SAT0372 CHANGE OF SUBCLINICAL ATHEROSCLEROSIS AFTER FIVE YEARS ANTI-TNF TREATMENTS IN PSORIATIC ARTHRITIS

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Background: Although cardiovascular (CV) diseases are very common in inflammatory arthritis like psoriatic arthritis (PsA), long-term impact of medication on CV outcomes is lacking.
Objectives: The aim of our study was to evaluate the long-term effects of anti-TNF-a drugs on subclinical atherosclerosis assessed by the flow-mediated dilatation (FMD) and carotid intima media thickness (IMT).
Methods: A total of 30 patients with PsA according to classification of psoriatic arthritis (CASPAR) criteria1 and 28 healthy controls were enrolled in this cross-sectional study between June 2011-July 2012. 22 out of 30 PsA patients completed the study. Demographic data (sex, age), PsA and psoriasis duration, joint pattern (monoarthritis, oligoarthritis or polyarthritis) and other PsA involvements (nail, enthesis, dactilytis) were noted. Tender joint count, swollen joint count and disease activity score (DAS)-28 were used for joint activity assessment. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were used for acute phase reactants. Sex and age matched healthy controls were selected as the control group for this study. Flow mediated dilatation (FMD) from brachial artery and carotid intima media thickness (IMT) were measured by an experienced cardiologist both at initial and 5-year follow-up visits.
Results: Psoriasis duration of PsA patients was 180±114 months. PsA disease duration was 108±33 months. The mean duration between two evaluations was 62±9 months. At first evaluation, 14 (63.6%) patients had peripheral joint, 1 (4.5%) patient had axial, and 7 (31.8%) patients had both peripheral and axial involvement among patients. Dactilytis in 6 (27.3%), enthesis in 7 (31.8%) and nail in 12 (54.5%) patients were other clinical involvements. FMD% was lower in PsA patients than healthy controls [9.3±3.9 vs 12.9±1.8, p<0.001] and carotid IMT was more obvious in PsA patients than healthy controls [0.64±0.17 vs 0.54 ±0.09, p=0.017] (Figure). All PsA patients used anti-TNF alpha treatment during the follow-up period. 68.1% of the PsA patients were in remission during the control. At 5-year follow-up visits, there was no CV event in study groups. However, FMD% was lower in PsA patients than healthy controls [7.6±4.8 vs 12.9±1.8, p<0.001] and carotid IMT was also similar between PsA patients and healthy controls [0.61±0.33 vs 0.54±0.09, p=0.306]. After 5-year follow-up visits, there was no statistically significant difference in FMD% compared to baseline [p = 0.254]. ΔFMD% was found to be moderately correlated with the ΔBASDAI (r= -0.45).
Conclusion: Our results showed that there was a significant impact of anti-TNF-a drugs on progression of subclinical atherosclerosis at the vascular wall level, but no impact on the endothelial dysfunction. Further large-scale randomized studies are needed to confirm our findings.

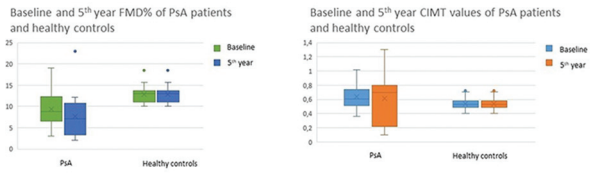

Figure.

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SAT0373 EFFECT OF FILGOTINIB ON PATIENT-REPORTED OUTCOMES IN ACTIVE PSORIATIC ARTHRITIS: RESULTS FROM EQUATOR, A RANDOMIZED, PHASE 2 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. FIL significantly improved multiple disease domains vs placebo (PBO) in patients with active psoriatic arthritis (PsA) in the multicenter, double-blind, phase 2 EQUATOR trial (NCT03101670) [1].
Objectives: To evaluate the effect of FIL vs PBO on patient reported outcomes (PROs) in EQUATOR and the extent to which effects on composite disease endpoints translate to clinically relevant improvements for patients.
Methods: Patients were randomized 1:1 to FIL 200 mg or PBO once daily for 16 weeks [1]. Patient's Global Assessment of Disease Activity (PtGADA), pain intensity (visual analog scale), Pruritus Numerical Rating Scale (NRS), Health Assessment Questionnaire Disability Index (HAQ-DI), 36-Item Short Form Survey (SF-36) Physical Component Summary (PCS) and Mental Component Summary (MCS), and Functional Assessment of Chronic Illness Therapy-Fatigue scale (FACIT-F) were assessed at week 16. Analysis of covariance was used to compare changes from baseline in outcomes between groups. Proportions of patients achieving normative PRO scores or minimal clinically important differences (MCIDs) were compared using Cochran-Mantel-Haenszel tests [2, 3].
Results: FIL significantly improved multiple PROs vs PBO at week 16 (Table). Proportions of patients reaching normative PRO values for FACIT-F and SF-36 PCS (≥40 or 50, respectively), and achieving MCIDs in HAQ-DI and SF 36 PCS, were significantly greater for FIL vs PBO (Table). Significant improvement in 6/8 SF 36 domains was observed at week 16 with FIL vs PBO (Fig a). Improvement in most individual FACIT F items was also observed (Fig b).
Conclusion: In EQUATOR, FIL-treated patients with active PsA reported greater and clinically meaningful improvements in most PROs at week 16 vs PBO, mirroring improvements previously reported with FIL in disease activity measures [1].

Table

Table

Week 16		FIL (n=65)	PBO (n=66)	Treatment difference (95% CI)	p
Mean change from baseline					
PtGADA (mm)		−27.2 (22.1)	−13.5 (25.8)	−15.2[a] (−22.3, −8.1)	<0.0001
Pain (mm)		−31.6 (21.3)	−11.1 (29.7)	−18.9[a] (−26.7, −11.1)	<0.0001
Pruritus NRS		−2.5 (2.1)	−0.6 (2.2)	−2.2[a] (−3.1, −1.4)	<0.0001
HAQ-DI		−0.6 (0.5)	−0.3 (0.5)	−0.3[a] (−0.4, −0.1)	0.0009
SF-36 PCS		7.4 (6.6)	2.4 (6.6)	4.7[a] (2.6, 6.8)	<0.0001
SF-36 MCS		4.3 (8.3)	3.2 (9.2)	1.2[a] (−1.7, 4.0)	0.4128
FACIT-F		8.2 (7.3)	5.5 (8.1)	3.2[a] (0.8, 5.5)	0.0086
Response rate, n/N (%)					
HAQ-DI	MCID ≥0.35	41/63 (65)	26/62 (42)	23.2[b] (5.7, 38.8)	0.0085
SF-36 PCS	Score ≥50	11/64 (17)	4/63 (6)	10.9[b] (−0.7, 22.5)	0.0471
	MCID ≥2.5	49/65 (75)	26/66 (39)	36.0[b] (19.2, 50.0)	<0.0001
SF-36 MCS	Score ≥50	13/46 (28)	14/47 (30)	−1.5[b] (−19.4, 16.6)	0.9879
	MCID ≥2.5	32/65 (49)	40/66 (61)	−11.4[b] (−27.4, 5.5)	0.2607
FACIT-F	Score ≥40	18/58 (31)	7/57 (12)	18.7[b] (3.6, 33.0)	0.0105
	MCID ≥4	43/65 (66)	37/66 (56)	10.1[b] (−6.5, 25.9)	0.1921

[a]Least-squares mean. [b]Arithmetic mean.
CI, confidence interval

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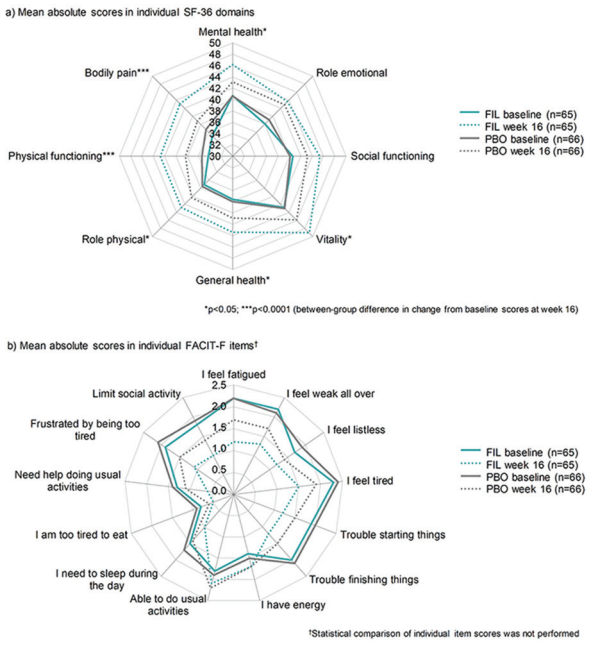

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SAT0374 IXEKIZUMAB, WITH OR WITHOUT CONCOMITANT METHOTREXATE, IMPROVES THE SIGNS AND SYMPTOMS OF PSA FOR UP TO 52 WEEKS OF TREATMENT

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Background: Ixekizumab (IXE) is a high affinity monoclonal antibody selectively targeting interleukin (IL)-17A. It was previously demonstrated that IXE, with or without concomitant methotrexate (MTX), was superior to placebo (PBO) in improving the signs and symptoms of patients with psoriatic arthritis (PsA) for up to 24 weeks[1,2].

Objectives: To evaluate the efficacy of IXE, with or without continuous concomitant MTX, for up to 52 weeks of treatment in patients with active PsA.

Methods: Patients with active PsA who were biologic naïve (SPIRIT-P1, NCT01695239) *or* had prior inadequate response or intolerance to tumour necrosis factor inhibitors (SPIRIT-P2; NCT02349295) were randomised to PBO (N=224), 80 mg IXE every 4 weeks (IXEQ4W, N=229) or every 2 weeks (IXEQ2W, N=226), after a 160 mg starting dose. In this post-hoc analysis, efficacy was assessed up to Week 52 for the following two subgroups: (i) patients who were treated with IXE as monotherapy i.e. no concomitant conventional disease-modifying anti-rheumatic drugs and (ii) patients who received constant dose of MTX from Weeks 0 to 52. Patients who had MTX dose change were excluded. Efficacy outcome measurements included American College of Rheumatology (ACR) 20/50/70 responses, minimal disease activity (MDA), and disease activity in psoriatic arthritis (DAPSA) low disease activity (LDA) (score ≤ 14). Patients who discontinued from treatment before Week 52 were included in the analysis. Missing values were imputed using non-responder imputation. All analyses were done post-hoc.

Results: Among patients randomised to IXE at Week 0, 177 (38.9%) patients were treated with IXE monotherapy while 183 (40.2%) patients received constant dose of MTX up to Week 52. The average MTX dose was 15.7 mg/week and 16.0 mg/week for IXEQ4W and IXEQ2W, respectively. Week 52 results are presented in Table 1. At Week 52, similar results were observed between the two groups of patients for the different disease activity measures (ACR, MDA, and DAPSA LDA) and there was also a trend for a numerical higher proportion of patients achieving ACR responses with IXE monotherapy compared to patients with concomitant MTX use. Over time (Weeks 0-52), ACR 20, 50, and 70 response rates increased from baseline and were largely similar between the two subgroups (data not shown).

Conclusion: In this post-hoc analysis, IXE treatment showed sustained efficacy in patients with PsA up to one year of treatment, with or without concomitant MTX therapy.

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Table 1. Efficacy Outcomes at Week 52

	IXEQ4W N=229		IXEQ2W N=226	
Concomitant Medication:	None (n=95)	MTX (n=85)	None (n=82)	MTX (n=98)
ACR 20	66.3%	55.3%	63.4%	55.1%
ACR 50	48.4%	38.8%	48.8%	38.8%
ACR 70	35.8%	27.1%	35.4%	23.5%
DAPSA LDA*	52.6%	52.9%	54.9%	41.2%
MDA	38.9%	35.3%	36.6%	22.7%

* score ≤ 14

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