Efficacy of Lebrikizumab in Adults and Adolescents With Moderate-to-Severe Atopic Dermatitis by Age of Onset: Analysis of Two Phase 3 Clinical Trials

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BACKGROUND

- AD can present at any age and has variable presentations and comorbidity profiles. It is known that the relationship between age of disease onset of AD and treatment efficacy is unknown.
- Lebrikizumab is a monoclonal antibody that binds with high affinity and slow dissociation rate to IL-13, thereby blocking the downstream effects of IL-13 with high potency 1-4.
- Lebrikizumab has demonstrated clinical benefit in patients with moderate-to-severe AD in the randomized, placebo-controlled, Phase 3 ADVocate 1 and ADVocate 2 trials 5-6.
- Lebrikizumab has been approved in the European Union, Japan, the UK, and United Arab Emirates, and is under review elsewhere for the treatment of moderate-to-severe AD in adults and adolescents, 212 years of age with a body weight of ≥40 kg, who are candidates for systemic therapy.

OBJECTIVE

- To evaluate the efficacy of lebrikizumab monotherapy at 16 weeks of age by age of onset in adults and adolescents with moderate-to-severe AD in an analysis of pooled data from ADVocate 1 and ADVocate 2 trials.

METHODS

Study Design: ADVocate 1 and ADVocate 2

- Induction Period
- Maintenance Treatment Period

Outcomes:

- Efficacy was assessed at Week 16 in the age of AD onset subgroups (>2 years, ≥12 years, and ≥18 years) and for each age group.
  - IGA-01 with 22-point improvement
    - EASI-75
    - Pruritus NRS 4-point improvement from baseline
  - EASI mean percent change from baseline

Statistical Analyses:

- Post hoc analyses were performed on the pooled mITT population of ADVocate 1 and ADVocate 2 trials.
- Data collected after any rescue medication use, or for patients discontinued due to lack of efficacy, were imputed as non-responders or set to baseline values, data collected after discontinuation due to other reasons were set as missing and analyzed using multiple imputation.
- Treatment-by-subgroup interaction was assessed with logistic regression, model included treatment, study, subgroup, and treatment by subgroup interaction.
- For each subgroup, binary outcomes were analyzed by the Cochran-Mantel-Haenszel method adjusted by study, and continuous outcomes were analyzed with ANCOVA with treatment, study, geographic region, age group, sex, race, and baseline IGA (≥4) score as fixed factors and baseline EASI score as a covariate.

RESULTS

Baseline Demographics

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Male (%)</th>
<th>Female (%)</th>
<th>White (%)</th>
<th>Black or African-American (%)</th>
<th>Hispanic (%)</th>
<th>Age of Onset (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;2 years</td>
<td>58.4 (10.6)</td>
<td>41.6 (10.6)</td>
<td>82.3 (10.7)</td>
<td>17.7 (10.7)</td>
<td>0.0 (10.7)</td>
<td>59.4 (10.6)</td>
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DISCLOSURES

- All authors or their immediate family members served as a consultant, investigator, and/or investigator for: AbbVie, Acrotech Biopharma, Advanced Derm Solutions, Alcon, Amgen, Arena Pharmaceuticals, BioCAD, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Cara Therapeutics, Castle Biosciences, Del Mar Pharmaceuticals, Dermavant, Dermira, Eli Lilly and Company, Galderma, Incyte Corporation, Janssen, Kyowa Kirin, Merck, Nektar, Novartis, Pfizer, RAPT Therapeutics, Rigel Pharmaceuticals, Regeneron, Revolo Biotherapeutics, Sanofi, SpinThera, Squibb, Surmodics, Takeda Pharmaceuticals, Telereach, Teva, UCB Pharma, Viela Bio, and Zura Bio.
- All authors or their immediate family members have received research support or fees for personal or institutional research or service related to the study from: AbbVie, Acrotech Biopharma, Advanced Derm Solutions, Alcon, Amgen, Arena Pharmaceuticals, BioCAD, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Cara Therapeutics, Castle Biosciences, Del Mar Pharmaceuticals, Dermavant, Dermira, Eli Lilly and Company, Galderma, Incyte Corporation, Janssen, Kyowa Kirin, Merck, Nektar, Novartis, Pfizer, RAPT Therapeutics, Rigel Pharmaceuticals, Regeneron, Revolo Biotherapeutics, Sanofi, SpinThera, Squibb, Surmodics, Takeda Pharmaceuticals, Telereach, Teva, UCB Pharma, Viela Bio, and Zura Bio.

CONCLUSION

- Regardless of age of onset of AD, lebrikizumab 250 mg Q2W monotherapy demonstrated consistent and robust efficacy on clinical and itch endpoints across the age range of patients with moderate-to-severe AD at Week 16.