453 Dupilumab Efficacy in Children With Atopic Dermatitis Aged 6 Months to 5 Years With and Without Atopic Comorbidities

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RATIONALE: Atopic dermatitis (AD) is a chronic inflammatory systemic disease that frequently occurs with atopic comorbidities. Here, we evaluate the efficacy of dupilumab with concomitant topical corticosteroids (TCS) for moderate-to-severe AD in children with and without asthma, allergic rhinitis, and food allergies.

METHODS: In LIBERTY AD PRESCHOOL (NCT03346434), a double-blind, 16-week, phase 3 trial, 162 children aged 6 months to 5 years were randomized 1:1 to dupilumab treatment (n = 83) every 4 weeks based on baseline weight (q4w; 200 mg: ≥5 to <15 kg; 300 mg: ≥15 to <30 kg) or placebo (n = 79), with concomitant low-potency TCS. Atopic comorbidity history was ascertained by caregiver report.

RESULTS: Atopic comorbidity history and disease severity at baseline were comparable in dupilumab and placebo groups. At Week 16, significantly more patients receiving dupilumab vs placebo, with or without atopic comorbidity, achieved Investigator's Global Assessment score 0 or 1 (with asthma: 23.8%/0%; without asthma: 29%/5.4%; with allergic rhinitis: 24.3%/ 0.1%; without allergic rhinitis: 30.4%/7.2%; with food allergies: 25.4%/1.8%; without food allergies: 33.3%/9.3%). At Week 16, significantly more patients receiving dupilumab vs placebo achieved ≥75% improvement in Eczema Area and Severity Index (with asthma: 52.4%/4.5%; without asthma: 53.2%/13.1%; with allergic rhinitis: 54.1%/ 3.2%; without allergic rhinitis: 52.2%/17.3%; with food allergies: 44.1%/ 7.5%; without food allergies: 75%/19.1%). Overall safety was consistent with the known dupilumab safety profile.

CONCLUSIONS: Dupilumab with concomitant TCS was equally efficacious in improving AD signs in children aged 6 months to 5 years with and without a history of atopic comorbidities.

454 Combinations of Probiotic Bacteria (Lactobacillus helveticus, Bifidobacterium longum, Lactobacillus rhamnosus, Sacchammyces boulardii) Restores the Skin Microbiome in Atopic Dermatitis

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RATIONALE: Combinations of probiotic bacteria may improve the quality of life and the effectiveness of standard treatment for atopic dermatitis.

METHODS: An open-label, placebo-controlled, randomized, pilot study in 2 parallel groups was conducted. The research group included 10 patients who received a combination of probiotic bacteria (*Lactobacillus helveticus, Bifidobacterium longum, Lactobacillus rhamnosus, Sacchammyces boulardii*) and 0.1% mometasone furoate cream for 28 days. The placebo group included 10 patients who received only 0.1% mometasone furoate cream. The study material was collected by the method of deep skin scraping. Identification of pure cultures of microorganisms was done using biochemical test systems.

RESULTS: The combination probiotic led to a decrease in the number of gram-positive bacteria *S. aureus* from $5x10^6$ to $1x10^2$ CFU and E. faecalis from $5x10^6$ to $3x10^3$ CFU, as well as gram-negative bacteria *Escherichia coli* from $1x10^{11}$ to $1x10^5$ CFU. In the probiotic group, at the end of the treatment, complete elimination of opportunistic gram-negative bacteria *Acinetobacter lwoffii* and microscopic fungi of the genus Candida were observed. On the 28th day of treatment, there was significant decrease in the SCORAD (16.5±4.1 vs 21.7±5.8, p=0.03) and DLQI index (6.6±2.2 vs 10.3±3.7, p=0.02) in the patients of probiotic group compared to the placebo group.

CONCLUSIONS: The use of probiotic bacteria (*Lactobacillus helveticus, Bifidobacterium longum, Lactobacillus rhamnosus, Sacchammyces boulardii*) helped to restore the natural healthy microbiota of the skin, improving the effectiveness of treatment in atopic dermatitis patients.

455 Efficacy of Lebrikizumab in Patients With Atopic Dermatitis and Atopic Comorbidities: Pooled Results From Two Phase 3 Monotherapy Randomized, Double-Blind, Placebo-Controlled 16-Week Studies (ADvocate1 and ADvocate2)

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RATIONALE: Atopic comorbidities are common in patients with atopic dermatitis (AD). We evaluated lebrikizumab, a high-affinity monoclonal antibody targeting interleukin-13, in patients with AD with and without atopic comorbidities in 2 Phase 3, randomized, double-blind trials (ADvocate1 [NCT04146363] and ADvocate2 [NCT04178967]).

METHODS: Adults and adolescents with moderate-to-severe AD were randomized 2:1 to subcutaneous lebrikizumab 250 mg (N=564) or placebo (N=287) every 2 weeks. Using pooled data, treatment comparisons in patients with and without atopic comorbidities were assessed at Week 16 by percentage of patients achieving Investigator's Global Assessment (IGA) (0,1) with ≥2-point improvement, Eczema Area and Severity Index 75% improvement (EASI75), and Pruritis Numeric Rating Scale (PNRS) ≥4-point improvement (in patients with baseline PNRS ≥4).

RESULTS: Of 851 patients, 614 (72.2%) reported ≥1 atopic comorbidity (1 [n=54], 2 [n=200], 3 [n=131], or >3 [n=229] atopic comorbidities), most commonly allergic rhinitis (49.6%), food allergy (32.1%), and asthma/asthma history (30.7%). At Week 16 among patients with ≥1 atopic comorbidity, more lebrikizumab- vs. placebo-treated patients reported IGA (0,1) with ≥2-point improvement (36.7% vs. 12.0%; p<0.001), EASI75 (55.6% vs. 16.7%; p<0.001), and PNRS ≥4-point improvement (42.2% vs. 10.1%; p<0.001). Similarly, among patients without atopic comorbidities, more lebrikizumab- vs. placebo-treated patients reported IGA (0,1) with ≥2-point improvement (41.8% vs. 11.1%; p<0.001), EASI75 (55.2% vs. 18.5%; p<0.001), and PNRS ≥4-point improvement (45.0% vs. 17.6%; p<0.001) at Week 16.

CONCLUSIONS: Lebrikizumab provided clinically meaningful improvements in skin and itch in patients with moderate-to-severe AD, regardless of coexisting atopic comorbidities.

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