AB0802 SAFETY PROFILES OF IXEKIZUMAB VERSUS ADALIMUMAB: 52-WEEK RESULTS FROM A HEAD-TO-HEAD COMPARISON IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

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Background: Ixekizumab (IXE) was shown to be superior to adalimumab (ADA) in achievement of simultaneous improvement of joint and skin disease (ACR50 and PASI100) in patients with active psoriatic arthritis (PsA) and inadequate response to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs).[1]

Objectives: To compare the safety and tolerability profile of IXE vs ADA in patients with PsA up to 52 weeks of treatment.

Methods: SPIRIT-H2H (NCT03151551) was an open-label, head-to-head, blinded assessor clinical trial which included patients with active PsA (≥3 tender joint count + ≥3 swollen joint count) and plaque psoriasis (BSA ≥3%) who were inadequate responders to csDMARD therapy but naïve to biologic DMARDs. Patients were randomized (1:1) to approved dosing of IXE or ADA. Safety events were assessed at each patient visit up to Week 52. Frequencies of adverse events (AEs) were based on the number of patients in the safety population (patients who received ≥1 dose of study drug). Cases of inflammatory bowel disease (IBD) and cerebro-cardiovascular events were adjudicated by external committees. Kaplan-Meier analysis of time to onset of serious adverse events (SAEs) was performed.

Results: Of the 283 patients randomized to each treatment, 87% (246/283) of patients who received IXE and 84% (237/283) of patients who received ADA completed 52 weeks of treatment. The frequency of treatment-emergent AEs (TEAEs) was similar between the groups (74% IXE vs 69% ADA), however fewer severe TEAEs were reported in the IXE group (3.2% IXE vs 7.1% ADA) (Table). SAEs were significantly more frequent in the ADA group compared to the IXE group (12% vs 4.2%; p<0.001), and the time to develop a patient's first SAE was significantly shorter for ADA versus IXE (p<0.001; Figure). Discontinuations due to AEs were numerically more frequent in the ADA group versus the IXE group (7.4% vs 4.2%; p=0.15). IXE-treated patients reported more injection-site reactions (ISR) than ADA-treated patients (11% vs. 3.5%; p=0.002). Study withdrawals due to ISR were comparable, and only one injection-site reaction was severe on ADA (Table). There were two IBD cases reported for IXE; one case was confirmed as IBD.

Conclusion: Safety results were consistent with previous trials with IXE and ADA. Compared with IXE, patients with PsA treated with ADA had significantly more serious AEs.

References:

[1] Mease PJ, et al. *Ann Rheum Dis.* 2020;79(1):123-31.

Table. Safety results at 52 weeks

	IXE N=283 n (%)	ADA N=283 n (%)
TEAEs	209 (74)	194 (69)
Severe[a]	9 (3.2)	20 (7.1)
Related to study treatment[b]	98 (35)	87 (31)
Serious adverse events	12 (4.2)	35 (12)***
Deaths	0	0
Discontinuation due to AE	12 (4.2)	21 (7.4)
Serious infections	3 (1.1)	4 (1.4)
Injection-site reactions[c]	30 (11)	10 (3.5)**
Severe	0	1 (0.4)
Resulted in discontinuation	2 (0.7)	3 (1.1)
Anaphylaxis	0	0
Inflammatory bowel disease	2 (0.7)	0
Ulcerative colitis	1 (0.4)[d]	0
Crohn's disease	1 (0.4)	0
Cerebro-cardiovascular events	5 (1.8)	7 (2.5)
MACE	0	2 (0.7)
Malignancies	0	4 (1.4)
Depression	5 (1.8)	9 (3.2)
Interstitial lung disease	0	1 (0.4)
Cytopenias	9 (3.2)	12 (4.2)
Hepatic events	18 (6.4)	20 (7.1)

[a]Patients with multiple occurrences of the same event are counted under the highest severity. [b]The TEAE's relationship to study treatment was judged by the investigator. [c]MedDRA high-level term. [d]This event was adjudicated but it was not a confirmed IBD. ***p<0.001; **p<0.01 by Fisher's exact test. ADA=adalimumab, AE=adverse event; IBD=inflammatory bowel disease; IXE=ixekizumab; MACE=major adverse cardiovascular event; TEAE=treatment-emergent adverse event.

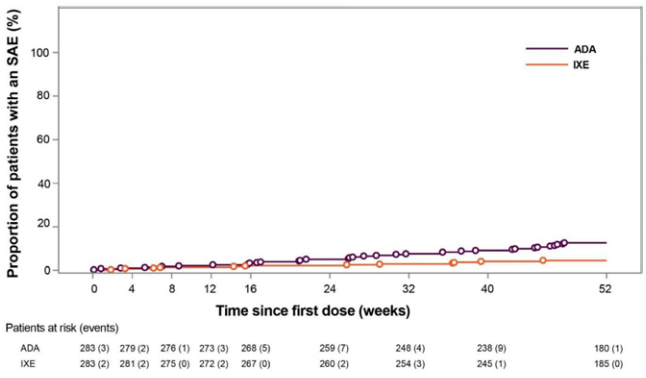

Figure: Time to onset of first SAE. Numbers below x-axis represent patients at risk at each time point. Open circles represent events. p<0.001 by log rank test. ADA=adalimumab; IXE=ixekizumab; SAE=serious adverse event.

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AB0803 EFFICACY OF TILDRAKIZUMAB IN PSA: DAS28-CRP SCORES THROUGH WEEK 52

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Background: Tildrakizumab (TIL), an anti–interleukin (IL)-23p19 monoclonal antibody, is approved in the US, EU, and Australia for treatment of moderate-to-severe plaque psoriasis.[1] A randomised, double-blind, placebo-controlled, multiple-dose, phase 2b study (NCT02980692) evaluating efficacy and safety of TIL for treatment of psoriatic arthritis (PsA) was recently completed.

Objectives: To evaluate the effect of TIL in PsA, using the DAS28-CRP responses up to week (W)52.

Methods: Patients (pts) ≥18 years old with PsA[2] and ≥3 tender and ≥3 swollen joints were randomised 1:1:1:1:1 to receive TIL (200 mg once every 4 weeks [Q4W], 200 mg every 12 weeks [Q12W], 100 mg Q12W, or 20 mg Q12W) or placebo (PBO Q4W) to W24. Thereafter, PBO Q4W and TIL 20 mg Q12W arms crossed over to TIL 200 mg Q12W to W52. DAS28-CRP was shown to be reliable in PsA studies,[3] and pts achieving scores <3.2 satisfied responder criteria.