Efficacy and Safety of Crisaborole in Patients With Mild-to-Moderate Atopic Dermatitis With and Without Comorbid Allergies or Asthma

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DISCLOSURES
PL has served as a clinical trial investigator for AbbVie, AOBiome, La Fondation pour la Dermatite Atopique, National Eczema Association, and Regeneron; has served on consulting/advisory boards for AbbVie, Altice, Amgen, Atlas Biome, Burt’s Bees, Dermawet, Dermitec, DermTan, Dermway, Eli Lilly, Exelixis, Franklin Biosciences, grower, Intercharm, Johnson & Johnson, Kimberly Clark, Kirinsh Pharmaceuticals, Leo Pharma, L'Oreal, Menlo Therapeutics, Micros Human Health, Modernizing Medicine, MyOR Diagnostics, National Eczema Association, Odessa, Reim Therapeutics, Regeneron, Sanofi US Services, SynerCell Skin Systems, Theraplex, UCB, Uniloy, Vertex Pharmaceuticals, and VyobraCare; has served as a speaker for Pfizer Inc., Eli Lilly, Galderma, La Roche-Posay, Leo Pharma, Pierre Fabre Dermatologie, and Regeneron; has received royalties from Theraplex; and is a stockholder of LearnHealth/LearnSkin, Medable, and Modernizing Medicine.

MJC has served as a clinical trial investigator for AstraZeneca, Galapagos, Johnson & Johnson, Leo Pharma, L’Oreal, Merck, Nett Pharma, Novartis, Pfizer, Regeneron, Sanofi Genzyme, and Stiefel; has served as an advisory board member; consultant, and/or invited lecturer for Pfizer Inc., Amgen, Astellas, Bayer, Johnson & Johnson, Leo Pharma, L’Oreal, MSD, Novartis, Regeneron, Sanofi Genzyme, and Stiefel; has received research funding from AstraZeneca, GlaxoSmithKline, Kamada, Novartis, Pfizer, Regeneron, and Sanofi Genzyme; and has served as a speaker for AbbVie, AOBiome, Amgen, Astellas, Bayer, BionX, Galapagos, GlaxoSmithKline, Johnson & Johnson, Leo Pharma, Novartis, Regeneron, Sanofi Genzyme, and Stiefel; and has received research funding from Bayer. MJB has served as a consultant for Pfizer Inc., ALX, Amgen, Armo, Merck, Regeneron, and Sanofi Genzyme. AK has served on advisory boards and has served as a speaker for AstraZeneca, GlaxoSmithKline, Kamada, Novartis, Astellas, BionX, and Merck.

WCC has served on advisory boards for Eli Lilly, Janssen, and Sun Pharma. JLH, MIO, CZ, and LT are employees and stockholders of Pfizer Inc.
Methods

- CrisADe CORE 1 (ClinicalTrials.gov, NCT02118766) and CORE 2 (NCT02118792) were identically designed, randomized, double-blind, vehicle-controlled, 28-day, phase 3 studies of crisaborole versus vehicle in patients aged ≥2 years with AD per Hanifin and Rajka criteria,\(^1\) mild-to-moderate disease per the ISGA, and %BSA ≥5 (excluding the scalp) who were randomly assigned 2:1 to receive crisaborole or vehicle twice daily\(^2\)

- In this post hoc analysis, patients were stratified by history of asthma/allergies (including but not limited to allergic rhinitis, food, and other allergies)

- Efficacy and safety outcomes included
  - **ISGA success**, defined as an ISGA of clear (0) or almost clear (1) with a ≥2-grade improvement from baseline, at day 29
  - **ISGA of clear (0) or almost clear (1) at day 29**
  - **SPS improvement**, defined as a weekly average SPS score ≤1 point with ≥1-point improvement from baseline, at week 4
  - **TEAEs** (all cause and treatment related), serious AEs, and AEs of special interest

Results

Baseline Characteristics

<table>
<thead>
<tr>
<th>Demographic or Characteristic</th>
<th>PMH of Asthma/Allergies</th>
<th>No PMH of Asthma/Allergies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vehicle n=304</td>
<td>Crisaborole n=585</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>12.1 (11.1)</td>
<td>12.4 (11.4)</td>
</tr>
<tr>
<td>%BSA, mean (SD)</td>
<td>19.5 (18.7)</td>
<td>19.7 (19.0)</td>
</tr>
<tr>
<td>ISGA, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild (2)</td>
<td>103 (33.9)</td>
<td>213 (36.4)</td>
</tr>
<tr>
<td>Moderate (3)</td>
<td>201 (66.1)</td>
<td>372 (63.6)</td>
</tr>
<tr>
<td>SPS, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate (2)</td>
<td>101 (33.2)</td>
<td>189 (32.3)</td>
</tr>
<tr>
<td>Severe (3)</td>
<td>86 (28.3)</td>
<td>183 (31.3)</td>
</tr>
<tr>
<td>Prior use of systemic corticosteroids, a n (%)</td>
<td>123 (40.5)</td>
<td>207 (35.4)</td>
</tr>
<tr>
<td>Concurrent use of antihistamines, n (%)</td>
<td>115 (37.8)</td>
<td>213 (36.4)</td>
</tr>
</tbody>
</table>

%BSA, percentage of treatable body surface area; AD, atopic dermatitis; AE, adverse event; ISGA, Investigator’s Static Global Assessment; PMH, past medical history; SPS, Severity of Pruritus Scale; TEAE, treatment-emergent adverse event.

\(^*\)Within 90 days before starting study treatment.

Significant Improvement in Severity of AD and Pruritus Was Observed With Crisaborole Compared With Vehicle in Patients With or Without a History of Asthma/Allergies

**ISGA Success**\(^a\)

- **PMH of asthma/allergies**
  - Vehicle: 20.1\% (95\% CI: 17.0-23.9)
  - Crisaborole: 29.4\% (95\% CI: 25.9-33.0)
  - \(P = 0.003\)

- **No PMH of asthma/allergies**
  - Vehicle: 24.6\% (95\% CI: 21.0-28.4)
  - Crisaborole: 35.8\% (95\% CI: 31.4-40.3)
  - \(P = 0.006\)

**ISGA Clear or Almost Clear**

- **PMH of asthma/allergies**
  - Vehicle: 32.0\% (95\% CI: 28.3-35.8)
  - Crisaborole: 48.4\% (95\% CI: 43.5-53.3)
  - \(P < 0.0001\)

- **No PMH of asthma/allergies**
  - Vehicle: 40.6\% (95\% CI: 36.3-44.9)
  - Crisaborole: 52.4\% (95\% CI: 47.5-57.3)
  - \(P = 0.01\)

**SPS Improvement**\(^b\)

- **PMH of asthma/allergies**
  - Vehicle: 20.4\% (95\% CI: 16.8-24.0)
  - Crisaborole: 33.6\% (95\% CI: 29.9-37.3)
  - \(P = 0.0003\)

- **No PMH of asthma/allergies**
  - Vehicle: 21.7\% (95\% CI: 18.1-25.4)
  - Crisaborole: 38.9\% (95\% CI: 34.2-43.6)
  - \(P = 0.0002\)

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*ISGA, Investigator’s Static Global Assessment; PMH, past medical history; SPS, Severity of Pruritus Scale; TEAE, treatment-emergent adverse event.*

\(^a\)ISGA success is defined as an ISGA of clear or almost clear with ≥2-grade improvement from baseline.

\(^b\)Improvement in SPS is defined as weekly average SPS score ≤1 point with a ≥1-point improvement from baseline.
Safety Profile and Discussion

- Among crisaborole-treated patients with asthma/allergies
  - 95 (16.2%) experienced mild TEAEs
  - 99 (16.9%) experienced moderate TEAEs
  - 14 (2.4%) experienced severe TEAEs

- The most common treatment-related TEAE was application site pain
  - Patients with asthma/allergies: crisaborole, 5.1%; vehicle, 1.7%
  - Patients without asthma/allergies: crisaborole, 3.5%; vehicle, 0.5%

- 6 crisaborole-treated patients with asthma/allergies experienced serious TEAEs (application site infection, asthma, laceration, Kawasaki disease, pneumonia, suicidal ideation; each n=1) considered unrelated to treatment
  - 1 vehicle-treated patient with asthma/allergies experienced a treatment-related serious TEAE (cellulitis)

- Exacerbation of asthma was reported in 9 patients in the asthma/allergies cohort, and exacerbation of allergic rhinitis was reported in 3 patients in the asthma/allergies cohort
  - Anaphylaxis was not reported in any subgroup

**AE (all cause), n (%)**

<table>
<thead>
<tr>
<th></th>
<th>Vehicle n=301</th>
<th>Crisaborole n=585</th>
<th>Vehicle n=198</th>
<th>Crisaborole n=427</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application site pain</td>
<td>5 (1.7)</td>
<td>30 (5.1)</td>
<td>1 (0.5)</td>
<td>15 (3.5)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>6 (2.0)</td>
<td>25 (4.3)</td>
<td>11 (5.6)</td>
<td>9 (2.1)</td>
</tr>
<tr>
<td>Viral upper respiratory tract infection</td>
<td>7 (2.3)</td>
<td>15 (2.6)</td>
<td>4 (2.0)</td>
<td>11 (2.6)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>4 (1.3)</td>
<td>11 (1.9)</td>
<td>4 (2.0)</td>
<td>13 (3.0)</td>
</tr>
<tr>
<td>Cough</td>
<td>6 (2.0)</td>
<td>11 (1.9)</td>
<td>3 (1.5)</td>
<td>5 (1.2)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>3 (1.0)</td>
<td>8 (1.4)</td>
<td>2 (1.0)</td>
<td>9 (2.1)</td>
</tr>
</tbody>
</table>

**TEAE of special interest, n (%)**

<table>
<thead>
<tr>
<th></th>
<th>Vehicle n=301</th>
<th>Crisaborole n=585</th>
<th>Vehicle n=198</th>
<th>Crisaborole n=427</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>1 (0.3)</td>
<td>8 (1.4)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>0</td>
<td>3 (0.5)</td>
<td>1 (0.5)</td>
<td>0</td>
</tr>
<tr>
<td>Anaphylaxis</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**DISCUSSION**

- Crisaborole is effective in treating patients aged ≥2 years with mild-to-moderate AD irrespective of a history of asthma/allergies, and no new safety concerns were identified
- Crisaborole may be suitable for the management of AD in patients with or without comorbid asthma/allergies

AD, atopic dermatitis; AE, adverse event; PMH, past medical history; TEAE, treatment-emergent adverse event.