

OP0220 RANDOMIZED, DOUBLE-BLIND, GLOBAL CLINICAL TRIAL TO EVALUATE EQUIVALENCE OF CHS-1420 TO ADALIMUMAB IN PATIENTS WITH PSORIASIS AND PSORIATIC ARTHRITIS

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Background: CHS-1420 is being developed as a proposed biosimilar to adalimumab for the treatment of rheumatoid arthritis, plaque psoriasis (PsO), and other auto-immune diseases.

Objectives: This phase 3, randomized, double-blind, active-controlled, multicenter study evaluated the equivalence of CHS-1420 to adalimumab in patients with active, moderate-severe, chronic plaque PsO, including patients with psoriatic arthritis (PsA).

Methods: Male and female patients (aged ≥ 18 years) were randomized to CHS-1420 or adalimumab. Patients received 40 mg x 2 on Day 0 and then 40 mg every other week (QOW) by subcutaneous injection. To establish the equivalence of CHS-1420 to adalimumab, the 95% CI of the treatment difference for the primary endpoint, PASI75 at Week 12, had to be within pre-specified equivalence margins of $\pm 15\%$. The 55-week study is ongoing, and blinded efficacy data at Week 12 and safety data through Week 16 are available. The study was not powered for statistical analysis of the PsA subgroup. Patients with PsA were evaluated based on change in the Health Assessment Questionnaire – Disability Index (HAQ-DI) and highly sensitive C-reactive protein (hs-CRP).

Results: The full analysis population for the primary efficacy endpoint consisted of 545 patients (mean age 43.9 years), with 274 and 271 in Group A and Group B, respectively. The mean BMI was 29.6 kg/m², and 72.3% were male. At Week 12, the proportion of patients achieving a PASI75 from Baseline was 77.7% in Group A and 74.5% in Group B. The 95% CI of the treatment difference [-3.63, 10.28] was within the pre-specified equivalence margin [-15.0, 15.0]. Sensitivity analyses supported equivalence of the two treatments.

PsA was present in 65 (23.7%) and 61 (22.5%) patients in Group A and Group B, respectively. A PASI75 was achieved by 81.5% and 77.0% of patients with PsA in Group A and Group B, respectively, at Week 12. Mean HAQ-DI scores decreased from Baseline by 0.6 and 0.7 (95% CI: -0.3, 0.3) at Week 12 in Group A and Group B, respectively. Mean hs-CRP (mg/L) decreased from Baseline by 8.9 and 6.3 at Week 12 in Group A and Group B, respectively.

In the safety population (n=545), adverse events were reported in 48.5% and 45.0% of patients, in Group A and Group B, respectively, through Week 16. Serious adverse events were reported in 1.1% and 2.2% of patients in Group A and Group B, respectively, through Week 16, and none were judged by the investigator to be related to treatment. The most common ($\geq 5\%$ of patients) adverse events were nasopharyngitis and upper respiratory tract infection.

Conclusions: This randomized, double-blind, global clinical trial demonstrated the equivalence of CHS-1420 to adalimumab in the treatment of chronic PsO. Both study drugs were well tolerated. Patients with PsA showed improvement with both study drugs.

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OP0221 RADIOGRAPHIC PROGRESSION OF STRUCTURAL JOINT DAMAGE IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS TREATED WITH IXEKIZUMAB OVER 52 WEEKS

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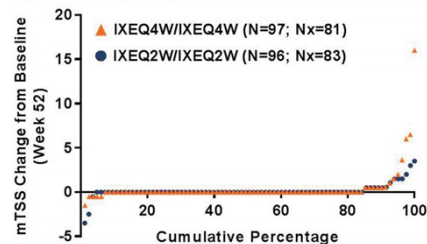
Background: Ixekizumab (IXE), an anti-interleukin-17A monoclonal antibody, was shown to be superior to placebo (PBO) in clinical responses and inhibiting the progression of structural joint damage in patients (pts) with psoriatic arthritis (PsA) treated for 24 weeks (wks).¹

Objectives: To assess progression of structural joint damage in PsA pts with IXE for up to 52 wks.

Methods: Biologic DMARD-naïve pts with active PsA (N=417) entered into SPIRIT-P1 (NCT01695239), a double-blind phase 3 trial. Pts must have had ≥ 1 joint erosion on the hand and foot x-rays confirmed by central reading or had a C-reactive protein level > 6 mg/L at screening. 417 pts were randomized to IXE 80 mg every 2 wks (Q2W; N=103) or 4 wks (Q4W; N=107) following a 160 mg initial dose, PBO (N=106), or adalimumab 40 mg every 2 wks (ADA; active reference arm; N=101) for 24 wks. In the Extension Period (EXT: Wks 24–52), PBO and ADA pts were re-randomized (1:1) to IXEQ2W or IXEQ4W at Wk 16 (inadequate responders) or Wk 24; ADA pts underwent a washout prior to IXE treatment. All pts were assessed for structural joint damage using the van der Heijde modified PsA Total Sharp Score (mTSS, 0–528 scale). X-rays at Wks 0, 24 and 52 were scored independently by 2 readers blinded to timepoint and clinical data (average of readers). mTSS was excluded from the pre-specified analysis if the radiograph was taken after the scheduled visit date. In a post-hoc analysis, mTSS from a radiograph taken after the scheduled visit date was interpolated and considered as observed data. Any missing data at Wk 52, in either presentation, were imputed using a linear extrapolation if they had at least 1 post-baseline value.

Results: Pts had active PsA at Week 0 (Table). 381 pts (91.3%) entered the EXT, with 374 (98.2%) having radiographs collected during the EXT. Wk 52 mean (SD) mTSS change from baseline were 0.54 (2.11) and 0.09 (1.0) for pts randomized to IXEQ4W and IXEQ2W at baseline, respectively. Similar changes at Wk 52 were obtained with the post-hoc analysis (Table). The majority of IXEQ2W or IXEQ4W pts exhibited no structural progression through 1 year of IXE treatment (Figure). In pts who switched from PBO or ADA to IXE, Wk 52 mean change from baseline mTSS values scores ranged from -0.03 to 0.41 (Table).

Observed mTSS Change from Baseline Values at Week 52, Cumulative Distribution Plot



N=EXT patients; Nx= Pts with baseline and Wk 52 radiograph assessments. mTSS values from radiographs taken after the Wk 52 scheduled visit date were interpolated and considered as observed data.

Conclusions: Over a 52 wk period, minimal changes in mTSS were observed in PsA pts entering the EXT and treated with IXEQ2W or IXEQ4W.

References:

[1] Mease P et al. 2017 ARD 76(1):79.

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Abstract OP0221 – Table 1. Radiographic Progression of Structural Joint Damage for EXT Pts

| | PBO/IXEQ4W (N=45) | PBO/IXEQ2W (N=46) | ADA/IXEQ4W (N=49) | ADA/IXEQ2W (N=48) | IXEQ4W/IXEQ4W (N=97) | IXEQ2W/IXEQ2W (N=96) |
|------------------------------------------------------|--------------------|--------------------|--------------------|---------------------|----------------------|----------------------|
| Baseline (Week 0) Disease Characteristics, Mean (SD) | | | | | | |
| mTSS | 11.5 (15.5) | 24.5 (37.3) | 15.6 (24.3) | 15.4 (30.2) | 19.6 (33.3) | 15.2 (29.1) |
| Tender Joint Count | 18.5 (11.6) | 19.2 (14.0) | 18.8 (11.9) | 18.8 (12.8) | 20.8 (13.6) | 21.3 (13.8) |
| Swollen Joint Count | 9.6 (6.2) | 10.7 (7.1) | 10.1 (7.4) | 9.6 (5.5) | 11.0 (7.3) | 12.2 (7.3) |
| mTSS, Pre-Specified, Mean (SD) | | | | | | |
| Week 52 Change from Baseline | n=31 0.27 (0.8) | n=37 0.41 (0.8) | n=36 0.32 (1.0) | n=34 -0.03 (0.4) | n=80 0.54 (2.1) | n=80 0.09 (1.0) |
| mTSS, Post-Hoc, Mean (SD) | | | | | | |
| Week 52 Change from Baseline | n=44 0.25 (0.8) | n=45 0.51 (1.1) | n=47 0.24 (0.9) | n=45 0.06 (0.5) | n=97 0.47 (1.9) | n=96 0.09 (0.9) |

N = EXT pts; n = pts with baseline and ≥ 1 post baseline radiograph assessments.

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OP0222 SECUKINUMAB PROVIDES SUSTAINED IMPROVEMENTS IN THE SIGNS AND SYMPTOMS OF ACTIVE PSORIATIC ARTHRITIS: 104 WEEKS RESULTS FROM A PHASE 3 TRIAL, FUTURE 2

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Background: Secukinumab significantly improved the signs and symptoms of psoriatic arthritis (PsA) over 52 weeks (wks) in FUTURE 2 study (NCT01752634).^{1,2}
Objectives: To present longer-term (104 wks) efficacy and safety data of secukinumab from FUTURE 2 study.

Methods: Overall, 397 patients (pts) with active PsA were randomised to secukinumab (300, 150, or 75 mg) or placebo at baseline, Wks 1, 2, 3, and 4, and every 4 wks thereafter. Assessments at Wk 104 are from pts originally randomised to secukinumab and included ACR20/50/70, PASI 75/90, DAS28-CRP, SF-36 PCS, HAQ-DI, dactylitis, and enthesitis. Multiple imputation was used for analysis of binary variables and mixed-model repeated measures for continuous variables. Analyses stratified by anti-TNF α status (naïve/inadequate response or intolerance to these agents) were prespecified and are reported as observed. Safety analysis included all pts who received ≥ 1 dose of secukinumab.

Results: In total, 86/100 (86.0%), 76/100 (76.0%) and 65/99 (65.7%) pts in the secukinumab 300, 150, and 75 mg groups respectively completed 104 wks. Sustained clinical improvements were observed through Wk 104 with secukinumab across all clinically important domains of PsA (Table). Responses were sustained through Wk 104 regardless of anti-TNF α status. Over the entire treatment period (mean [SD] exposure to secukinumab of 709 \pm 210.99 days), the exposure adjusted incidence rates for serious infections/infestations, candida infections, inflammatory bowel disease and malignant/unspecified tumors with secukinumab were 1.6, 2.3, 0.5 and 1.3, respectively.

Table 1. Summary of Efficacy Results at Wk 104

| Variable* | Secukinumab | | |
|----------------------------------------|------------------------|------------------------|----------------------|
| | 300 mg s.c. (N=100) | 150 mg s.c. (N=100) | 75 mg s.c. (N=99) |
| ACR20 | 69.4 | 64.4 | 50.3 |
| ACR50 | 50.6 | 36.0 | 28.2 |
| ACR70 | 33.1 | 23.1 | 14.9 |
| ^a PASI 75 | 79.5 | 73.3 | 58.4 |
| ^a PASI 90 | 69.6 | 52.5 | 33.7 |
| SF-36 PCS, LS mean change from BL (SE) | 6.8 (0.85) | 5.0 (0.87) | 4.1 (0.91) |
| DAS28-CRP, LS mean change from BL (SE) | -1.9 (0.12) | -1.7 (0.12) | -1.5 (0.13) |
| HAQ-DI, LS mean change from BL (SE) | -0.58 (0.05) | -0.48 (0.06) | -0.27 (0.06) |
| ^b Resolution of enthesitis | 71.5 | 61.8 | 68.4 |
| ^c Resolution of dactylitis | 79.9 | 78.0 | 88.6 |

*% responders unless otherwise specified. ^aAssessed in pts with psoriasis affecting $\geq 3\%$ body surface area at BL (300 mg: n=41; 150 mg: n=58; 75 mg: n=50). ^bAssessed in pts (n=56 [300 mg], 64 [150 mg] and 68 [75 mg]) with this symptom at BL. ^cAssessed in pts (n=46 [300 mg], 32 [150 mg] and 33 [75 mg]) with this symptom at BL. BL, baseline; DAS28-CRP, 28-joint disease activity score using C-reactive protein; HAQ-DI, health assessment questionnaire-disability index; LS, least squares; N, number of pts randomised; PASI, psoriasis area and severity index; SE, standard error; SF-36 PCS, short form-36 physical component summary.

Conclusions: Secukinumab 300 and 150 mg provided sustained improvements in signs and symptoms and multiple clinical domains of active PsA through 2 years of therapy. Secukinumab was well tolerated, with a safety profile consistent with that reported previously.

References:

- [1] McInnes IB, et al. Lancet 2015;386:1137–46.
- [2] McInnes IB, et al. Ann Rheum Dis. 2015;74:352–3.

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OP0223 ABATACEPT IN THE TREATMENT OF ACTIVE PSORIATIC ARTHRITIS: 1-YEAR RESULTS FROM A PHASE III STUDY

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Background: In the Phase III ASTRAEA trial (NCT01860976), abatacept (ABA), a selective T-cell co-stimulation modulator, significantly increased ACR20 response (primary endpoint; PE) and had an overall beneficial effect vs placebo (PBO) on musculoskeletal symptoms in patients (pts) with active psoriatic arthritis (PsA) at 24 weeks (W).¹

Objectives: To analyse 1-year results from ASTRAEA.

Methods: Pts with active disease (≥ 3 swollen and ≥ 3 tender joints), ≥ 2 cm target lesion of plaque psoriasis and inadequate response/intolerance to ≥ 1 non-biologic DMARD were randomized (1:1) to SC ABA 125 mg weekly or PBO for 24W, followed by open-label (OL) SC ABA up to 52W. Randomization was stratified by MTX use, prior TNF inhibitor (TNFi) use and skin involvement $\geq 3\%$ of body surface area. Pts without $\geq 20\%$ improvement in joint counts at W16 were switched to OL ABA (early escape; EE) for 28W (total study time: 44W). Pre-specified exploratory endpoints included: ACR20/50/70 responses at W44; adjusted mean changes from baseline (BL) in DAS28 (CRP; post hoc analysis) and HAQ-DI at W44 and PsA-modified total Sharp/van der Heijde score (SHS) at W44 (EE pts)/W52 (non-EE pts); complete resolution of BL enthesitis and dactylitis at W44 (EE pts)/W52 (non-EE pts); and Psoriasis Area and Severity Index (PASI) 50/75 responses at W44. Analyses used the ITT population with non-responder imputation for missing values and actual data at each time point for all pts (denominator at each time point equal to number of pts in ITT population). All missing responses were imputed as non-responders, except if the missing value was between 2 visits for which the pt was a responder. In that case the missing value was imputed as a responder.

Results: Of 424 pts enrolled, 213 received ABA and 211 PBO. Most (>60%) pts had received prior TNFis. Of pts in the ABA and PBO groups, 76 (36%) and 89 (42%) were EE, 12 (6%) and 24 (11%) discontinued by PE of W24;

Figure. ACR 20/50/70 Responses to Week 44 (ITT Population)

