CLOSER LOOK

MEMORANDUM

Lilly announces positive phase 3b TOGETHER-PsA trial results evaluating Taltz (ixekizumab) and Zepbound for psoriatic arthritis – January 9, 2026

Nearly a third of participants who received the combination treatment experienced 50% improvement in PsA activity and ≥10% weight reduction

Lilly just announced positive topline results from the 52-week phase 3b TOGETHER-PsA trial (n=271) that studied the combination of Taltz (ixekizumab) and Zepbound (tirzepatide) compared to Taltz alone in adults with active psoriatic arthritis (PsA) and obesity or overweight with at least one weight-related condition. As background, Taltz is a monoclonal antibody that selectively binds with interleukin 17A (IL-17A) cytokine, inhibiting its interaction with the IL-17 receptor.

At 36 weeks, the combination of Taltz and Zepbound met the primary and key secondary endpoints for superiority to Taltz monotherapy.

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Phase 3b TOGETHER-PsA trial studied the efficacy and safety of concomitant use of Taltz and Zepbound

The 52-week phase 3b TOGETHER-PsA trial studied the efficacy and safety of the concomitant use of Taltz and Zepbound compared with Taltz alone in adults with PsA and obesity or overweight. Study participants were randomized 1:1 to receive either Taltz in combination with Zepbound, both administered subcutaneously, or Taltz alone. The primary endpoint of the trial included the proportion of individuals achieving both an American College of Rheumatology 50 (ACR50)[1] response and ≥10% weight reduction at Week 36.

Study participants included those with a high disease burden at baseline and an average BMI of 37.6 kg/m^2 across both groups. More than 60% of study participants had prior experience with one or more advanced therapies, indicating a population with difficulty managing their conditions. Throughout the trial, participants in both groups also received guidance on a reduced-calorie diet and increased physical activity.

Combination of Taltz and Zepbound conferred 50% improvement in PsA activity, compared to 1% improvement with Taltz monotherapy

In the TOGETHER-PsA trial, 32% of participants who received the combination treatment of Taltz and Zepbound experienced a significant 50% improvement in PsA activity (measured by the ACR50) and ≥10% weight reduction, compared to 1% of participants on Taltz monotherapy ($p<0.001$). On the key secondary endpoint, the combination of Taltz and Zepbound treatment showed a 64% relative increase over Taltz monotherapy among patients who achieved

ACR50 (34% of patients vs. 20%, respectively, $p<0.05$).

These results reflect promising interventions for PsA, especially as 65% of adults with PsA also live with obesity or overweight in the US. We are encouraged by the trial results showing additive benefits of tirzepatide for people with PsA. In addition to mechanical effects through weight loss, we are curious if tirzepatide's benefits could be due to anti-inflammatory effects.

Adverse events consistent with the known safety profiles of each therapy

Regarding safety, adverse events associated with the combination of Taltz and Zepbound were mostly mild to moderate, and the types of adverse events were consistent with the known safety profiles of each treatment. The most common adverse events occurring in ≥5% of participants were nausea, diarrhea, constipation, and injection site reactions with combined treatment, and injection site reactions and upper respiratory tract infections with Taltz monotherapy.

Expanding role of tirzepatide beyond T2D, obesity, and sleep apnea

While treatment guidelines for PsA currently recommend interventions for obesity management, the separate management of PsA and obesity has remained challenging. Therefore, findings from the TOGETHER-PsA trial highlight an integrated therapeutic approach that could lead to better outcomes for those living with both PsA and obesity. Tirzepatide continues to demonstrate efficacy across various conditions, following its approval for T2D (under the brand name Mounjaro), obesity (under the brand name Zepbound), and obstructive sleep apnea (under the brand name Zepbound).

Close Concerns' Questions

1. *What are some challenges that might arise with a combined therapeutic approach, and how could those be mitigated and addressed?*
2. *How does Lilly plan to proceed with findings from the TOGETHER-PsA trial? Does the company plan to submit tirzepatide for approval for individuals with PsA and obesity?*
3. *With an eye on tirzepatide's expanding indications, how does Lilly prioritize its pipeline and development candidates?*

-- by Esther Min, Kat Moon, and Kelly Close

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[1] The ACR50 (American College of Rheumatology 50) response represents at least a 50% improvement in tender and swollen joint counts and 50% improvement in three of the five additional criteria: (i) Patient Global Assessment of Disease Activity; (ii) Physician Global Assessment of Disease Activity; (iii) Patient Assessment of Pain; (iv) Health Assessment Questionnaire score; and (v) C-Reactive Protein or Erythrocyte Sedimentation Rate.