IXEKIZUMAB WITH OR WITHOUT TIRZEPATIDE IN ADULTS WITH PSORIASIS AND OVERWEIGHT OR OBESITY: THE TOGETHER-PSO PHASE 3B RANDOMIZED CLINICAL TRIAL

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Keywords: *Ixekizumab, Tirzepatide.*

Introduction. Overweight and obesity affect 60%-78% of patients with psoriasis, impacting disease severity, treatment response (i.e., complete skin clearance), and clinical outcomes. This trial evaluated efficacy and safety of ixekizumab (IXE) with or without tirzepatide (TZP) in participants with psoriasis and overweight or obesity.

Methods. This is a Phase 3b, randomized, US-based, open-label, 52-week trial (NCT06588283) in adults with moderate-to-severe plaque psoriasis and overweight with ≥1 weight-related comorbidity or obesity. Participants were randomized (1:1) to IXE+TZP (n=138) or IXE (n=136) with diet and exercise in both treatment arms. At Week 36, primary endpoint was simultaneous achievement of PASI 100 and ≥10% weight reduction. Key secondary endpoints were PASI 100, simultaneous PASI 75 and ≥5% weight reduction, and ≥10% weight reduction.

Results. Among 274 randomized participants (mean age, 45.6 years; 44.9% women; BMI, 39.2 kg/m2; psoriasis duration, 14.6 years; PASI, 19.7), 84.3% completed treatment through Week 36. Overall, 27.1% achieved primary endpoint with IXE+TZP vs 5.8% with IXE (P<.001). 40.6% *vs* 29.0% achieved PASI 100 (P=.044), 79.9% *vs* 17.9% simultaneous PASI 75 and ≥5% weight reduction (P<.001), and 69.2% *vs* 9.1% achieved ≥10% weight reduction (P<.001), respectively. Adverse events were generally consistent with established drug safety profiles, the most common being gastrointestinal events and injection site reactions. Gastrointestinal events occurred more frequently with IXE+TZP vs IXE.

Conclusions. IXE+TZP vs IXE produced clinically meaningful, statistically significant improvements in skin clearance and weight in participants with challenging psoriasis and overweight or obesity, with no new safety concerns, while providing potential to elevate outcomes.