Lebrikizumab in Combination with Topical Corticosteroids Improves Quality of Life in Patients with Moderate-to-Severe Atopic Dermatitis: Results from a Phase 3, Randomized, Double-Blinded, Placebo-Controlled Trial (ADhere)

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Introduction: Lebrikizumab is a novel, high-affinity IgG-4 monoclonal antibody targeting interleukin 13 that selectively prevents the formation of the 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 in combination with topical corticosteroids (TCS) versus placebo/TCS from the ADhere study.

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 subcutaneous lebrikizumab 250 mg + TCS (loading dose [LD] of 500 mg given at baseline and Week 2) or placebo + TCS every 2 weeks (Q2W). Improvement in patients' QoL was assessed at Weeks 4, 8, 12 and 16 using the Dermatology Life Quality Index (DLQI) and EQ-5D scores. Missing data were imputed using non-responder imputation for categorical endpoints. Mixed model repeated measure approach was used for DLQI change from baseline (CFB) analysis. For the EQ-5D visual analogue scale (VAS) and EQ-5D-5L US Health State Index CFB analysis, ANCOVA model was used with missing data imputed by last observation carried forward.

Results*:* Patients assigned to lebrikizumab + TCS (N=145) and placebo + TCS (N=66) had similar baseline mean scores for DLQI (14.9 and 13.5), EQ-5D-5L US Health State Index (0.8 and 0.8), and EQ-5D VAS (72.7 and 72.8), respectively. At Week 16, the proportion of patients with ≥4-point improvement from baseline in DLQI score was 76.2% for the lebrikizumab + TCS group and 50.0% for the placebo + TCS group (p-value <0.01), among those patients with baseline DLQI ≥4. The DLQI (0,1) response was achieved at Week 16 by 27.5% of patients receiving lebrikizumab + TCS and 8.0% of patients receiving placebo + TCS (p-value <0.01), among those patients with baseline DLQI >1. The DLQI total score mean CFB at Week 16 was improved by -10.5 for patients treated with lebrikizumab + TCS and by -7.1 for patients treated with placebo + TCS (p-value <0.001). Statistically significant differences were observed as early as Week 4, the first assessment after baseline, and continued through Week 16 for DLQI ≥4-point improvement and total score CFB. The EQ-5D-5L US Health State Index CFB at Week 16 was 0.10 for patients receiving lebrikizumab + TCS and 0.03 for patients receiving placebo + TCS (p-value <0.001); corresponding means for EQ-5D VAS score CFB were 10.1 and 6.5 (p-value 0.131), respectively.

Conclusion: Lebrikizumab 250 mg Q2W in combination with TCS for 16 weeks provided improvements in quality of life for patients with moderate-to-severe AD.

References:

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