228. SECUKINUMAB, A HUMAN ANTI-INTERLEUKIN-17A MONOCLONAL ANTIBODY, IMPROVES ACTIVE PSORIATIC ARTHRITIS AND INHIBITS RADIOGRAPHIC PROGRESSION: EFFICACY AND SAFETY DATA FROM A PHASE 3 RANDOMIZED, MULTICENTRE, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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Background: Secukinumab has demonstrated significant and rapid efficacy in the treatment of psoriasis in two phase 3 studies. We present the first randomized, multicentre, double-blind, placebo (PBO)-controlled phase III study to assess the efficacy and safety of secukinumab in patients (pts) with PsA (FUTURE 1; NCT01392326).

Methods: 606 adults with active, moderate to severe PsA were randomized to secukinumab or PBO. Pts on secukinumab received 10 mg/kg i.v. loading dose at baseline, week 2 and week 4, then either 75 mg s.c. (10 i.v.→75 s.c.) or 150 mg s.c. (10 i.v.→150 s.c.) every 4 weeks from week 8. PBO was given on the same schedules. Patients naïve to anti-TNF therapy (~70%) and those intolerant of or inadequate responders to anti-TNF therapy (TNF-IR; ~30%), were stratified across groups. Statistical analyses for the primary and multiple secondary endpoints used non-responder imputation (binary variables), mixed-effects repeated measures model (continuous variables) and linear extrapolation (radiographic data), following a pre-defined hierarchical hypothesis testing strategy to adjust for multiplicity.

Results: Demographics and baseline characteristics were balanced between groups. Both 10 i.v.→75 s.c. and 10 i.v.→150 s.c. demonstrated significantly higher ACR20 responses *vs* PBO at week 24 (50.5% and 50.0% *vs* 17.3%, respectively; $P < 0.0001$ *vs* PBO). All prespecified secondary endpoints, including dactylitis, enthesitis, SF36-PCS, HAQ-DI, DAS for 28 joints (DAS28)-CRP, ACR50, PASI 75, PASI 90 and mTSS score were achieved by week 24 and reached statistical significance; active dose separated from PBO as early as week 1 for ACR20, DAS28-CRP and HAQ-DI. Drug exposure levels were similar in the secukinumab groups up to the primary endpoint due to i.v. loading. Improvements in all primary and secondary endpoints were sustained through week 52. At week 52, ACR 20/50/70 responses, using an observed analysis, were 66.9%, 38.4% and 25.6% for 10 i.v.→75 s.c. and 69.5%, 50.0% and 28.2% for 10 i.v.→150 s.c. In both TNF-naïve and TNF-IR groups, secukinumab demonstrated superiority at week 24 in ACR20/50/70, PASI 75/90, HAQ-DI, SF36-PCS, dactylitis and enthesitis at both doses and the effect was maintained through week 52. Secukinumab significantly inhibited radiographic structural joint damage at week 24 *vs* PBO. AEs at week 16: 60.4% (10 i.v.→75 s.c.), 64.9% (10 i.v.→150 s.c.) and 58.4% (PBO); non-fatal serious adverse event rates: 2.5%, 4.5% and 5.0%, respectively. Mean, median and maximum exposures: 438.5, 456.0 and 721 days; AE/non-fatal serious adverse event rates: 78.1%/8.6% and 82.4%/12.9% in patients who received secukinumab 75 mg s.c. or 150 mg s.c., respectively, at any point in the study.

Conclusion: In this first phase 3 trial to evaluate highly selective IL-17A inhibition in pts with PsA, secukinumab provided rapid, clinically significant and sustained improvements in signs and symptoms, and inhibited joint structural damage. Secukinumab was well tolerated through 52 wks.

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