FRI0284

EFFECTIVENESS AND SAFETY OF SECUKINUMAB IN NAÏVE OR TNF-INHIBITORS FAILURE PSORIATIC ARTHRITIS PATIENTS IN REAL LIFE: A 24-MONTHS PROSPECTIVE MULTICENTER STUDY

M. Lorenzin¹, A. Carletto², R. Foti³, M. S. Chimenti⁴, A. Semeraro⁵, L. Costa⁶, L. Santo⁷, E. Fracassi², I. Montanari², M. Felicetti¹, G. L. Fonti⁴, F. Caso⁶, A. Doria¹, A. Ortolan¹, R. Ramonda¹. ¹University of Padova, Padova, Italy; ²University of Verona, Verona, Italy; ³a.O.U. Policlinico Vittorio Emanuele, Catania, Italy; ⁴University of Rome "Tor Vergata", Roma, Italy; ⁵ASL Taranto, Taranto, Italy; ⁶University Federico II, Napoli, Italy; ⁷aSL BT andria - DSS4, Barletta-Andria-Trani, Italy

Background: Secukinumab (SEC) is a novel treatment for psoriatic arthritis (PsA), but data from real life are still missing.

Objectives: 1) to evaluate the effectiveness and safety of a wide cohort of PsA patients on SEC followed in 7 Italian rheumatologic centers for 24 months; 2) to compare the features and disease activity indices of SEC-treated PsA patients subdivided in naïve biological drugs (**group A**) and in TNF-inhibitors (TNFi) failure patients (**group B**).

Methods: Consecutive patients with moderate-severe PsA, who begun SEC treatment were evaluated prospectively. Data on disease characteristics, previous and ongoing treatments, comorbidities and duration of follow-up were collected. Disease activity, functional and clinimetric scores and biochemical values were recorded at baseline (t0), at 6 (t6), 12 (t12), and 24 (t24) months. Anova (Kruskal Wallis) and generalized linear models were used to compare variables over time. Infections and adverse events were also collected.

Results: PsA 345 patients [38.84% men; mean age 52.9 (11.27) years] were enrolled; mean treatment duration was 18.53 (9.97) years. SEC was prescribed as first line biologic treatment in 133 (38.55%) patients and as second or more line biological treatment in 212 (61.45%) patients. Enthesitis was present as a prominent manifestation in 61.44% of patients (Figure 1). In all population significant decrease in tender/swollen joints; Visual Analogue Scale of pain (VASp) and general health (VASgh); Psoriasis Area Severity Index (PASI); Leeds Enthesitis Index (LEI); number of dactylitis; Health Assessment Questionnaire modified for spondyloarthritis (HAQ-S); Bath Ankylosing Spondylitis Disease Activity Index (BASDAI); Bath Ankylosing Spondylitis Functional Index (BASFI); C-reactive protein (CRP) was achieved. Effectiveness of all PsA patients was associated to an improvement in Ankylosing Spondylitis disease activity score (ASDAS) [t0=3.45 (0.69) vs t24=1.48 (0.23); p<0.01] and in Disease Activity in PsA (DAPSA) [t0=29.52 (12.56) vs t24=11.41 (7.63); p<0.001]. At t0 **group B** had a more erosive (p=0.04) and polyarticular pattern (p=0.04), a longer disease duration (p=0.001), a greater prevalence (p=0.04) of psoriasis and dactylitis (p=0.01), a higher PASI score (p=0.01), while no significant difference was observed for uveitis, inflammatory bowel diseases, enthesitis. At t24 **group A** showed better physical functioning and lower disease activity compared to **group B** [HAQs A vs B=0.03 (0.16) vs 0.69 (0.73); BASDAI A vs B=2.37 (0.66) vs 4.27 (2.33); ASDAS A vs B=1.4 (0.62) vs 1.99 (0.86); CRP A vs B=2.03 (1.94) vs 3.11 (1.55) mg/L; DAPSA A vs B=7.03 (3.57) vs 12.41 (8.05)]. After t24 of treatment 74.6% of **Group A** and 72.8% of **Group B** articular had an inactive/low disease activity (MDA), accordingly to ASDAS and DAPSA respectively. Forty-three patients (12.46%) stopped the treatment during the follow-up mainly because of primary or secondary loss of efficacy (29 and 24, respectively). Only 14 patients suspended SEC because of adverse events (of which 9 for reactions at site of injection). A low number of episodes of mild infections (16) occurred; SEC was instead permanently discontinued in 7 cases for: oral refractory mucositis (3); recurrent aphthosis (2); diverticulitis (2). The retention rate at t24 was good in the whole population. Interestingly no differences were found between **Group A** and **B** (p=0.815).

Conclusion: In a real life clinical setting, SEC was safe and effective in PsA. as shown by a significant decrease of DAPSA and ASDAS over a 24-months follow up.

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Baseline characteristics of 345 PsA patients of AOP treated with secukinumab in the period September 2016- November 2019.

PsA Features	Total patients	GROUP A	GROUP B	p
Male sex (N,%)	134 (38.84%)	52 (39.09%)	82 (38.68%)	ns
Age (years), mean (SD)	52.90 (11.27)	48.59 (13.79)	53.30 (7.99)	0.05
Age of diagnosis (years), mean (SD)	38.86 (12.98)	39.20 (13.82)	37.69 (9.98)	ns
Disease duration (years), mean (SD)	10.68 (7.64)	9.18 (6.82)	15.76 (8.32)	0.001
PsA (n)	345	133	212	NA
Polyarticular	209 (60.58%)	74 (55.63%)	135 (63.68%)	0.04
Mono/Oligoarticular	106 (30.72%)	45 (33.83%)	61 (28.77%)	ns
Axial	84 (24.35%)	28 (21.05%)	56 (26.42%)	ns
Enthesitis	212 (61.44%)	81 (60.91%)	131 (61.79%)	ns
Dactylitis	50 (14.49%)	13 (9.77%)	37 (17.45%)	0.01
Psoriasis, N (%)	247 (71.59%)	91 (68.42%)	156 (73.58%)	0.04
Onicopathy, N (%)	138 (40%)	47 (35.34%)	91 (42.93%)	0.05
IBD, N (%)	4 (1.15%)	0 (0%)	4 (1.89%)	ns
Uveitis, N (%)	14 (4.06%)	9 (6.77%)	5 (2.36%)	ns
Erosions, N (%)	174 (50.43%)	59 (44.36%)	115 (54.25%)	0.04
Weight (kg), mean (SD)	75.32 (12.73)	75.64 (13.09)	74.23 (11.84)	ns
Height (m), mean (SD)	1.71 (0.08)	1.74 (0.05)	1.69 (0.19)	ns
BMI, mean (SD)	25.86 (3.73)	25.84 (3.58)	25.93 (4.37)	ns
TI [0-68], mean (SD)	6.94 (5.07)	6.65 (3.63)	7.56 (5.74)	ns
SI [0-66], mean (SD)	3.77 (2.67)	2.28 (2.87)	4.21 (2.16)	0.04
LEI [0-6] mean (SD)	1.92 (1.5)	1.81 (1.56)	2.14 (1.48)	ns
Dactylitis [0-20] number digit, mean (SD)	0.68 (0.87)	0.66 (0.95)	0.85 (0.77)	ns
PASI [0-72] mean (SD)	3.21 (5.59)	1.05 (2.25)	4.5 (6.64)	0.01
ESR [0-25] (mm/h), mean (SD)	18.57 (12.56)	16.45 (11.61)	19.73 (12.19)	ns
CRP [0-6] (mg/L), mean (SD)	8.81 (8.29)	8.69 (8.72)	9.57 (8.17)	0.05
DAPSA [0-164], mean (SD)	29.52 (12.56)	28.59 (13.34)	31.25 (11.10)	0.05
ASDAS [0-6], mean (SD)	3.45 (0.69)	3.35 (0.78)	3.51 (0.65)	0.04
HAQ-S [0-8], mean (SD)	1.08 (0.55)	0.96 (0.55)	1.14 (0.59)	0.05
VAS-pain [0-10], mean (SD)	6.96 (1.37)	6.92 (1.44)	7.13 (1.35)	ns
VAS-gh [0-10], mean (SD)	6.47 (1.84)	6.15 (1.93)	6.68 (1.79)	ns
BASDAI [0-10], mean (SD)	7.02 (1.54)	6.62 (1.44)	7.23 (1.51)	ns
BASFI [0-10], mean (SD)	6.43 (1.94)	5.77 (2.08)	6.82 (1.78)	ns
Mean treatment duration (months), mean (SD)	17.24 (11.25)	16.13 (10.17)	18.53 (9.97)	ns
1 st line (N,%)	134 (38.84%)	134 (100%)	0 (0%)	NA
2 nd line (N,%)	66 (19.13%)	0 (0%)	66 (31.13%)	NA
3 rd line (N,%)	67 (19.42%)	0 (0%)	67 (31.60%)	NA
4 th line (N,%)	45 (13.04%)	0 (0%)	45 (21.23%)	NA
5 th line (N,%)	15 (4.34%)	0 (0%)	15 (7.08%)	NA
6 th line (N,%) or more	19 (5.50%)	0 (0%)	19 (8.96%)	NA
Concomitant NSAIDs, N (%)	211 (61.16%)	95 (71.43%)	116 (54.72%)	0.04
Concomitant steroid, N (%)	95 (27.54%)	28 (21.05%)	67 (31.60%)	0.05
Concomitant csDMARDs, N (%)	159 (46.08%)	67 (50.37%)	92 (43.39%)	ns
Methotrexate	118 (34.20%)	51 (38.35%)	67 (31.60%)	ns
Sulfasalazine	41 (11.88%)	18 (13.53%)	23 (10.85%)	ns
Leflunomide	17 (4.93%)	6 (4.51%)	11 (5.19%)	ns
Hydroxychloroquine	3 (0.86%)	2 (1.50%)	1 (0.47%)	ns
Cyclosporine	6 (1.73%)	1 (0.75%)	5 (2.36%)	ns

Legend: Data are expressed as mean (standard deviation=SD) unless otherwise specified; range of possible values are indicated in square brackets. p: Anova (Kruskal Wallis) a t0; p<0.05; GROUP A= naïve to anti-TNFalpha inhibitors; GROUP B= TNFalpha failure inhibitors; PsA, psoriatic arthritis; IBD, inflammatory bowel disease; PASI, Psoriasis Area Severity Index; TI, Tender joint; SI, Swollen joint; LEI, Leeds Enthesitis Index; DAPSA, Disease Activity Index for Psoriatic Arthritis; BMI, body mass index; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; ASDAS, Ankylosing Spondylitis disease activity score; HAQ-S, Health Assessment Questionnaire modified for spondyloarthritis; NSAIDs, non-steroidal anti-inflammatory drugs; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs. ns=not statistically significant. NA=not applicable

FRI0285

FILGOTINIB TREATMENT RESULTS IN REDUCTION OF BIOMARKERS ASSOCIATED WITH DISEASE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

W. P. Maksymowych¹, Y. Tian², O. K. Yoon², W. Barchuk², R. Galien³, R. Besuyen⁴, Y. Liu², A. M. Mirza², V. Malkov², A. Hertz². ¹University of Alberta, Edmonton, Canada; ²Gilead Sciences Inc., Foster City, United States of America; ³Galapagos SASU, Romainville, France; ⁴Galapagos BV, Leiden, Netherlands

Background: Ankylosing spondylitis (AS) is a chronic, immune-mediated disease characterized by inflammation of the sacroiliac joints and spine, and a young age of onset of 20–40 years. In the recent TORTUGA study, filgotinib (FIL), an oral, selective Janus kinase 1 (JAK1) inhibitor, significantly reduced AS disease activity compared with placebo (PBO).¹ Selective JAK1 inhibition by FIL has the potential to simultaneously block multiple inflammatory pathways, thus we analyzed biomarker concentrations in serum samples from TORTUGA.

Objectives: To evaluate the impact of selective JAK1 inhibition with FIL on circulating disease associated biomarkers in adult patients with active AS enrolled in the TORTUGA study.

Methods: TORTUGA (Clinicaltrials.gov identifier NCT03117270) was a 12-week, randomized, double-blind, placebo-controlled, phase 2 study. Patients were randomized 1:1 to FIL 200mg (n=58) or PBO (n=58) once-daily. Serum samples (FIL n=56, PBO n=53) were collected at baseline (BL) and weeks 1, 4 and 12, and analyzed using the Meso Scale Discovery immunoassay platform (Meso Scale Diagnostics, Rockville, MD, USA) to evaluate 135 biomarkers. Biomarker concentration changes from BL were analyzed on paired patient data and reported for weeks 1, 4 and 12, and clustering analysis was performed. Correlation between the 135 biomarkers and selected clinical scores at BL was assessed by Spearman rank correlation analysis.

Results: FIL treatment produced significant reductions in serum concentrations of multiple biomarkers associated with AS disease activity. Five clusters of biomarker response were identified based on the kinetics and magnitude of percent changes from BL. These clusters also represented discrete biological functions:

cluster 1 (rapid, strong >50% decrease in all three time points) included systemic inflammation biomarkers eg. CRP, SAA; cluster 2 (>20% decrease in at least one time point) included immune cell biomarkers eg. MIP3B, IL12p40; cluster 3 (<20% decrease in all three time points) included cellular adhesion biomarkers eg. ICAM-1, VCAM-1; cluster 4 (delayed decrease) included matrix remodelling biomarkers eg. MMP1, TIMP1; and cluster 5 included biomarkers that exhibited a gradual increase in serum concentration with FIL treatment.

Spearman rank correlation analyses showed that at BL, the systemic inflammation biomarkers CRP and SAA, as well as a number of biomarkers including ICAM-1 and MMP3, were positively correlated with BL AS disease activity score (ASDAS); conversely, only a few biomarkers showed a negative correlation with BL ASDAS, the cytokine receptor FLT3 and the chemotactic cytokine fractalkine (FRCTAL).

Conclusion: In patients with active AS, FIL treatment significantly decreased levels of circulating biomarkers associated with active AS disease, including proinflammatory cytokines and chemokines, cell adhesion molecules, and markers of matrix remodelling. Clustering analysis revealed early and late biomarker changes associated with disease. These data are consistent with reduced AS disease activity in TORTUGA and suggest that FIL treatment leads to a rapid and sustained reduction of inflammation in AS.

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[1] van der Heijde D *et al.* *Lancet* 2018;392:2378–87

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FRI0286

IXEKIZUMAB TREATMENT IMPROVES FATIGUE, SPINAL PAIN, STIFFNESS, AND SLEEP IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

P. J. Mease¹, A. Deodhar², P. Rahman³, H. Marzo-Ortega⁴, V. Strand⁵, T. Hunter⁶, D. Adams⁶, D. Sandoval⁶, A. Kronbergs⁶, B. Zhu⁶, A. Leung⁷, S. Liu Leage⁶, V. Navarro-Compán⁸. ¹Swedish Medical Center/Providence St. Joseph Health, Seattle, United States of America; ²Oregon Health & Science University, Division of Arthritis and Rheumatic Diseases, Portland, United States of America; ³Memorial University of Newfoundland, Department of Medicine, Saint John's, Canada; ⁴University of Leeds, NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals Trust, and Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom; ⁵Stanford University, Division of Immunology/Rheumatology, Palo Alto, United States of America; ⁶Eli Lilly and Company, Indianapolis, United States of America; ⁷Syneos Health, Morrisville, United States of America; ⁸Hospital Universitario La Paz IdiPaz, Madrid, Spain

Background: Common symptoms of axial spondyloarthritis (axSpA) include fatigue, spinal pain, stiffness, and sleep problems, which can impair health-related quality of life. Ixekizumab (IXE) treatment shows efficacy in active non-radiographic axSpA (nr-axSpA).¹

Objectives: To assess fatigue, spinal pain, stiffness, and sleep with IXE treatment versus (vs) placebo (PBO) in patients (pts) with active nr-axSpA up to 16 and 52 weeks (wks).

Methods: In COAST-X, pts with active nr-axSpA were randomized to 52 wks of double-blind IXE 80 mg once every 4 wks (Q4W) or 2 wks (Q2W), or PBO. Data were collected from baseline to Wk 52.

Results: At Wk 16, IXE Q4W significantly improved fatigue, spinal pain, and stiffness, and IXE Q2W improved spinal pain, spinal pain at night, and stiffness vs PBO (Table). At Wk 52, IXE Q4W significantly improved stiffness, and IXE Q2W improved spinal pain, spinal pain at night, and stiffness vs PBO. Numeric improvements in sleep were not significant vs PBO. Wk 1, and up to Wk 16, IXE

Q4W and Q2W significantly reduced spinal pain and stiffness vs PBO; stiffness was significantly reduced vs PBO up to Wk 52 (Figure).

Least squares mean (standard error) change from BL-ITT population (mixed-effect model of repeated measures)

Measure	Timepoint	PBO N=105	IXE Q4W N=96	IXE Q2W N=102
Spinal pain ^a	Wk 16	-1.45 (0.244)	-2.35 (0.248)*	-2.59 (0.244)†
	Wk 52	-2.29 (0.350)	-2.92 (0.305)	-3.32 (0.304)*
Spinal pain at night ^a	Wk 16	-1.71 (0.262)	-2.43 (0.267)	-2.79 (0.263)*
	Wk 52	-2.25 (0.358)	-3.04 (0.312)	-3.58 (0.311)*
BASDAI-stiffness ^{b,c}	Wk 16	-1.44 (0.242)	-2.44 (0.246)*	-2.89 (0.242)†
	Wk 52	-1.94 (0.332)	-3.15 (0.290)*	-3.48 (0.289)†
Fatigue severity NRS ^d	Wk 16	-1.4 (0.24)	-2.1 (0.24)*	-1.9 (0.24)
	Wk 52	-2.1 (0.38)	-2.6 (0.32)	-2.7 (0.32)
Sleep disturbance ^e	Wk 16	-2.3 (0.45)	-2.0 (0.45)	-2.5 (0.45)
	Wk 52	-2.9 (0.63)	-3.6 (0.52)	-3.6 (0.53)
Pt Global Assessment of Disease Activity ^f	Wk 16	-1.30 (0.246)	-2.32 (0.251)*	-2.64 (0.247)†
	Wk 52	-1.81 (0.378)	-2.77 (0.320)	-3.30 (0.321)*

*P<.05 vs PBO; †P≤.001 vs PBO. ITT population: all randomized pts. Pts needing rescue treatment after Wk 16 per investigator could switch to open-label IXE Q2W; observations at visits thereafter not included in analyses. BL values similar across treatments. Numerical improvements in BASDAI-fatigue not significant vs PBO.

^aScored 0 (no pain) to 10 (most severe pain) on NRS

^bMean score BASDAI questions 5 (intensity) and 6 (duration)

^cScored 1–10 on NRS

^dScored 0 (no fatigue) to 10 (as bad as you can imagine)

^eJenkins Sleep Evaluation Questionnaire scored 0 to 20: each of 4 items scored 0 (0 days) to 5 (22–30 days)

^fScored 0 (not active) to 10 (very active) on NRS

BASDAI=Bath Ankylosing Spondylitis Disease Activity Index BL=baseline ITT=intent-to-treat IXE=ixekizumab N=number of pts in ITT population NRS= numeric rating scale PBO=placebo pt=patient Q2W=every 2 wks Q4W=every 4 wks vs=versus wk=week

*P<.05 vs PBO; †P≤.001 vs PBO. Significant differences between placebo and IXE Q4W and IXE Q2W are shown by orange and blue symbols, respectively. Changes from BL (least squares mean) up to Wk 52 were analyzed using MMRM analysis in the ITT population, which includes all randomized pts. BASDAI=Bath Ankylosing Spondylitis Disease Activity Index BL=baseline ITT=intent-to-treat IXE=ixekizumab MMRM=mixed-effects model of repeated measures PBO=placebo pt=patient Q2W=every 2 weeks Q4W=every 4 weeks vs=versus wk=week

Conclusion: IXE Q4W and/or Q2W significantly improved spinal pain, spinal pain at night, and stiffness vs PBO at 16 and 52 wks in pts with nr-axSpA. IXE Q4W also improved fatigue at 16 wks in these pts. Numerical improvements in sleep were not significant vs PBO.

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