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SAT0270 LOW INCIDENCE OF BOTH NEW-ONSET AND FLARES OF UVEITIS IN SECUKINUMAB-TREATED PATIENTS WITH ANKYLOSING SPONDYLITIS: CLINICAL TRIAL AND POST-MARKETING SAFETY ANALYSIS

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Background: Uveitis, a common extra-articular manifestation of SpA, has an estimated prevalence in patients (pts) with ankylosing spondylitis (AS) of 33.2%, which increases with disease duration and positive HLA-B27 status.¹ Uveitis occurs in 10%–50% of SpA pts.¹ The exposure-adjusted incidence rate [EAIR] of uveitis (combined new-onset and flares) reported in AS pts treated with TNF inhibitors is 2.6–3.5 per 100 patient-years (pt-yrs).^{2–5}

Objectives: To assess the incidence of uveitis in secukinumab-treated AS pts in long-term pooled clinical data from three phase 3 trials (MEASURE 1–3 [NCT01358175, NCT01649375, NCT02008916]) and from post-marketing analyses.

Methods: Analysis included pooled pt-level data from all pts in MEASURE 1 who received any dose (≥1) of secukinumab up to the last pt attending Week 156 study visit, and up to visit Week 156 in MEASURE 2 and visit Week 104 in MEASURE 3 for each patient, respectively. Post-marketing data were from the most recent periodic safety surveillance report. Incidence of uveitis is reported as EAIR per 100 pt-yrs of secukinumab exposure.

Results: In the phase 3 AS clinical trials, 135 (17%) pts reported pre-existing (but not active or ongoing) uveitis at baseline and 589 (74.2%) pts were HLA-B27 positive. The EAIR for uveitis was 1.4 per 100 pt-yrs over the entire treatment period (n=794). Among all cases of uveitis (n=26), 14 (54%) were flares in pts with a history of uveitis at baseline (Table). The EAIR of uveitis in the post-marketing data (based on cumulative secukinumab exposure of 96 054 pt-yrs) was 0.03 per 100 pt-yrs.

Abstract SAT0270 – Table 1. Safety Analysis for Uveitis with Secukinumab in AS

Data from Clinical Studies	
Number of clinical studies/pts included	3/794
Uveitis cases reported, n (%)	
Total	26 (3.3%)
New onset cases	14 (1.8%)
Treatment discontinuation	2 (0.3%)
Treatment interruption	1 (0.1%)
EAIR (95% confidence interval) per 100 pt-yrs ^a	1.4 (0.9–2.0)
Post-Marketing Data ^b	
Cumulative estimated market experience (pt-treatment yrs) ^c	96 054
Cumulative number of cases reported	29
Crude incidence rate per 100 pt-yrs	0.03

^aRates are for uveitis MedDRA preferred term

^bData from the periodic safety update report (PSUR) dated 10th August 2017 – includes all indications

^cEstimated based on cumulative worldwide sales volume and the average maintenance dose

Conclusions:

In secukinumab-treated pts with active AS, a low incidence of uveitis was observed, including new-onset cases and flares, in both clinical trials and post-marketing analyses.

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SAT0271 SECUKINUMAB, A FULLY HUMAN ANTI-INTERLEUKIN-17A MONOCLONAL ANTIBODY, EXHIBITS LOW IMMUNOGENICITY IN PATIENTS WITH PSORIATIC ARTHRITIS AND ANKYLOSING SPONDYLITIS DURING A 52-WEEK TREATMENT PERIOD

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Background: Secukinumab (SEC), a fully human monoclonal antibody (mAb) that selectively targets IL-17A, is highly efficacious for the treatment of psoriatic arthritis (PsA) and ankylosing spondylitis (AS). mAb therapies may be associated with immunogenicity (IG) and production of anti-drug antibodies (ADAs) that may cause adverse events (AEs), and affect drug pharmacokinetics (PK) and clinical response.

Abstract SAT0271 – Table 1. Overview of pts with TE-ADA¹

PsA studies	Study	SEC dose	Prior biologics	ADA (titer)/ Neut-Ab	AE IG related	Impact on efficacy ²	PK behaviour ³
	F2306	PBO-75 mg	0	W24 (no titer)/Y	N	None	Normal
	F2312	PBO-150 mg	0	W52 (2.99)/N	N	None	Normal
	F2318	150 mg	Infliximab	W52 (2.14)/N	N	None	Normal
		150 mg	0	W24 (1.00)/N	N	None	Normal
		150 mg	0	W52 (2.59)/N	N	None	Normal
AS studies	F2305	10 mg/kg–150 mg	0	W52 (2.39)/N	N	None	Normal
		PBO-150 mg	0	W52 (10.61)/N	N	None	Normal
	F2310	PBO-75 mg	0	W52 (39.39)/N	N	None	Normal
	F2314	PBO-300 mg	0	W52 (1.02)/N	N	None	Normal
	F2320	150 mg	0	W16 (6.35)/N	N	None	Normal
				W52/ (2.96)/N			
		150 mg	0	W16 (2.70)/N	N	None	Normal
		No Load	0	W24/ (2.80)/N	N	None	Normal
		150 mg	0	W52/ (2.89)/N	N	None	Normal
		PBO–150 mg	0		N	None	Normal

Neut-Ab=neutralising antibodies; PBO, placebo; Y, yes; N, No. ¹Only positive ADA results at the respective study week are shown; ²Impact on efficacy is defined as: PsA, failure to achieve >20% reduction, compared to baseline, in both tender and swollen joint counts; AS, failure to achieve ASAS20, after previously achieving such improvement for at least 2 consecutive visits prior to the first detection of ADA; ³Normal PK: Concentrations in ADA-positive pts within observed range for all pts without ADA

Objectives: To assess the IG of SEC in PsA and AS patients (pts) treated with SEC for up to 52 weeks (W).

Methods: IG in pts with PsA (FUTURE 1–3 studies, n=1414) and AS (MEASURE 1–4 studies, n=1163) exposed to SEC was evaluated at baseline (BL) and at W 12, 16 (AS only), 24 and 52. Treatment emergent (TE)-ADA were defined as a positive ADA signal in ≥ 1 post-treatment sample in pts negative at BL. TE-ADA positive samples were analysed for drug-neutralising potential, SEC impact on PK, IG-related AEs and TE-ADA impact on efficacy through W52.

Results: Of 1414 treated PsA and 1163 treated AS pts with samples for IG evaluation, 5 (0.35%) and 8 (0.68%) developed TE-ADAs respectively, over 52 weeks (Table). All but 1 PsA pt were biologic naïve; 2/5 PsA and 1/8 AS pts received concomitant methotrexate, 2/8 AS pts received concomitant sulfasalazine. Associations between TE-ADAs and SEC dose, frequency or mode of administration were not observed. Other than 1 PsA pt, all TE-ADAs were non-neutralising and none were associated with any IG-related AE. All TE-ADAs were associated with normal PK and none were associated with loss of SEC efficacy over 52 weeks.

Conclusions: SEC treatment was associated with a low incidence of IG in PsA and AS pts, as shown by TE-ADA detection in only 0.35% PsA pts and 0.68% AS pts over 52 weeks in a database of >2500 pts, which is consistent with the low incidence of IG (0.4%) seen with SEC in pts with plaque psoriasis.¹

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SAT0272

DO TNF INHIBITORS IMPACT THE COMORBIDITIES AND EXTRA-ARTICULAR MANIFESTATIONS, AND THEREBY ALTER THE NATURAL HISTORY OF ANKYLOSING SPONDYLITIS?

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Background: Anti-tumour necrosis factor (anti-TNF) treatment has led to reduction in signs and symptoms, and improvements in physical function and quality of life in ankylosing spondylitis (AS) patients (pts). Whether anti-TNFs impact the incidence of AS-related comorbidities and extra-articular manifestations (EAMs) is not known.

Objectives: To evaluate the incidence and prevalence of AS-related comorbidities and EAMs in AS pts in the US.

Methods: This was a retrospective cohort study of 3 commercial insurance claims databases (Multi-Payer Claims Database [MPCD 2007–2010], Truven MarketScan [2010–2014], and US Medicare Fee-for-Service Claims [2006–2014]) to evaluate EAMs (uveitis, psoriasis, inflammatory bowel disease) and physician-diagnosed comorbidities (cardiac, renal, pulmonary, neurologic) in AS pts diagnosed by a rheumatologist (index date), having 6 months' baseline data prior to the index date, and drug-specific exposures after AS diagnosis (ICD-9 720.0). Three mutually exclusive hierarchical exposure groups were examined (low to high):¹ no therapy or prescription NSAIDs;² conventional DMARDs;³ anti-

TNFs. Prevalence of comorbidities was ascertained in a 12 month period (6 months pre- and post-index date). Incidence of comorbidities and EAMs was assessed during the period between treatment initiation and the earliest of death, loss of medical coverage, end of study, first outcome occurrence, treatment discontinuation or initiation of therapy at a higher level in exposure hierarchy. Pts with a history of prior events (except infections) were excluded from the incidence assessment for that event. Hazard ratios comparing anti-TNFs vs DMARDs and NSAIDs/no therapy were estimated using inverse probability treatment weighted Cox proportional hazards models.

Results: A total of 37,566 AS pts were included. Prevalence of AS in the MPCD population was 0.26% and in the Medicare population was 1.21%. As expected, comorbidities were more common in Medicare AS pts vs those in MPCD or MarketScan databases in all exposure groups. The propensity score-weighted incidences of solid cancers, myocardial infarction, conduction block, cord compression and vertebral fractures were lower in anti-TNF treated pts vs those treated with NSAIDs or DMARDs alone, although anti-TNF treated Medicare pts had a higher incidence of EAMs such as psoriatic arthritis, uveitis and ulcerative colitis (figure 1).

Abstract SAT0272 – Figure 1. Propensity score-weighted hazard ratios of physician-diagnosed outcomes and EAMs by treatment exposures

Conclusions: This investigation of the prevalence and incidence of comorbidities and EAMs of AS in US pts suggests that anti-TNF use is associated with a lower incidence of some comorbidities, and a trend of higher incidence of EAMs, which may reflect channelling of more severe AS pts to anti-TNFs. Although results vary somewhat by data source and may be explained by different baseline characteristics (e.g. Medicare pts were older), our results suggest that anti-TNF use is associated with lower incidence of those comorbidities that confer substantial morbidity in AS.

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