduction in pain. Fatigue was significantly reduced by 15% following a physical activity protocol on a cycleergometer for 11 weeks. Muscle strength and maximum VO₂ were significantly improved after participation in the physical activity protocol in two of the clinical trials. Four retrospective studies evaluated the effect of physical activity on the risk of enthesitis or dactylitis. None were associated with an increased risk of enthesitis. However, physical activity was found to be a risk factor for structural remodelling of the Achilles tendon. And, avoiding physical activity seems to be a protective factor against the risk of enthesitis. On the other hand, the three clinical trials did not mention any increase in the disease's activity score. Finally, the effects of four rehabilitation programs have been evaluated in psoriatic arthritis and other inflammatory rheumatism. The beneficial effects were modest and concerned the reduction of pain for all the programs and of fatigue for two of the programs.

Conclusion: The studies showed a beneficial effect of physical activity on disease activity, on well-being and on comorbidities. The data on the risk of enthesitis are reassuring. Further investigations are necessary to confirm these results and to precise the modalities of exercise.