Deucravacitinib, an Oral, Selective Tyrosine Kinase 2 (TYK2) Inhibitor, Versus Placebo and Apremilast in Moderate to Severe Plaque Psoriasis: Efficacy Analysis by Baseline Disease Characteristics From the Phase 3 POETYK PSO-1 and PSO-2 Trials

Introduction

- Deucravacitinib is a novel, oral, selective tyrosine kinase 2 (TYK2) inhibitor with a unique mechanism of action distinct from Janus kinase (JAK) 1/2/3 inhibition (Figure 1).
- Bonds to the TYK2 regulatory domain with high selectivity and inhibits TYK2 in an allosteric mechanism.
- Has >60-fold greater selectivity for TYK2 vs JAK 1/3 and JAK 2/3/6.
- Reduced selectivity for TYK2 was observed in the Phase 2 trials.
- Inhibits TYK2-mediated signaling of cytokines involved in psoriasis pathogenesis, including IL-12, IL-23, IL-10, and Type I interferons.

Results

Baseline patient demographics and disease characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Placebo</th>
<th>Deucravacitinib 6 mg BID</th>
<th>Apremilast 5 mg QD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, median (IQR)</td>
<td>46.5 (13.5)</td>
<td>47.1 (13.4)</td>
<td>47.5 (13.3)</td>
</tr>
<tr>
<td>Weight, kg, median (IQR)</td>
<td>81.0 (11.2)</td>
<td>80.7 (10.9)</td>
<td>81.8 (10.6)</td>
</tr>
<tr>
<td>Sex, % males</td>
<td>55.0</td>
<td>55.3</td>
<td>56.7</td>
</tr>
<tr>
<td>Age at disease onset (&lt;20 y, &gt;20 y)</td>
<td>52.9 (21.9)</td>
<td>55.1 (22.6)</td>
<td>51.1 (20.6)</td>
</tr>
<tr>
<td>Duration of disease (&lt;10 y, &gt;10 y)</td>
<td>55.2 (21.5)</td>
<td>52.9 (22.6)</td>
<td>55.1 (22.0)</td>
</tr>
</tbody>
</table>

Methods

Key design elements

- The POETYK PSO-1 and PSO-2 study designs are shown in Figure 2.
- Key eligibility criteria:
  - Moderate to severe plaque psoriasis (PSO)-IIA (N=324, body surface area [BSA] >10%)
  - Stratified by geographic region, body weight, and prior biologic use
-Coprsynergists: The proportion of patients who achieved PASI 75 and PASI 90, and IGA 0/1 response was similar between deucravacitinib and placebo.

Data from subgroups with the following baseline disease characteristics in PSO-1 and PSO-2 were pooled and analyzed for the coprsynergists vs placebo and BID in patients treated at week 16:

- PASI score: 0 to 100
- BSA score: 0 to 4

Conclusions

- Patients treated with deucravacitinib had PASI 75 and IGA 0/1 responses that were superior to placebo and bupropion, and statistically similar or better for all other disease measures, including measures of baseline disease severity, comorbidities, and age at disease onset.
- These data support the potential treatment of choice for moderate to severe plaque psoriasis.

References


Acknowledgments

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- Grants and personal fees: AbbVie, Bristol Myers Squibb, Eli Lilly, Janssen, Leo Pharma, and Novartis; Personal fees: Boehringer Ingelheim/Parexel, Celgene, Eli Lilly, Janssen, Leo Pharma, Merck, Pfizer, and UCB

Figure 1. Mechanism of action of deucravacitinib

Figure 2. Study designs

Figure 3. PASI 75 and IGA 0/1 response at Week 16 for Placebo and PSO-2

Figure 4. PASI 75 and IGA 0/1 response at Week 16 for PSO-1 and PSO-2

Figure 5. PASI 75 and IGA 0/1 response at Week 16 for Placebo and PSO-1

Figure 6. PASI 75 response at Week 16: PSO-1 and PSO-2 pooled analysis – efficacy of deucravacitinib in patients and placebo in pre-specified subgroups

Figure 7. IGA 0/1 response at Week 16: PSO-1 and PSO-2 pooled analysis – efficacy of deucravacitinib in patients and placebo in pre-specified subgroups

Figure 8. IGA 0/1 response at Week 16: PSO-1 and PSO-2 pooled analysis – efficacy of deucravacitinib in patients and placebo in all pre-specified subgroups

Figure 9. IGA 0/1 response at Week 16: PSO-1 and PSO-2 pooled analysis – efficacy of deucravacitinib in patients and placebo in pre-specified subgroups

Figure 10. PASI 75 response at Week 16: PSO-1 and PSO-2 pooled analysis – efficacy of deucravacitinib in patients and placebo in all pre-specified subgroups

Figure 11. PASI 75 response at Week 16: PSO-1 and PSO-2 pooled analysis – efficacy of deucravacitinib in patients and placebo in pre-specified subgroups

Figure 12. PASI 75 response at Week 16: PSO-1 and PSO-2 pooled analysis – efficacy of deucravacitinib in patients and placebo in all pre-specified subgroups

Figure 13. PASI 75 response at Week 16: PSO-1 and PSO-2 pooled analysis – efficacy of deucravacitinib in patients and placebo in pre-specified subgroups

Figure 14. PASI 75 response at Week 16: PSO-1 and PSO-2 pooled analysis – efficacy of deucravacitinib in patients and placebo in all pre-specified subgroups

Figure 15. PASI 75 response at Week 16: PSO-1 and PSO-2 pooled analysis – efficacy of deucravacitinib in patients and placebo in pre-specified subgroups

Figure 16. PASI 75 response at Week 16: PSO-1 and PSO-2 pooled analysis – efficacy of deucravacitinib in patients and placebo in all pre-specified subgroups

Figure 17. PASI 75 response at Week 16: PSO-1 and PSO-2 pooled analysis – efficacy of deucravacitinib in patients and placebo in pre-specified subgroups

Figure 18. PASI 75 response at Week 16: PSO-1 and PSO-2 pooled analysis – efficacy of deucravacitinib in patients and placebo in all pre-specified subgroups

Figure 19. PASI 75 response at Week 16: PSO-1 and PSO-2 pooled analysis – efficacy of deucravacitinib in patients and placebo in pre-specified subgroups

Figure 20. PASI 75 response at Week 16: PSO-1 and PSO-2 pooled analysis – efficacy of deucravacitinib in patients and placebo in all pre-specified subgroups

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Figure 23. PASI 75 response at Week 16: PSO-1 and PSO-2 pooled analysis – efficacy of deucravacitinib in patients and placebo in pre-specified subgroups

Figure 24. PASI 75 response at Week 16: PSO-1 and PSO-2 pooled analysis – efficacy of deucravacitinib in patients and placebo in all pre-specified subgroups

Figure 25. PASI 75 response at Week 16: PSO-1 and PSO-2 pooled analysis – efficacy of deucravacitinib in patients and placebo in pre-specified subgroups

Figure 26. PASI 75 response at Week 16: PSO-1 and PSO-2 pooled analysis – efficacy of deucravacitinib in patients and placebo in all pre-specified subgroups