Lebrikizumab, a High-Affinity IL-13 Inhibitor, Improves Clinical Manifestations in Moderate-to-Severe Atopic Dermatitis: Primary Results From a Randomized, Double-Blinded, Placebo-Controlled, Dose-Ranging, Phase 2b Study


INTRODUCTION

- Moderate-to-severe atopic dermatitis (AD) is a prevalent, debilitating condition characterized by a broad range of clinical manifestations, including skin lesions and intense, persistent pruritus that can have a significant, multi-dimensional impact on quality of life.
- interleukin-13 (IL-13) is a central pathogenic mediator driving multiple facets of AD pathology, underlying the range of clinical manifestations.
- Lebrikizumab (LEB) is a novel, high-affinity monoclonal antibody targeting IL-13 that selectively prevents formation of the IL-13Rα1/IL-4Rα heterodimer signaling complex while leaving undisturbed regulation of IL-4.

OBJECTIVE

- To report the efficacy and safety of LEB from a randomized, double-blinded, placebo-controlled, dose-ranging, phase 2b study in adults with moderate-to-severe AD.

METHODS

- Study Design:
  - This phase 2b study consisted of a 16-week treatment period with 16-week follow-up. Patients were randomized 3:3:3:2 to subcutaneous LEB 125 mg every 4 weeks (Q4W), 250 mg Q4W (LEB 250 mg Q4W (Q2W), or placebo (Q2W).
  - Randomized patients received ≥1 dose of study drug.

- Study Patients:
  - Eligible patients were 18 years of age or older, with Eczema Area Severity Index (EASI) ≥16, Investigator’s Global Assessment (IGA) 3 or 4, (5-point scale), ≥10% body surface area (BSA) affected, and active AD for >1 year for which topical treatment provided inadequate control or was medically inadvisable.

- Efficacy and Safety Assessments:
  - The primary endpoint was percent change in EASI at Week 16.
  - Additional endpoints included proportions of patients achieving EASI75, EASI90, IGA 0/1, no. ( NA), change in pruritus NRS from Baseline at Week 16, and percent change in pruritus NRS from Baseline.

- Statistical Analyses:
  - Efficacy analyses used the modified intent-to-treat (mITT) population (all patients who were randomized and received study drug).

RESULTS

- **Patient demographics and baseline disease characteristics were well matched across groups (Table 1).**

- **Patients were randomized 3:3:3:2 to subcutaneous LEB 125 mg every 4 weeks (Q4W), 250 mg Q4W (LEB 250 mg Q4W (Q2W), or placebo (Q2W).**

- **Patients requiring rescue therapy were allowed to use topical corticosteroids (TCS) for an interim period as possible and could remain in the study; those requiring systemic rescue therapy were discontinued.**

- **Rescue medication was infrequently required in LEB-treated patients (LEB 125 mg Q4W: 12.3%, 250 mg Q4W: 12.5%, 250 mg Q2W: 12.3%, placebo: 34%).**

- **Topical medication was used by 28.6% of placebo versus 3.4%, 3.4%, and 8.0% of LEB 125 mg Q4W, 125 mg Q2W, and 250 mg Q2W, respectively.**

- **Mean duration of topical medication use was 6 days for placebo versus 4.9, 1.0, and 2.5 days for LEB 125 mg Q4W, 250 mg Q4W, and 250 mg Q2W, respectively.**

- **These findings suggest that TCS use would not have confounded study results.**

Primary Endpoint

- **All LEB groups demonstrated a dose-dependent, statistically significant improvement in the primary endpoint versus placebo at Week 16 (least squares mean percent change in EASI: LEB 125 mg Q4W: -62.3%, LEB 250 mg Q4W: -57.1%, LEB 250 mg Q2W: -31.3%, placebo: 10.0%).**

- **Across all endpoints measured, LEB demonstrated a dose-dependent and statistically significant improvement over placebo at Week 16 (least squares mean percent change).**

Secondary Endpoints

- **A greater proportion of LEB versus placebo-treated patients achieved EASI75, EASI90, and IGA 0/1 at Week 16, with statistically significant improvements seen with LEB 250 mg Q4W and Q2W (Figure 4).**

- **LEB demonstrated a dose-dependent response across all endpoints measured, with marked improvement at both 250 mg Q2W and Q4W doses; for skin symptoms, an effect was seen at Week 4.**

- **Effects on itch were observed as early as Day 2 in patients who received a 500 mg loading dose at Day 0.**

- **LEB was well tolerated, and consistent with previous studies, TEAE rates were low across all LEB AD studies.**

CONCLUSIONS

- **In this phase 2b, placebo-controlled study, all LEB groups showed dose-dependent and statistically significant improvement in the primary endpoint (percent change in EASI from Baseline at Week 16).**

- **LEB demonstrated a dose-dependent response across all endpoints measured, with marked improvement at both 250 mg Q2W and Q4W doses; for skin symptoms, an effect was seen at Week 4.**

- **Effects on itch were observed as early as Day 2 in patients who received a 500 mg loading dose at Day 0.**

- **LEB was well tolerated, and consistent with previous studies, TEAE rates were low across all LEB AD studies.**

- **These data highlight that selective blockade of IL-13 with LEB leads to improvements in key AD clinical severity scores and pruritus while maintaining a favorable safety profile.**

**REFERENCES**


