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LB0005

MULTICENTRE, RANDOMISED, OPEN-LABEL, ASSESSOR-BLINDED, PARALLEL-GROUP HEAD-TO-HEAD COMPARISON OF THE EFFICACY AND SAFETY OF IXEKIZUMAB VERSUS ADALIMUMAB IN PATIENTS WITH PSORIATIC ARTHRITIS NAIVE TO BIOLOGIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS: 24-WEEK RESULTS

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Background: There have been few head-to-head clinical trials comparing different biologic disease-modifying anti-rheumatic drugs (bDMARDs) in patients (pts) with psoriatic arthritis (PsA).
Objectives: To report 24-week (wk) results of a study directly comparing efficacy and safety of ixekizumab (IXE), an IL-17A inhibitor, and adalimumab (ADA), a TNF inhibitor, in bDMARD-naïve pts with PsA.
Methods: The study (NCT03151551; SPIRIT-H2H) included pts with active PsA (≥ 3 TJC + ≥ 3 SJC) and plaque psoriasis (BSA $\geq 3\%$) who were bDMARD naïve and inadequate responders to csDMARD therapy. Patients were randomised (1:1) to IXE or ADA for 52 wks (on-label dosing based on presence/absence of moderate to severe psoriasis). The primary objective was superiority of IXE vs ADA measured by the proportion of pts achieving both ACR50 and PASI100 responses at wk 24. Key secondary objectives versus ADA at wk 24 were (1) non-inferiority of IXE for ACR50 (noninferiority margin -12%) and (2) superiority of IXE for PASI100. Additional PsA, skin, composite treat-to-target (T2T: MDA, DAPSA 4), PASDAS remission and patient-reported outcomes, and safety were assessed. Nine pts had PASI=0 and BSA $\geq 3\%$ (a medical inconsistency) at baseline; these pts were considered PASI100 responders if PASI=0 and BSA=0 at wk 24. Categorical variables were evaluated using logistic regression analyses with NRI in the ITT population. Continuous variables were analysed using mixed models for repeated measure analysis.
Results: 566 pts were randomised (283 to IXE and 283 to ADA). Baseline demographics and disease characteristics were generally well balanced between groups (Table 1). All primary and key secondary efficacy endpoints at wk 24 were met (Figure). The proportion of pts achieving both ACR50 and PASI100 was significantly greater for IXE than ADA (36% vs 28%; $p<0.05$). IXE was non-inferior to ADA for ACR50 response and superior for PASI100 response (Figure). While improvements from baseline were achieved with both treatments, significantly better results were seen with IXE vs ADA for skin and composite T2T outcomes, enthesitis resolution (Figure 1), and skin-related quality of life (Table 2). No unexpected safety signals were observed.

Table 1. Patient baseline demographics/characteristics

	IXE (N=283)	ADA (N=283)
Age, years	47.5 (12.0)	48.3 (12.3)
Male, n (%)	162 (57)	150 (53)
PsA duration since diagnosis, years	6.6 (7.4)	5.9 (6.4)
Concomitant csDMARD use, n (%)	193 (68)	199 (70)
TJC	19.1 (12.7)	21.3 (15.4)
SJC	10.1 (7.5)	10.7 (8.1)
PASI	7.9 (8.7)	7.7 (7.3)

Data are mean (SD), unless stated otherwise

Figure

Pts were stratified by conventional synthetic DMARD use and presence of moderate to severe psoriasis.
*There were 193 IXE- and 171 ADA-treated pts with SPARCC enthesitis index scores ≥ 2 at baseline; these patients were evaluated at wk 24. *There were 62 IXE- and 58 ADA-treated pts with LDI scores ≥ 2 at baseline; these patients were evaluated at wk 24. ADA, adalimumab 40 mg qd 0 then 40 mg every 2 wk from wk 1 for pts with moderate to severe psoriasis or 40 mg qd 0 then 40 mg every 2 wk for pts without moderate to severe psoriasis; IXE, ixekizumab 160 mg qd 0, then 80 mg every 2 wk to wk 12 and every 4 wk thereafter for pts with moderate to severe psoriasis or 160 mg qd 0, then 80 mg every 4 wk for pts without moderate to severe psoriasis; ACR, American College of Rheumatology criteria; PASI, Psoriasis Area Severity Index score; MDA, minimal disease activity - PsA; DAPSA, Disease Activity for Psoriatic Arthritis; PASDAS VLDL, Psoriatic Arthritis Disease Activity Score very low disease activity; SPARCC, Spondyloarthritis Research Consortium of Canada; LDI, Leeds Dactylitis Instrument; * $p<.05$, ** $p<.01$ IXE vs ADA

Table 2. Patient reported outcomes

	IXE (N=283)		ADA (N=283)	
	Baseline	LS mean change at wk 24	Baseline	LS mean change at wk 24
HAQ-DI	1.20	-0.63	1.27	-0.56
SF-36 PCS	36.80	9.96	36.12	8.82
SF-36 MCS	45.40	4.47	44.85	3.93
Dermatology Life Quality Index	9.77	-7.81*	9.82	-6.48
Fatigue Severity Numeric Rating Scale	5.87	-2.66	6.46	-2.53

LS, least square; * $p<.001$ vs ADA

Conclusion: In bDMARD naïve pts with active PsA and skin disease, IXE showed superior efficacy to ADA based on simultaneous achievement of ACR50 and PASI100 responses at wk 24. Greater improvements with IXE vs ADA were also attained in individual PsA domains and composite T2T outcomes.
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LB0006

SUBCUTANEOUS SECUKINUMAB 300MG AND 150MG PROVIDES SUSTAINED INHIBITION OF RADIOGRAPHIC PROGRESSION IN PSORIATIC ARTHRITIS OVER 2 YEARS: RESULTS FROM THE PHASE 3 FUTURE-5 TRIAL

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Background: Secukinumab (SEC) provided sustained clinical efficacy, and inhibition of radiographic progression over 52 Weeks (Wks) in patients (pts) with psoriatic arthritis (PsA) in the FUTURE 5 study¹.

Objectives: To report the effect of SEC on radiographic progression at Wk 104 (2 years) in PsA pts in the FUTURE 5 study.

Methods: Adults (N=996) with active PsA, stratified by prior anti-TNF therapy (naïve and inadequate response/intolerance [IR]) were randomised 2:2:2:3 to subcutaneous SEC 300mg with loading dose (LD; 300mg), 150mg LD (150mg), 150mg no LD, or placebo at baseline (BL), Wks 1, 2, 3, 4, and every 4 wks thereafter. Pts could have SEC dose escalated from 150 to 300 mg starting from Wk 52, based on physicians' judgement. Data are shown for pts originally randomised to SEC; 150mg groups include pts who had dose escalated to 300mg. Concomitant MTX (≤25 mg/week) was allowed. Radiographic progression (mean change in van der Heijde-modified total Sharp score [vdH-mTSS] and its components: erosion and joint space narrowing [JSN] scores, was based on hand/wrist/foot X-rays obtained at BL and Wk 104, and assessed by two blinded readers (plus an adjudicator if required). Other efficacy endpoints included ACR20/50, PASI90 and resolution of dactylitis and enthesitis.

Table. Summary of Efficacy Results

Mean change in vdH-mTSS scores from BL to Wk 104 (BL score)			
	300mg N=222 n=191	150mg group* N=220 n=181	150mg no LD group* N=222 n=169
vdH-mTSS	0.37 (12.07)	0.52 (11.47)	0.41 (13.99)
Erosion	0.27 (7.15)	0.27 (6.67)	0.38 (8.07)
JSN	0.11 (4.92)	0.24 (4.79)	0.03 (5.92)
Clinical responses at Wk 104 (% responders [n])			
	300 mg N = 222	150 mg group* N = 220	150 mg no LD group* N = 222
ACR20	77.0 (187)	79.4 (175)	78.0 (168)
ACR50	51.9 (187)	52.6 (175)	57.7 (168)
PASI90 ¹	70.1 (97)	59.2 (103)	62.6 (91)
Resolution of enthesitis ²	78.0 (118)	80.3 (117)	69.5 (95)
Resolution of dactylitis ³	82.8 (64)	85.5 (62)	89.3 (75)
Observed data			
* 150mg and 150mg no load arms include 86 and 92 pts, respectively, who were dose escalated at Wk 52 or later.			
N, number of pts randomised; n, number of pts with data at BL and Wk 104.			
Data from pts with: ¹ BL psoriasis ≥3% body surface area, ² enthesitis at BL, ³ dactylitis at BL			

Results: Overall, 84.7% (300mg), 82.3% (150mg) and 75.2% (150mg no LD) pts completed 2 years of treatment. A total of 86 (39%) and 92 (41%) pts had their dose escalated to 300mg in the 150mg and 150mg no LD groups, respectively. Inhibition of radiographic progression was sustained with SEC through 2 years (Table 1). Proportions of pts with no radiographic progression (change from BL in mTSS ≤0.5) with SEC were 89.5% (300 mg), 82.3% (150 mg), and 81.1% (150 mg no LD) at 2 years; corresponding proportion of pts for change from BL in mTSS ≤0.0 were: 81.2%, 69.1% and 73.4%, respectively. Clinical responses were also sustained through 2 years (Table 1).

Conclusion: Subcutaneous secukinumab provided sustained inhibition of radiographic progression and sustained clinical responses through 2 years of treatment in pts with active PsA.

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[1] Mease PJ *et al. Arthritis Rheumatol* 2018;70(suppl 10).

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LB0007

SUBCUTANEOUS TANEZUMAB FOR OSTEOARTHRITIS PAIN: A 24-WEEK PHASE 3 STUDY WITH A 24-WEEK FOLLOW UP

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Background: Tanezumab, a monoclonal antibody against nerve growth factor, is in development for treatment of osteoarthritis (OA) pain.

Objectives: To assess efficacy and safety of tanezumab in patients with moderate to severe OA pain who have not responded to or cannot tolerate standard of care analgesics.

Methods: A randomized, double-blind, placebo-controlled study (24 week treatment; 24 week follow-up) was conducted in patients in Europe and Japan with moderate to severe OA pain of the knee or hip and history of insufficient pain relief or intolerance to acetaminophen, oral nonsteroidal anti-inflammatory drug, and either tramadol or opioids (or unwilling to take opioids). Patients received subcutaneous tanezumab (2.5 or 5 mg) or placebo at baseline, week 8, and week 16. Co-primary endpoints were change from baseline in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain, WOMAC Physical Function, and Patient Global Assessment of OA (PGA-OA) scores at week 24. Safety, including independent adjudication of joint safety events, was assessed.

Results: Tanezumab 5 mg met all co-primary endpoints (Fig. 1). Tanezumab 2.5 mg met WOMAC Pain and Physical Function endpoints but not the PGA-OA endpoint; thus, this dose did not meet pre-specified efficacy criteria. The occurrence