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Ixekizumab Provides Sustained Improvement in Signs and Symptoms in Patients with Active Psoriatic Arthritis: Two-Year Results from a Phase 3 Trial

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Objective: To assess the efficacy and safety of ixekizumab (IXE), a monoclonal antibody that inhibits interleukin-17A, over 2 years in SPIRIT-P1 Phase 3 study (NCT01695239) enrolling patients with active psoriatic arthritis (PsA). Previous results showed that IXE was superior to placebo (PBO) in achieving ACR20 response at Week 24 in biologic disease-modifying antirheumatic drugs (bDMARD)-naïve PsA patients.

Methods: During the SPIRIT-P1 double-blind treatment (DBTP; Weeks 0-24), 417 bDMARD-naïve patients with active PsA were randomized 1:1:1:1 to subcutaneous 80-mg IXE (160-mg starting dose at Week 0) every 4 weeks (Q4W), every 2 weeks (Q2W), 40-mg adalimumab (ADA) Q2W (active arm), or PBO. Of these, 381 patients entered the extension period (Weeks 24-52), followed by the long-term extension period (Weeks 52-156). Here, data are presented for combined extension periods (CEP; Weeks 24-108) in patients who completed the initial 24-week treatment and received ≥1 dose of study drug during CEP. IXE-randomized patients continued on IXE throughout CEP and, if receiving PBO and ADA, were re-randomized (1:1) to IXEQ4W/Q2W at Week 16 (inadequate responders) or Week 24; ADA patients had 8-week washout period before receiving IXE. Efficacy measures included ACR20/50/70 responses, HAQ-Disability Index (HAQ-DI) score, DAS28 based on C-reactive protein (DAS28-CRP), 75%/90%/100% improvement in the Psoriasis Area and Severity Index (PASI 75/90/100), Leeds-Enthesitis Index (LEI), and Leeds-Dactylitis Index-Basic (LDI-B). Categorical data were compared using a logistic regression model with missing values imputed by non-responder imputation, which treats inadequate responders as non-responders.

Results: IXE provided persistent improvement in ACR 20/50/70 response rates through 2 years of treatment (Total-IXEQ4W and Total-IXEQ2W: 61% and 62%; 46% and 53%; 31% and 35%). Similar improvements were seen for PASI 75/90/100 (Total-IXEQ4W and Total-IXEQ2W: 62% and 68%; 53% and 63%; 43% and 56%). The mean changes from baseline in Total-IXEQ4W and Total-IXEQ2W groups for LDI-B and LEI were -61.4 and -50.0 and -1.6 and -1.8,

respectively. Frequency of treatment-emergent adverse events (AEs) were similar across treatment arms; majority were mild/moderate and serious AEs occurred in 46 patients. One death occurred (ADA/IXEQ4W patient suffered a cerebrovascular accident at Week 108).

Conclusion: In bDMARD-naïve patients, IXE demonstrated clinically significant improvement in the signs and symptoms of PsA across both the groups. The safety profile of IXE was similar to that in the DBTP of SPIRIT-P1, SPIRIT-P2, and other Phase 3 studies of IXE in patients with plaque psoriasis.

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