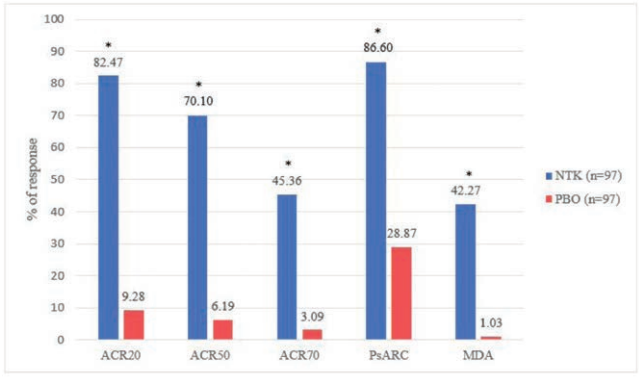

* p<0.0001 for comparison with placebo

Figure 1. Treatment response at Wk 24

Conclusion: NTK is a well-tolerated monoclonal antibody, that provided sustained improvements in signs and symptoms of active PsA through 24 Wks of therapy.

Table 2. Safety data

Arm	NTK (N=97)	PBO (N=97)	p-value
Treatment-related AEs	12 (12.37)	7 (7.22)	0.227[1]
Treatment-related SAEs	0 (0)	0 (0)	1.00[2]
Treatment-related AEs (grade 3-4)	1 (1.03)	2 (2.06)	1.00[2]
Local reactions	0 (0)	0 (0)	-
Grade 3-4 treatment-related AEs			
blood pressure increased	1 (1.03)	0(0)	1.00[2]
lymphopenia	0 (0)	2 (2.06)	0.497[2]

n (%) are presented, [1] Pearson's χ^2 test, [2] Fisher's exact test; N=number of patients, AE=adverse event, SAE=serious adverse event, ALT=Alanine transaminase

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OP0227

SECUKINUMAB VERSUS ADALIMUMAB HEAD-TO-HEAD COMPARISON IN BIOLOGIC-NAÏVE PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS THROUGH 52-WEEKS (EXCEED): A RANDOMISED, DOUBLE-BLIND, PHASE-3B STUDY

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Background: Secukinumab (SEC), an interleukin-17A inhibitor, has demonstrated improvements on multiple domains of psoriatic arthritis (PsA).[1] Adalimumab (ADA), a TNF inhibitor, is widely used as a first–line biologic in PsA.

Objectives: To report efficacy and safety outcomes from the head-to-head EXCEED trial (NCT02745080) that compares SEC *vs.* ADA as first–line biologic monotherapy through 52-weeks (wks), with a musculoskeletal primary endpoint in pts with active PsA.

Methods: Head-to-head, phase-3b, randomised, double-blind trial: biologic naïve active PsA pts were randomised to receive SEC 300mg subcutaneous at baseline, Wk1-4, and then every 4wks (q4w) until Wk48 or ADA 40mg subcutaneous at baseline and then q2w until Wk50. The primary endpoint was superiority of SEC *vs.* ADA on ACR20 response at Wk52. Binary and continuous variables were analysed using logistic-regression model and MMRM, respectively. Safety analysis included patients who received ≥1 dose of study-drug.

Results: 853 pts were randomised to receive SEC (n=426) or ADA (n=427). Baseline demographics and disease characteristics were comparable between treatment-groups except higher proportion of female pts and pts without enthesitis in the SEC group. ACR20 response at Wk52 for SEC *vs.* ADA were 67·4% *vs.* 61·5%, respectively (p=0·0719) (Figure). Higher clinical responses were observed with SEC *vs.* ADA for a range of musculoskeletal, skin, and higher-hurdle outcomes (Table). A higher retention rate was observed for SEC (85.7%) *vs.* ADA (76.3%). Safety profiles of SEC and ADA were consistent with previous reports.[2,3]

Conclusion: Results suggest that SEC is at least as efficacious as ADA on musculoskeletal endpoints whilst providing higher responses on skin endpoints, and is associated with a higher retention rate. No new safety signals were reported.

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[1] van der Heijde, et al. Rheumatol. (Oxford).2019; DOI10.1093/rheumatology/kez420.

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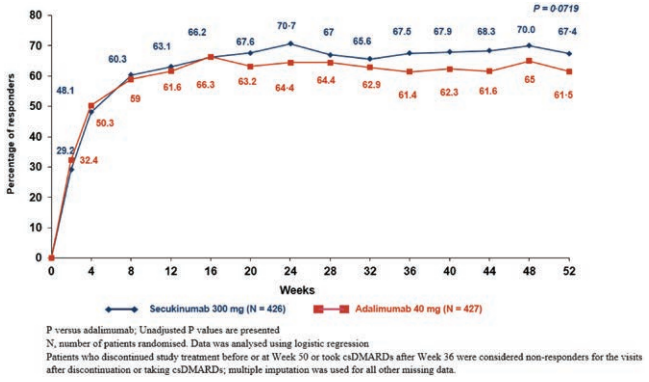

Figure. ACR20 Response through Wk 52

Table. Efficacy Outcomes at Wk 52

Endpoints, % response unless specified otherwise	SEC 300 mg (N=426)	ADA 40 mg (N=427)	P-value (unadjusted)*
ACR20	67·4	61·5	0·0719
[a]ACR20	66·9	59·5	0·0239
Key Secondary			
[b]PASI 90	65·4	43·2	<0·0001
ACR50	49·0	44·8	0·2251
HAQ-DI mean change from baseline ± SE	-0·58 ± 0.03	-0·56 ± 0.03	0·5465
[c]Resolution of enthesitis (based on LEI)	60·5	54·2	0·1498
Exploratory			
MDA	43·0	37·9	0·1498
VLDA	18·1	16·6	0·6107
DAPSA LDA+Remission	61·7	53·1	0·0178
PASDAS LDA+Remission	51·1	44·1	0·0557

*Unadjusted P-values *vs* ADA

Binary variables were analysed using logistic regression. Pts who discontinued study treatment prematurely or took csDMARDs after week-36 were considered non-responders. Multiple imputation was used for all other missing data. HAQ-DI mean change from baseline was analysed using mixed-effect model repeated measures

[a]Non-responder imputation was used for pre-specified sensitivity analysis

[b]N=215 in SEC and N=202 in ADA in psoriasis subset

[c]N=234 in SEC and N=264 in ADA in enthesitis subset

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OP0228

EFFICACY AND SAFETY OF IXEKIZUMAB VERSUS ADALIMUMAB (SPIRIT-H2H) WITH AND WITHOUT CONCOMITANT CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (DMARD) IN BIOLOGIC DMARD-NAÏVE PATIENTS WITH PSORIATIC ARTHRITIS: 52-WEEK RESULTS

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Background: Ixekizumab (IXE), a high-affinity monoclonal antibody selectively targeting IL-17A, was superior to adalimumab (ADA) at Week (Wk) 24 for simultaneous achievement of ACR50 and 100% improvement from baseline in the Psoriasis Area and Severity Index (PASI 100) (primary endpoint) in patients (pts) with active PsA from SPIRIT-H2H[1]. SPIRIT-H2H had two major secondary endpoints and achieved both: noninferiority of IXE to ADA for ACR50 at Wk 24, and superiority of IXE to ADA for PASI 100 at Wk 24.

Objectives: To determine how concomitant conventional synthetic DMARD (csDMARD) use affects safety and efficacy of IXE and ADA in prespecified subgroups defined by biologic monotherapy, concomitant MTX use, and concomitant csDMARD use through Wk 52 in SPIRIT-H2H.

Methods: SPIRIT-H2H (NCT03151551) was a 52-week, multicentre, randomised, open-label, assessor-blinded, parallel-group study evaluating the efficacy and safety of IXE versus ADA in adults with PsA and naïve to biologic DMARDs. Patients were required to have active PsA fulfilling Classification for Psoriatic Arthritis (CASPAR) criteria and ≥3/68 tender and ≥3/66 swollen joints, ≥3% plaque psoriasis BSA involvement, no prior treatment with bDMARDs, and with prior inadequate response to ≥1 csDMARD (but not necessarily current treatment with csDMARDs). Randomization (1:1) was stratified by concomitant use of csDMARD and the presence/absence of moderate to severe PsO (baseline: BSA≥10% + PASI≥12, + static Physician's Global Assessment≥3). Patients (N=566) received IXE/ADA through 52 wks according to the labelled dose dependent on presence/absence of moderate-to-severe PsO. In this prespecified subgroup analysis by presence or absence of csDMARDs, efficacy outcomes through wk 52 were compared between IXE and ADA using logistic regression models and Fisher's exact tests. Missing data were imputed using non-responder imputation.

Results: At baseline, 167 of 283 IXE-treated patients and 169 of 283 ADA-treated patients had concomitant MTX use. Of these, 9.0% (15/167) and 7.1% (12/169) treated with IXE and ADA, respectively, were taking an additional csDMARD (sulfasalazine, cyclosporine, or leflunomide). A significantly greater proportion of patients on IXE versus ADA achieved the primary endpoint or PASI 100 when used as monotherapy or in combination with csDMARD (Figure 1A and 1C). At Wk 52, the proportion of patients achieving ACR50 was not statistically different between IXE and ADA, regardless of monotherapy or concomitant csDMARD use (Figure 1B). A significantly higher proportion of patients achieved MDA on IXE compared to ADA in the monotherapy subgroup (49% vs 33%), while the response rates were similar in both combination subgroups (Figure 1D). These data support consistent ACR50, PASI 100, and MDA response for IXE across all three subgroups. Frequencies of adverse events were similar across the three subgroups for IXE and ADA (Figure 2).

Conclusion: As with prior studies,[2,3] consistent efficacy across multiple PsA disease-specific endpoints was observed with IXE in SPIRIT-H2H, regardless of whether IXE was taken as monotherapy or in combination with MTX or another csDMARD. No unexpected safety signals were found for either agent.

References:

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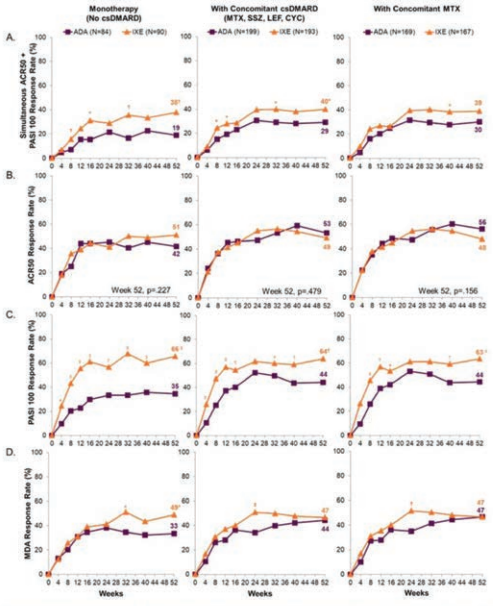

Figure 1. Proportion patients through 52 weeks with simultaneous achievement of ACR50 + PASI 100, ACR50, PASI 100, and MDA-18 Entheseal Points. Nine patients with active PsO and BSA≥3% were assessed as PASI=0 at baseline, a medical inconsistency that was resolved using medical judgement. These patients were considered PASI 100 responders if PASI=0 and BSA=0 at post baseline visit. *p≤.05 vs. ADA; †p<.01 vs. ADA; ‡p≤.001 vs. ADA.

Abbreviations: ACR, American College of Rheumatology criteria; ADA, adalimumab; csDMARD, conventional synthetic DMARD; IXE, ixekizumab; MTX, methotrexate; MDA, minimal disease activity – PsA; PASI, Psoriasis Area Severity Index score.