Efficacy and Safety of Lebrikizumab in Combination with Topical Corticosteroids in Patients with Moderate-to-Severe Atopic Dermatitis: A Phase 3, Randomized, Placebo-Controlled Trial (ADhere)

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Background: Atopic dermatitis (AD) is a chronic, relapsing, heterogenous skin disease with a global prevalence of 2-10% in adulthood[1-4] and >20% in children[5]. Lebrikizumab, a novel high-affinity monoclonal antibody directed against IL-13, is being considered for treatment of patients with moderate-to-severe AD. Here, we evaluated the efficacy and safety of lebrikizumab vs. placebo in combination with topical corticosteroids (TCS) in patients with moderate-to-severe AD in the Phase 3 ADhere study (NCT04250337).

Methods: Eligible patients included adults (≥18 years) and adolescents (≥12 years weighing ≥40 kg) with moderate-to-severe AD. During the 16-week treatment period, 228 patients were stratified and randomized 2:1 to treatment with either 250 mg lebrikizumab (loading dose of 500 mg given at Baseline and Week 2) plus TCS (LEB250mg+TCS) or placebo by subcutaneous (SC) injection every 2 weeks (Q2W) plus TCS (PBO+TCS). The co-primary efficacy endpoints were the percentage of patients with an IGA score of 0/1 at Week 16 and the proportion of patients achieving 75% improvement in EASI from baseline (EASI75) at Week 16. Key secondary endpoints were assessed at Week 16 and included the percentage of patients achieving 90% improvement in EASI from baseline (EASI90), the percentage change in EASI from baseline, the Pruritus Numeric Rating Scale (NRS) ≥4-points improvement score and the Pruritus NRS percent change from baseline, the percentage of patients with a Pruritus NRS score of ≥4 points at baseline who achieve both EASI-75 and ≥4-point reduction in Pruritus NRS score from baseline, the Dermatology Life Quality Index (DLQI) ≥4-point improvement score, the change from baseline in Sleep-loss score, measuring interference of itch on sleep. Safety was assessed by monitoring adverse events, serum chemistry, hematology and urinalysis laboratory evaluations, physical examination, and vital signs.

Results: In ADhere, 17 patients from a single site were excluded from analyses due to GCP issues. Thus, efficacy and safety analyses were conducted for 211 patients. At Week 16, IGA 0/1 was achieved by 41.2% (N=60/145) of patients receiving LEB250mg+TCS vs. 22.1% (N=15/66) receiving PBO+TCS (p=0.011). Similarly, there was a significantly higher

($p<0.001$) proportion of patients achieving EASI75 for LEB250mg+TCS (69.5%) vs. PBO+TCS (42.2%), and EASI90 (41.2% vs. 21.7%, respectively; $p<0.008$). In addition, there was a significant decrease ($p<0.001$) in the percent change in EASI from baseline for the LEB250mg+TCS vs. PBO+TCS group (-76.8 vs. -53.1, respectively). A higher proportion of those receiving LEB250mg+TCS achieved ≥4 points reduction in Pruritus NRS score at Week 16 vs. PBO+TCS (50.6% vs. 31.9%, respectively [$p=0.017$]) and a significant percent change from baseline ($p=0.017$) was observed in the LEB250mg+TCS group compared to the PBO+TCS group for the Pruritus NRS at week 16 (-50.7 vs. -35.5, respectively). Patients receiving LEB250mg+TCS had a significantly greater combined EASI75 & Pruritus NRS score at Week 16 compared to the PBO+TCS group (38.3% vs. 16.8% [$p=0.005$], respectively). Furthermore, those receiving LEB250mg+TCS achieved significant DLQI ≥4-point improvement vs. PBO+TCS group (77.4% vs. 58.7% [$p=0.036$]). A significant change from baseline in Sleep-loss score was also observed in patients receiving LEB250mg+TCS compared to PBO+TCS (-1.1 vs. -0.8 [$p=0.025$]). TEAEs reported in ≥2% in either treatment group were conjunctivitis, headache, hypertension, nasopharyngitis, atopic dermatitis, dry eye, and upper respiratory tract infection. Conjunctivitis (4.8% vs. 0%), headache (4.8% vs. 1.5%), hypertension (2.8% vs. 1.5%) and dry eye (2.1% vs. 0%) were more frequently reported in the LEB250mg+TCS group compared to the PBO+TCS group. Nasopharyngitis (2.1% vs. 6.1%), atopic dermatitis (2.1% vs. 4.5%) and upper respiratory tract infection (0.7% vs. 3.0%) were less commonly reported in the LEB250mg+TCS group compared to the PBO+TCS group. SAEs (serious adverse events) were similar in the PBO+TCS group (1.5%) and the LEB250mg+TCS group (1.4%). In the LEB250mg+TCS group, sinus node dysfunction or arrhythmias (0.7%) and fall (0.7%) were reported. In the PBO+TCS group, dehydration (1.5%) and acute kidney injury (1.5%) were reported. The LEB250mg+TCS group did report AE's leading to treatment discontinuation (2.1%) which included injection site rash (0.7%), drug hypersensitivity (0.7%), and conjunctivitis (0.7%).

Discussion: LEB250mg+TCS demonstrated efficacy and safety in a placebo-controlled phase 3 trial, consistent with previous lebrikizumab monotherapy studies in patients with moderate-to-severe AD.

References:

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