Lebrikizumab Treatment Improves Quality of Life in Patients with Moderate-to-Severe Atopic Dermatitis: Results from Two Phase 3, Randomized, Double-Blinded, Placebo-Controlled Trials (ADvocate1 and ADvocate2)

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Introduction: Lebrikizumab is a novel, high-affinity IgG-4 monoclonal antibody targeting interleukin 13 that selectively prevents the formation of IL-13Rα1/IL-4Rα heterodimer receptor signaling complex. Lebrikizumab demonstrated efficacy and a favorable safety profile at 16 weeks in patients with moderate-to-severe atopic dermatitis (AD) in two ongoing 52-week, randomized, double-blinded, placebo-controlled Phase 3 trials[1], ADvocate1 (NCT04146363) and ADvocate2 (NCT04178967), as monotherapy and in a 16-week randomized, double-blinded, placebo-controlled Phase 3 trial, ADhere (NCT04250337)[2], as combination therapy. Here, we report 16-week quality of life (QoL) outcomes of lebrikizumab monotherapy in AD patients from ADvocate1 and ADvocate2.

Methods*:* Eligible patients with moderate-to-severe AD (adults and adolescents [≥12 to <18 years of age and weighing ≥40 kg]) were randomized 2:1 to receive two loading doses of 500 mg subcutaneous lebrikizumab, followed by 250 mg of lebrikizumab or placebo every two weeks (Q2W). Dermatology Life Quality Index (DLQI) and EQ-5D scores were assessed at Weeks 4, 8, 12 and 16. Missing data were imputed with nonresponder imputation for categorical endpoints. Mixed model repeated measure was used for DLQI total score change from baseline (CFB) analysis. For EQ-5D visual analogue scale (VAS) and US Health State Index CFB analysis, ANCOVA model was used with missing data imputed by last observation carried forward.

Results*:* In ADvocate1, the mean DLQI score at baseline in patients treated with lebrikizumab 250 mg (N=283) and placebo (N=141) was 15.3 and 15.7, respectively. Corresponding baseline means for EQ-5D VAS score were 68.2 and 67.0; for EQ-5D-5L US Health State Indices were 0.7 and 0.7, respectively. At Week 16, the proportion of patients with ≥4-point improvement from baseline in DLQI score at Week 16 was 71.2% and 29.3% in lebrikizumab and placebo groups, among those patients with baseline DLQI score ≥4, respectively. The proportion of patients receiving lebrikizumab and placebo with DLQI (0,1) response was 26.3% and 4.2%, among those patients with baseline DLQI>1, respectively. The DLQI total score mean CFB at Week 16 was improved by -10.0 for lebrikizumab-treated patients and by -4.4 for placebo-treated patients. Statistical significance was achieved as early as Week 4, the first assessment after baseline, and continued through Week 16 for all DLQI analyses. There was also a significant difference between EQ-5D VAS score mean CFB (10.5 and 2.2, respectively) and EQ-5D-5L US Health State Index CFB (0.13 and 0.03, respectively) at Week 16 for patients assigned to lebrikizumab and placebo.

In ADvocate2 (lebrikizumab, N=281, placebo, N=146), baseline means for DLQI score were 15.4 and 15.9; EQ-5D VAS score were 66.7 and 68.6; EQ-5D-5L US Health State Index were 0.8 and 0.7, respectively. At Week 16, proportion of patients with ≥4-point improvement from baseline in DLQI score at Week 16 was 60.5% and 31.3% in lebrikizumab and placebo groups, among those patients with baseline DLQI score ≥4, respectively. The proportion of patients assigned to lebrikizumab and placebo achieving DLQI (0,1) response was 16.1% and 7.7%, among those patients with baseline DLQI>1, respectively. The DLQI total score mean CFB at Week 16 was improved by -9.3 for lebrikizumab-treated patients and by -4.9 for placebo-treated patients. Statistical significance was achieved as early as Week 4, the first assessment after baseline, and continued through Week 16 for DLQI ≥4-point improvement and total score CFB. Significant differences were also observed at Week 16 for EQ-5D VAS score mean CFB (9.0 and 5.2, respectively) and EQ-5D-5L US Health State Index CFB (0.08 and 0.03, respectively) for patients receiving lebrikizumab and placebo.

Conclusion: Lebrikizumab 250 mg Q2W treatment for 16 weeks resulted in clinically significant improvements in quality of life in patients with moderate-to-severe AD.

1. Silverberg, et al. "*Efficacy And Safety of Lebrikizumab in Moderate-to-Severe Atopic Dermatitis: Results from Two Phase 3, Randomized, Double-Blinded, Placebo-Controlled Trials*". American Academy of Dermatology (AAD), 2022
2. Simpson, et al. "*Efficacy and Safety of Lebrikizumab in Combination with Topical Corticosteroids in Patients with Moderate-to-Severe Atopic Dermatitis: a Phase 3, Randomized, Placebo-Controlled Clinical Trial (Adhere)*". Revolutionizing Atopic Dermatitis (RAD), 2022