Cumulative benefit over 52 weeks comparing initiation with deucravacitinib versus apremilast in patients with moderate to severe plaque psoriasis: A post hoc analysis of POETYK PSO-1 trial results stratified by prior treatment

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Introduction
- Deucravacitinib, an oral, selective, alanine: tyrosine kinase 2 inhibitor, is approved in the US, EU, and other countries for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy. 1
- Recent phase 3 clinical trial results of POETYK PSO-1 demonstrated superior response rates for deucravacitinib in patients treated for 24 weeks, and deucravacitinib responses were maintained at 52 weeks with continuous treatment. 2
- Calculating the cumulative clinical benefit from the area under the curve (AUC) allows clinicians and researchers to measure the totality of an intervention's effect in a patient population over a defined time period based on a patient's time-to-event history. 3
- A recent study found that initiating deucravacitinib as the first-line rather than second-line treatment after failure to respond with a prior treatment may optimize the clinical benefit of the drug. 4

Objective
- To evaluate the cumulative clinical benefit of deucravacitinib or apremilast (as randomized) from baseline to Week 52, stratified by prior biologic and systemic therapies used based on data from POETYK PSO-1

Methods

Data source
- POETYK PSO-1 was a multinational, randomized, double-blind, placebo- and active comparator controlled phase 3 study to evaluate safety and efficacy of deucravacitinib compared with apremilast in adults with moderate to severe plaque psoriasis. 2

Study design
- This post hoc analysis used patient-level data from the POETYK PSO-1 trial (Figure 1):
  - Deucravacitinib arm: patients initiated with and continued on deucravacitinib, regardless of response status.
  - Apremilast initiators arm: patients initiated with apremilast; at Week 24, responders with ≥50% improvement from baseline in Psoriasis Area and Severity Index (PASI) 50 continued with apremilast, while PASI 50 nonresponders crossed over to deucravacitinib for 28 weeks. Both the placebo arm and the deucravacitinib arm were included in the cumulative clinical benefit analysis. 2

Study population
- Patients were ≥18 years of age and had moderate to severe plaque psoriasis, PASI score of ≥12, static Physician Global Assessment (sPGA) score of ≥3, and body surface area involvement of ≥10%

Figure 1. Study design comparing data from 3 arms of POETYK PSO-1

Statistical analysis
- Cumulative clinical benefit from randomization to Week 52 was determined by the total area under the curve for clinical response over 52 weeks (AUCclinical) in each arm:
  - Clinical response was measured by the change in PASI score from baseline to Week 52 (PASI 75) and the proportion of patients with PASI 75 responder status at each time point over 52 weeks.
  - Prior biologic and systemic use subgroups were analyzed for each efficacy endpoint.
  - Total AUCclinical was calculated for each patient, separating for each efficacy endpoint, using the trapezoidal rule:
    \[ \text{Total } AUC_{\text{clinical}} = \sum_{i=1}^{n} \left[ \frac{Y_i + Y_{i+1}}{2} \right] \Delta t_{i} \]
    where \( Y_i \) denotes the responder status at time point \( i \), \( \Delta t_i \) denotes the time interval from the previous to the current time point.

- Analysis of covariance (ANOVA) models were used to adjust for each stratification factor (geographic region, prior biologic initiators, systemic naive status, prior systemic initiators) at time point
- Adjusted AUCclinical results were standardized as a percentage of the maximum possible benefit (% of baseline to Week 52) to facilitate interpretation
- Nonparametric Kaplan-Meier survival curves were used for the time to achievement of the primary endpoint

Results

Table 1. AUCclinical, Week 75, by prior treatment use

<table>
<thead>
<tr>
<th>Prior treatment use</th>
<th>Deucravacitinib</th>
<th>Apremilast</th>
<th>Difference in clinical responder percentage</th>
<th>p-value</th>
<th>Benefit ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic naive</td>
<td>60.0%</td>
<td>38.1%</td>
<td>21.9%</td>
<td>&lt; 0.001</td>
<td>1.57</td>
</tr>
<tr>
<td>Systemic experienced</td>
<td>51.7%</td>
<td>38.0%</td>
<td>13.7%</td>
<td>&lt; 0.001</td>
<td>1.34</td>
</tr>
</tbody>
</table>

Discussions

- Deucravacitinib initiators obtained greater cumulative clinical benefit than apremilast initiators in all subgroups and for all efficacy outcomes examined.
- The results of this study may help clinicians select an optimal oral treatment pathway for patients with psoriasis

Strengths and limitations

Strengths
- Evaluation of cumulative clinical benefit using AUC clinical allowed continuous capture of treatment impact for patients with psoriasis
- Estimating cumulative clinical benefit utilizing treatment crossover data from the POETYK PSO-1 trial provided insights into the cumulative clinical benefit of different treatment pathways
- The crossover data better reflect real-world treatment patterns of patients with multiple lines of therapy

Limitations
- Calculating AUC required complete data for each patient at each measured time point; in line with the study protocol, missing data were imputed using carryover assumption; a conservative approach to imputation
- This post hoc analysis may have been introduced bias

Conclusions

- Initiating treatment with deucravacitinib resulted in greater cumulative clinical benefit over 52 weeks than apremilast for patients with moderate to severe plaque psoriasis
- The greater cumulative clinical benefit was observed, regardless of prior treatment
- The benefit ratio of initiating with deucravacitinib or apremilast was between 1.32 and 1.56 across all efficacy endpoints and all prior treatment subgroups examined

- Initiating with deucravacitinib as the first-line therapy rather than switching to deucravacitinib as the second-line therapy after response failure with apremilast may improve clinical outcomes in patients

References

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