Efficacy of Apremilast, an Oral Phosphodiesterase 4 Inhibitor, for Palmoplantar Psoriasis in Patients With Moderate to Severe Plaque Psoriasis in Phase 2 and Phase 3 (ESTEEM) Trials

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Disclosures

• Dr. Robert Bissonnette has been an investigator and consultant for AbbVie, Amgen, Celgene, Eli Lilly, Galderma, Incyte, Janssen, LEO Pharma, Merck, Novartis, Pfizer, and Tribute.

• Dr. Jennifer Cather has been an investigator and consultant for Amgen, Celgene, Galderma, Merck, Novartis, and Pfizer, and has served on the advisory board for AbbVie and Janssen OrthoBiotech.

• Dr. Phoebe Rich has been an investigator for AbbVie, Amgen, Celgene, Eli Lilly, Janssen-Ortho, Merck, Novartis, and Pfizer.

• Dr. Alan Menter has been an investigator and consultant for AbbVie, Allergan, Amgen, Convoy Therapeutics, Eli Lilly, Janssen Biotech, LEO Pharma, Novartis, Pfizer, Syntrix, and Wyeth; served on the advisory board for AbbVie, Allergan, Amgen, Boehringer Ingelheim, Genentech, Janssen Biotech, LEO Pharma, and Pfizer; has been a speaker for AbbVie, Amgen, Janssen Biotech, LEO Pharma, and Wyeth; has been an investigator for ApoPharma, Celgene, Merck, and Symbio; and has been a consultant for XenoPort.

• Dr. Michael Sebastian has been an investigator and/or consultant for Amgen, Celgene, Eli Lilly, Galderma, Janssen-Cilag, Merck, Novartis, and Pfizer.

• Dr. Mark Goodfield has received honoraria as an advisory board member and has been an investigator for AbbVie, Celgene, Galderma, Janssen-Cilag, LEO Pharma, Novartis, and Pfizer.

• Dr. Carlos Ferrandiz has no financial relationships to disclose.

• ChiaChi Hu and Dr. Robert M. Day are employees of Celgene Corporation.
Abstract

**Background:** Apremilast (APR), an oral phosphodiesterase 4 inhibitor, works intracellularly to regulate inflammatory mediators. The efficacy of APR for the treatment of palmoplantar psoriasis was evaluated in a subset of pts from 1 phase 2B trial (PSOR005) and 2 phase 3 trials (ESTEEM 1 and 2) who also had palmoplantar psoriasis.

**Methods:** Pts with moderate to severe plaque psoriasis (PASI ≥12, BSA ≥10%, sPGA ≥3 [sPGA ≥3 for ESTEEM 1 and 2 only]) were randomized (PSOR005, 1:1:1:1 to APR 10 mg BID, APR 20 mg BID, APR 30 mg BID [APR30], or placebo [PBO]; ESTEEM 1 and 2, 2:1 to APR30 or PBO). At Week 16 PBO pts were re-randomized to APR 20 mg BID or APR30 to Week 24 (PSOR005), or switched to APR30 to Week 32 (ESTEEM 1 and 2). This was followed by an active treatment extension study (PSOR005) or a randomized treatment withdrawal phase (ESTEEM 1 and 2) to Week 52. Analyses at Week 16 included (1) Palmoplantar Psoriasis Physician Global Assessment (PPPGA; range: 0 [clear] to 4 [severe]) score of 0 (clear) or 1 (almost clear) in pts with baseline (BL) PPPGA ≥3; (2) PPPGA of 0 or 1 with ≥1-point improvement among pts with BL PPPGA ≥1; and (3) ≥2-point improvement from BL in PPPGA regardless of severity at BL.

**Results:** In pts with BL PPPGA ≥3, achievement of a PPPGA score of 0 or 1 was significantly greater with APR30 than PBO in PSOR005 (6/9 [66.7%] vs 2/10 [20.0%], \(P=0.0397\)) and ESTEEM 2 (17/26 [65.4%] vs 5/16 [31.3%], \(P=0.0315\)); however there was no significant difference in ESTEEM 1 (22/57 [38.6%] vs 8/26 [30.8%], \(P=0.4912\)). In pts with BL PPPGA ≥1, a PPPGA score of 0 or 1 with ≥1-point improvement was achieved by a significantly larger proportion of pts treated with APR30 than PBO in PSOR005 (19/27 [70.4%] vs 7/22 [31.8%], \(P=0.0072\)); ESTEEM 1 (107/169 [63.3%] vs 38/85 [44.7%], \(P=0.0047\)); and ESTEEM 2 (55/78 [70.5%] vs 17/46 [37.0%], \(P=0.0003\)). Regardless of severity at BL, a larger proportion of pts treated with APR30 than PBO demonstrated a ≥2-point improvement from BL in PPPGA in PSOR005 (12/27 [44.4%] vs 4/22 [18.2%], \(P=0.051\)); ESTEEM 1 (58/169 [34.3%] vs 18/85 [21.2%], \(P=0.031\)); and ESTEEM 2 (36/78 [46.2%] vs 8/46 [17.4%], \(P=0.0012\)). Across all 3 trials, the most common adverse events with APR30 were diarrhea, nausea, URTI, nasopharyngitis, tension headache, and headache.

**Conclusion:** APR30 improved the severity of palmoplantar psoriasis in a subset of pts from 3 trials evaluating APR in pts with moderate to severe plaque psoriasis.
Psoriasis is a chronic, systemic inflammatory disease that affects 1% to 3% of the world’s population.\textsuperscript{1-3}

Palmoplantar psoriasis is among the most challenging forms to treat.\textsuperscript{4}

Apremilast, an oral PDE4 inhibitor, works intracellularly to regulate inflammatory mediators\textsuperscript{5}

Apremilast was approved by the FDA in 2014 and by the EC in 2015 for treatment of psoriasis and psoriatic arthritis.\textsuperscript{6,7}

ESTEEM is a phase 3 clinical trial program comprising 2 randomized placebo-controlled studies evaluating the efficacy, safety, and tolerability of apremilast for the treatment of moderate to severe plaque psoriasis.

The objective of this presentation is to evaluate the efficacy of apremilast at Week 16 for the treatment of palmoplantar psoriasis in a subset of patients with palmoplantar psoriasis from the 2 ESTEEM trials as well as a phase 2B trial (PSOR-005).

Adult patients aged 18 years and older with moderate to severe plaque psoriasis

**Randomize** (1:1:1:1)
- Apremilast 30 mg BID *
- Apremilast 20 mg BID *
- Apremilast 10 mg BID *
- Placebo

**Screen**

**Period A**
- Week 0

**Period B**
- Week 16
- Week 24

Optional enrollment in long-term extension study
Observational 4-week follow-up phase §

*Doses of apremilast were titrated during the first week of administration and at Week 16 when placebo patients were switched to apremilast. § For patients who do not enter the long-term extension study.*
• Adult patients aged 18 years and older with moderate to severe plaque psoriasis

*Doses of apremilast were titrated during the first week of administration and at Week 16 when placebo patients were switched to apremilast. §Patients restarted apremilast at the time of loss of effect vs. baseline (loss of PASI-75, ESTEEM 1; loss of 50% of the PASI improvement obtained at Week 32, ESTEEM 2) but no later than Week 52. ‡Patients initially on placebo or randomized to apremilast 30 mg BID who did not attain PASI-75/PASI-50 were able to add topicals and/or ultraviolet B at Week 32 at the discretion of the investigator.
PPPGA 0 or 1 Achievement at Week 16 in Patients With Baseline PPPGA ≥3

*P<0.05 vs. placebo.

Includes patients with Palmoplantar Psoriasis Physician Global Assessment (PPPGA) ≥3, indicating moderate or severe palmoplantar psoriasis, at baseline; all data are last observation carried forward. n/m=number of patients with response/number of patients with sufficient data for evaluation.
PPPGA 0 or 1 Achievement (With ≥1-Point Improvement) at Week 16 in Patients With Baseline PPPGA ≥1

- Includes patients with PPPGA ≥1, indicating the presence of any palmoplantar psoriasis, at baseline; all data are last observation carried forward. n/m=number of patients with response/number of patients with sufficient data for evaluation.

*P<0.01 vs. placebo.
PASI-75 in Patients Who Achieved PPPGA 0 or 1 at Week 16 (With Baseline PPPGA ≥3)

Includes patients with PPPGA ≥3, indicating moderate or severe palmoplantar psoriasis, at baseline, and PPPGA 0 or 1 at Week 16; all data are last observation carried forward. PASI-75=75% decrease from baseline in Psoriasis Area and Severity Index; n/m=number of patients with response/number of patients with sufficient data for evaluation.
## Most Common Adverse Events (≥5%) in Period A (Weeks 0 to 16*)

### PSOR-005 and ESTEEM 1 & 2 (Pooled)

<table>
<thead>
<tr>
<th>Patients, n (%)</th>
<th>Placebo n=506</th>
<th>EAIR/100 Patient-Years</th>
<th>Apremilast 30 mg BID n=920</th>
<th>EAIR/100 Patient-Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>32 (6.3)</td>
<td>24.1</td>
<td>160 (17.4)</td>
<td>72.4</td>
</tr>
<tr>
<td>Nausea</td>
<td>35 (6.9)</td>
<td>26.4</td>
<td>155 (16.8)</td>
<td>69.8</td>
</tr>
<tr>
<td>URTI</td>
<td>31 (6.1)</td>
<td>22.8</td>
<td>84 (9.1)</td>
<td>33.7</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>36 (7.1)</td>
<td>26.8</td>
<td>66 (7.2)</td>
<td>26.3</td>
</tr>
<tr>
<td>Tension headache</td>
<td>21 (4.2)</td>
<td>15.5</td>
<td>75 (8.2)</td>
<td>30.9</td>
</tr>
<tr>
<td>Headache</td>
<td>19 (3.8)</td>
<td>14.0</td>
<td>55 (6.0)</td>
<td>22.1</td>
</tr>
</tbody>
</table>

*Placebo-controlled period.
AE=adverse event; EAIR= exposure-adjusted incidence rate; URTI=upper respiratory tract infection.
In this analysis of the phase 2B PSOR-005 and phase 3 ESTEEM 1 and 2 clinical trials:

• Apremilast 30 mg BID improved palmoplantar psoriasis in a subset of patients with moderate to severe chronic plaque psoriasis who had palmoplantar involvement.

• Apremilast demonstrated an acceptable safety profile and was generally well tolerated in this population.