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OP0237

INTERLEUKIN-17 OR TNF BLOCKADE IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS AFTER WITHDRAWAL OF AT LEAST ONE TNF INHIBITOR

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Background: Secukinumab (SEC), an interleukin-17A inhibitor, is approved for the treatment of ankylosing spondylitis (AS) and has been integrated into the current treatment recommendations of patients with axial spondyloarthritis (axSpA) as an alternative to tumor necrosis factor inhibitors (TNFi). The optimal use of one mode of action over the other remains unclear and longitudinal real-life data are lacking to date.

Objectives: To compare drug survival of SEC versus TNFi in axSpA patients having previously stopped at least one TNFi in a large prospective cohort.

Methods: Patients with a clinical diagnosis of axSpA in the Swiss Clinical Quality Management cohort were included if they had previously stopped treatment with at least one TNFi, initiated therapy with either SEC or a next TNFi after approval of SEC and had a baseline clinical visit. Drug survival was evaluated by Cox proportional hazards models adjusted for sex, age, Bath ankylosing spondylitis disease activity index (BASDAI), Maastricht ankylosing spondylitis enthesitis score (MASES), proportion of patients with elevated CRP, number of previous TNFi and interaction between mode of action and number of previous TNFi.

Results: Baseline characteristics of 382 axSpA patients included (N=107 for SEC and N=275 for next TNFi) are shown in Table 1. The proportion of patients with ≥ 2 TNFi administered previously was significantly higher in the SEC group. Patients starting SEC had higher baseline disease activity, more enthesitis and greater impairment of spinal mobility, function and quality of life. A history of uveitis was more prevalent in the TNFi group. No differences between the groups could be detected with regards to the reason for discontinuation of the previous TNFi. Unadjusted median (interquartile range) drug maintenance was 1.1 (0.9; 1.3) years for SEC and 2.0 (1.7; 2.2) years for TNFi ($p=0.03$). The adjusted hazard ratio to stop SEC vs. TNFi in patients without missing data (N=233, 61%) was 1.05 (95% CI 0.42; 2.61; $p=0.91$) (Table 2).

Table 1. Baseline characteristics of axSpA patients having stopped ≥ 1 TNFi at start of a next biologic after approval of SEC in Switzerland, stratified by the mode of action.

Parameter	N 382	TNFi N=275	SEC N=107	p
Male sex,%	374	43.3	43.0	1.00
Age, years	382	45.3 (12.6)	45.7 (11.5)	0.81
Symptom duration, years	369	14.0 (10.8)	14.8 (11.3)	0.47
HLA-B27 positive,%	338	58.9	60.0	0.90
BASDAI	276	4.8 (2.1)	6.1 (1.9)	<0.001
ASDAS	239	2.7 (0.9)	3.5 (1.0)	<0.001

Elevated CRP,%	336	31.5	41.0	0.13
BASFI	266	3.0 (2.4)	4.9 (2.6)	<0.001
BASMI	205	1.8 (1.6)	2.6 (1.9)	0.01
Number of swollen joints	348	1.0 (3.0)	1.4 (3.7)	0.32
MASES	352	2.8 (3.3)	3.9 (3.9)	0.02
Uveitis ever,%	369	16.9	8.7	0.05
Psoriasis ever,%	366	9.8	13.0	0.45
Inflammatory bowel disease ever,%	371	10.6	4.7	0.10
≥ 2 previous TNFi used,%	382	37.8	77.6	<0.001
Ineffectiveness of previous TNFi,%	334	60.7	67.3	0.24

Table 2. Multivariable adjusted cox regression model for drug survival of next biologic DMARD.

	HR	95% CI	p
Secukinumab vs. TNFi	1.05	0.42; 2.61	0.91
Age	1.01	0.99; 1.03	0.42
Female sex	1.60	0.98; 2.61	0.06
BASDAI	1.15	1.02; 1.31	0.03
Elevated CRP	1.15	0.71; 1.86	0.56
Number of previous TNFi	0.83	0.61; 1.13	0.23
Interaction between bDMARD mode of action and number of previous TNFi	1.20	0.83; 1.73	0.34

Conclusion: SEC was predominantly initiated in axSpA after use of at least 2 TNFi. Patients starting SEC had a higher mean disease activity than patients starting a next TNFi. Adjusted drug survival after previous withdrawal of TNFi was comparable for SEC or a next TNFi.

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OP0238

WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT AMONG PATIENTS WITH ACTIVE ANKYLOSING SPONDYLOARTHRITIS AND TREATED WITH IXEKIZUMAB FOR 16 WEEKS: RESULTS FROM COAST-V AND COAST-W

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Background: Axial spondyloarthritis (axSpA) negatively impacts work productivity and IL-17A antagonists, such as ixekizumab (IXE), may improve paid and unpaid work productivity.^{1,2} Also, it is unknown if improvements with IXE differ between biologic-naïve and TNF inhibitor (TNFi) experienced patients.

Objectives: We investigated the effect of IXE treatment for 16-weeks on work productivity and activity impairment among patients with radiographic axSpA (r-axSpA) using data from the biologic-naïve and TNFi-experienced patients receiving either placebo (PBO), IXE, or adalimumab (ADA; if biologic-naïve).

Methods: Both COAST-V and COAST-W investigated the efficacy and safety of IXE among patients with r-axSpA that either were biologic-naïve patients (COAST-V, NCT02696785) or TNFi-experienced patients (COAST-W, NCT02696798), as defined by prior inadequate response or intolerance to 1 or 2 TNFi. Patients were required to have a diagnosis of axSpA. Patients fulfilled ASAS criteria for r-axSpA and mNY criteria for ankylosing spondylitis. Active disease was defined by BASDAI ≥ 4 and back pain ≥ 4 on a numeric ratings scale (NRS).^{1,2} Full eligibility criteria were previously reported.^{1,2} Patients were treated with placebo (PBO), 40-mg adalimumab (ADA) every 2 weeks (Q2W; COAST-V only), 80-mg IXE Q2W (IXEQ2W) or every 4 weeks (IXEQ4W) for 16 weeks. Work productivity was investigated using the Work Productivity and Activity Impairment Questionnaire for Ankylosing Spondylitis (WPAI:SpA). Individual and integrated

study data were analyzed using analysis of covariance models. Results reported as least squares mean (LSM) change from baseline±standard error (SE). Integrated data of COAST-V and -W were analyzed for inferential statistics due to small sample sizes in the individual studies. ADA was included in COAST-V as an active reference arm only, and the study was not powered to allow comparisons between the IXE and ADA arms.

Results: Overall, 365 (64.5%) PBO- and IXE-treated patients reported paid work (part-time or full-time) at baseline in COAST-V and COAST-W. Based on integrated data, Absenteeism was significantly lower in IXEQ2W treated patients than PBO and Presenteeism, Work Productivity Loss, and Activity Impairment were significantly reduced in IXEQ2W and IXEQ4W treated patients versus PBO (Table 1). WPAI-SpA outcomes for biologic-naïve and TNFi-experienced were similar with some exceptions (Table 2). The active reference arm (ADA) exhibited numerical improvements for presenteeism, work productivity, and activity impairment versus PBO.

Table 1. Integrated WPAI-SpA results for patients with r-axSpA

	PBO	IXEQ2W	IXEQ4W
Absenteeism	-1.7±1.7 n=107	-7.3±1.8* n=95	-1.5±1.7 n=104
Presenteeism	-14.0±2.3 n=104	-24.0±2.4*** n=99	-22.0±2.3* n=99
Work Productivity Loss	-14.7±2.4 n=104	-24.9±2.5*** n=99	-22.0±2.4* n=99
Activity Impairment	-13.3±1.7 n=105	-22.4±1.7*** n=179	-20.8±1.7*** n=192

IXEQ2W = ixekizumab every 2 weeks; IXEQ4W = ixekizumab every 4 weeks; n = number of patients in the analysis category; PBO = placebo

Table 2. WPAI-SpA results for biologic-naïve and TNFi-experienced patients with r-axSpA

	PBO	IXEQ2W	IXEQ4W	ADA
Biologic Naïve (COAST-V)				
Absenteeism	-1.3±2.3 n=50	-6.7±2.3 n=49	1.2±2.2 n=57	-1.2±2.0 n=65
Presenteeism	-17.7±3.1 n=50	-23.3±3.1 n=47	-22.7±2.9 n=55	-20.9±2.8 n=60
Work Productivity Loss	-17.8±3.3 n=50	-24.1±3.3 n=47	-21.4±3.1 n=55	-21.4±2.9 n=60
Activity Impairment	-14.1±2.3 n=86	-23.4±2.3 n=83	-23.0±2.4 n=80	-21.1±2.2 n=88
TNFi Experienced (COAST-W)				
Absenteeism	-1.2±2.8 n=57	-6.9±3.1 n=46	-4.7±2.9 n=47	
Presenteeism	-8.9±3.6 n=54	-22.2±4.1 n=43	-19.5±3.9 n=44	
Work Productivity Loss	-9.8±3.7 n=54	-23.5±4.2 n=43	-21.0±4.0 n=44	
Activity Impairment	-10.1±2.6 n=99	-18.4±2.7 n=96	-16.5±2.4 n=112	

IXEQ2W = ixekizumab every 2 weeks; IXEQ4W = ixekizumab every 4 weeks; n = number of patients in the analysis category; PBO = placebo

Conclusion: In this integrated analysis of patients with active r-axSpA, IXE treatment for 16 weeks yielded significant improvements in work productivity and activity impairment versus PBO. The effect is similar in biologic-naïve and TNFi-experienced patients. A limitation for evaluations of work productivity in the individual studies was the relatively low number of employed patients.

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SSc and Myositis – novel therapeutic options_____

OP0239

PROGRESSIVE LUNG FIBROSIS IN PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE IN THE EUSTAR DATABASE

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Background: Some patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD) develop progressive ILD, but the prevalence is unknown and no validated algorithms for early detection exist.

Objectives: To assess the frequency of, and parameters associated with, progressive SSc-ILD in the EUSTAR database.

Methods: Patients from the EUSTAR database registered after 2010, ≥18 yrs old, fulfilling SSc classification criteria, with serial lung function, HRCT assessments and disease duration recordings were eligible. Progressive ILD, assessed as absolute changes in %predicted, was defined as: significantly progressive (FVC decline >10% or FVC decline 5–10% and DL_{CO} decline ≥15%); moderately progressive (FVC decline 5–10%); or stable (<5% FVC change in either direction). Lung fibrosis changes from baseline to 12±3 months, disease course and cumulative frequency of progressive ILD during the 5-yr follow-up were assessed. Candidate predictors of significant progressive ILD were selected by expert opinion, and logistic regression applied. Time to event was evaluated by Kaplan-Meier estimates.

Figure: Time to first SSc-ILD progression events of A. Moderately progressive ILD and B. Significantly progressive ILD in the EUSTAR database over a 5-year follow-up period

Results: 826 SSc-ILD patients were included; 219/826 (26.5%) showed moderate/significant ILD progression at 12±3 months' follow-up. Baseline FVC, erythrocyte sedimentation rate, modified Rodnan skin score (mRSS), GERD and disease duration were significantly associated with significant progressive fibrosis in uni- and multivariable modelling (area under curve 0.67). Serial lung function data with median follow-up of 5 yrs were available in 411/826 (49.8%) patients. In 128/411 with initial progressive ILD at 12±3 months, 59/128 (46.1%) showed further progression, while 69/128 (53.9%) were stable. Baseline FVC, mRSS and disease duration were significantly associated with further ILD progression. The incident cumulative frequency of moderate and significant ILD progression was 22.9% (n=189/826) and 28.5% (n=235/826) during the median 5-yr follow-up and time to first progressive event (Figure).

Conclusion: This study provides novel insights into the frequency, severity and association of progressive fibrosis in patients with SSc-ILD in the EUSTAR database.

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