Safety and Efficacy of Apremilast Through 104 Weeks in Patients With Moderate to Severe Psoriasis Who Continued on Apremilast or Switched From Etanercept Treatment in the LIBERATE Study

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INTRODUCTION

• Psoriasis is a chronic, systemic, inflammatory disease affecting 1% to 4% of the world population. –
• Currently estimated to affect over 150,000,000 people worldwide. Studies have shown that moderate-to-severe psoriasis is associated with decreased quality of life and an increased risk of comorbidities, including obesity, diabetes, cardiovascular disease, and depression. –
• Psoriasis is driven by the overproduction of cytokines that activate keratinocytes and inflammatory cell infiltration. –
• Apremilast, an oral small-molecule phosphodiesterase 4 inhibitor, was intrinsically more efficacious in the production of inflammatory mediators. –
• Apremilast was approved by the US Food and Drug Administration and by the European Commission for treatment of psoriatic arthritis.

METHODS

Patients

Key Inclusion Criteria

• Participants who had chronic plaque psoriasis for ≥12 months who were candidates for phototherapy and had no prior exposure to biologic therapy for the treatment of psoriatic arthritis or plaque psoriasis.

• Moderate to severe plaque psoriasis, as determined by the Physician Global Assessment of Psoriasis (PGA) score ≥3 (very severe) or ≥4 (severe).

• ≥10% body surface area (BSA) involvement.

• Moderate to severe psoriatic arthritis, as determined by the Physician Global Assessment of Psoriatic Arthritis (PGA).

• ≥12 months of prior systemic therapy, ≥1 post-treatment PASI evaluations; Week 16 analysis included patients with PASI score >20.

Key Exclusion Criteria

• Other clinically significant or major uncontrolled diseases, serious infections, including latent, active, or history of incompletely treated tuberculosis.

• Receipt of biologic for psoriatic arthritis within 8 weeks or biologic for psoriasis within 4 weeks of randomization.

Study Design

• Trial consisted of a screening/phase 1 (12-week) run-in phase, double blind, placebo-controlled phase, and an open-label extension phase (28 weeks).

• PASI, PGA, DLQI, and NAPSI were assessed at baseline and at weeks 12, 16, and 24. PASI was analyzed using a last observation carried forward (LOCF) methodology.

Statistical Analysis

• Comparisons between groups were conducted for the PASI controlled phase in the modified intent-to-treat (mITT) population. All intent-to-treat patients were included in all primary and secondary analysis with the last observation carried forward (LOCF) methodology. Week 16 analysis included patients with ≥12 months of prior systemic therapy and ≥1 post-treatment PASI evaluations.

• The setting population consisted of patients who were randomized and received ≥1 dose of study medication.

• An internal endpoint committee was used to evaluate the results of NAPSI scores in patients with psoriatic arthritis.

• Missing values were imputed using the last observation carried forward (LOCF) methodology.

RESULTS

Table 1. Baseline Patient and Demographic Characteristics

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Placebo</th>
<th>Apremilast</th>
<th>Placebo</th>
<th>Apremilast</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>35 (1)</td>
<td>36 (7)</td>
<td>34 (1)</td>
<td>35 (7)</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>19/21</td>
<td>20/19</td>
<td>19/21</td>
<td>20/19</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>10 (3)</td>
<td>10 (2)</td>
<td>10 (3)</td>
<td>10 (2)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>28.5 (5)</td>
<td>28.7 (5)</td>
<td>28.5 (5)</td>
<td>28.7 (5)</td>
</tr>
</tbody>
</table>

Efficacy

PASI 75 Response

• At Week 16, a ≥75% reduction from baseline in PASI score (PASI-75) was achieved by significantly more patients receiving APR compared with ETN (PASI-75 (cont’d)

• The PASI-75 response achieved at Week 16 was sustained through Week 164 in patients continuing APR vs switching to ETN at Week 104 (AUROC) (Figure 6).

Scalp and Nail Response

• Improvements in nail psoriasis were achieved with APR at Week 16, and continued APR treatment over 104 weeks resulted in sustained through Week 104.

• No increase in incidence of adverse events was found comparing APR with ETN and no increase in serious adverse events in patients in the APR group, with mild-to-moderate psoriasis and possibly mild-to-moderate etanercept.

• At end of Week 16 and near the end of the ARN extension phase, 20% of patients were still in situ, and possibly in the previous treatment.

DISCLOSURES

• All authors contributed to the design of the study and the analysis and drafting of the manuscript.

• All authors have read and approved the final version of the manuscript.

• Contributions of the authors are described in the acknowledgments section.

• All authors have no relevant conflicts of interest or financial relationships to disclose.

REFERENCES


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