Optimizing the treatment sequence: the cumulative clinical benefit of treatment initiation with deucravacitinib versus apremilast over 52 weeks in patients with moderate to severe plaque psoriasis from the POETYK PSO-1 trial

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1Keck School of Medicine, University of Southern California, Los Angeles, CA; 2Bristol Myers Squibb, Princeton, NJ; 3OPEN Health, Bethesda, MD; 4Bristol Myers Squibb, Boussy, Switzerland

Synopsis

• Deucravacitinib is an oral, selective, allosteric tyrosine kinase 2 inhibitor approved by the US Food and Drug Administration for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

• In the recent phase 3 clinical trial POETYK PSO-1, patients with moderate to severe plaque psoriasis were randomized 2:1:1 to deucravacitinib, placebo, or apremilast1—Patients receiving apremilast who did not achieve at least 50% improvement from baseline in Psoriasis Area and Severity Index score (PSI) by Week 24 crossed over to deucravacitinib—At Week 52, 46.3% of these patients achieved at least 75% improvement from baseline in PSI score (PSI-J) 75), and 41.6% achieved a change in PGA score of 0 vs 1; PSI-J/PGA 0/11—Patients receiving apremilast who achieved PSI-J 50 at Week 24 continued with apremilast—Patients who received placebo are not represented in this analysis—This study evaluated the cumulative clinical benefit of initiating with deucravacitinib vs apremilast to determine the treatment pathway that provides greater benefit to the patient—The cumulative clinical benefit reflects the total time patients spend in a state of therapeutic response1

• The results of this study indicate that initiating deucravacitinib as a first-line treatment offers greater benefits over time compared with initiating with apremilast.

Objective

• To evaluate the cumulative clinical benefit of initiating with deucravacitinib vs apremilast from baseline to Week 52 based on data from POETYK PSO-1

Methods

• POETYK PSO-1 was a multicenter, randomized, double-blind, placebo- and active comparator-controlled study1

— Patients were aged ≥18 years and had moderate to severe plaque psoriasis (PSI score ≥12, PGA score ≥3), and body surface area involvement ≥10%

— Co-morbid efficacy endpoints were PSI-J 75 and PSI-J/PGA 0/1

— Nonresponder imputation was used for missing data

• This post hoc analysis compared data from 2 arms in 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, PSI-J 50 responders continued with apremilast while PSI-J 50/nonresponders crossed over to deucravacitinib

• Cumulative clinical benefit from randomization to Week 52 was determined by the total area under the curve of clinical response over 52 weeks (AUC0–52) in each arm

— AUC analysis has been employed to evaluate outcomes over time in clinical trials, as the AUC reflects the intensity and duration, as well as the magnitude, of response2

• While assessments of discrete time points identify static responses, the AUC approach captures cumulative treatment effects over time

— This study determined the AUC using data at a patient level (responder status at each time point over 52 weeks)

• Total AUC0–52 was calculated separately for each efficacy endpoint, using the trapezoidal rule

— Total AUC0–52 = \sum_{i=1}^{12} (T_i-0.5) \cdot \left( P_i + P_{i+1} \right) \cdot \left( 0.5 \right)

— Where \( T_i \) denotes the time points of Weeks 0, 1, 2, 4, 6, 12, and 16, then every 4 weeks thereafter through Week 52, and P denotes the response (yes, no) at each time point,

— The result was standardized as a percentage of maximum possible AUC(J/PGA 0/1) [× weeks] and aggregated to the population level

— Adjusted AUC0–52 were calculated, representing the relative cumulative clinical benefit of the 2 treatment pathways for achieving PSI-J 75 or PGA 0/1 over the 52-week period

Results

Table 1. Cumulative clinical benefit measured by PASI 75 response over 52 weeks

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Deucravacitinib</th>
<th>Apremilast</th>
<th>Difference in estimate</th>
<th>P-value</th>
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<tr>
<td>Adjusted AUC0–52 wk, % × weeks</td>
<td>2978.72</td>
<td>1988.06</td>
<td>990.66</td>
<td>0.001</td>
<td>1.50</td>
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Figure 2. Standardized adjusted AUC0–52 wk

Table 2. Cumulative clinical benefit measured by sPGA 0/1 response over 52 weeks

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Figure 3. Standardized adjusted AUC0–52 wk

Conclusions

• Initiating with deucravacitinib resulted in greater cumulative benefits over 52 weeks than initiating with apremilast

— Deucravacitinib initiators spend ≈150% more time in therapeutic response over 52 weeks compared with apremilast initiators

— Initiating with deucravacitinib as the first line rather than switching to deucravacitinib as the second line after failure to respond with apremilast may optimize the clinical benefit that patients receive

References


Acknowledgments

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Disclosures

• AMA: Grants and personal fees: AbbVie, Bristol Myers Squibb, Eli Lilly, Janssen, Leo Pharma, and Novartis; Personal fees: Boehringer Ingelheim/Pfizer, Crucence, Dermotamir, Genentech, GlaxoSmithKline, Hema Therapeutics, Merck, Modernizing Medicine, Onco-Dermatologics, Pﬁzer, Regeneron, Sanofi Genzyme, Science 37, Sun Pharma, and Valeant; Grants: Derrera, Kyowa Hakko Kirin, and UCB, outside the submitted work

• SFP, VF, PM: AUC Employees of and may own stock options in Bristol Myers Squibb

• WM, NC: Employees of OPEN Health, which has received consulting fees from Bristol-Myers Squibb
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Methods
• In the recent phase 3 clinical trial POETYK PSO-1, patients with moderate to severe plaque psoriasis were initiated either with deucravacitinib or apremilast.
• This post hoc analysis compared data from 2 arms in the POETYK PSO-1 trial.

Synopsis
Optimizing the treatment sequence: the cumulative clinical benefit of treatment initiation with deucravacitinib versus apremilast over 52 weeks

Results
• This study evaluated the cumulative clinical benefit of initiating with deucravacitinib vs apremilast to determine the treatment pathway that provides greater benefit to the patient.
• Standardized average cumulative sPGA 0/1 response over 52 weeks among patients initiating with deucravacitinib was 57.3% compared with 38.2% in patients initiating with apremilast (including 87 patients who continued apremilast while PASI 50 nonresponders crossed over to deucravacitinib).

Discussion
• While assessments at discrete time points identify static responses, the AUC approach captures cumulative pathways for achieving PASI 75 or sPGA 0/1 over the 52-week period.
• This study determined the AUC using data at a patient level (responder status at each time point over the 52-week period).
• Apremilast initiators arm: 4, 8, 12, and 16, then every 4 weeks thereafter through Week 52, and Pi denotes the response (yes = 1; no = 0).

Table 1

<table>
<thead>
<tr>
<th>Region (United States, China, Japan, rest of the world [ROW])</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deucravacitinib initiators, n = 332</td>
</tr>
<tr>
<td>PASI 50 at Week 24</td>
</tr>
<tr>
<td>PASI 75 at Week 52</td>
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Figure 1
Figure 1. Study design comparing data from 2 arms of POETYK PSO-1

Table 2

<table>
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<tr>
<th>Deucravacitinib, n = 332</th>
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<tbody>
<tr>
<td>Standardized average cumulative response, %</td>
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<tr>
<td>Standardized adjusted AUC0–52wk, % × weeks</td>
<td>2612.82</td>
</tr>
<tr>
<td>CI</td>
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<td>P</td>
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Table 2 shows the cumulative clinical benefit measured by sPGA 0/1 response over 52 weeks.
Synopsis

- Deucravacitinib is an oral, selective, allosteric tyrosine kinase 2 inhibitor approved by the US Food and Drug Administration for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

- In the recent phase 3 clinical trial POETYK PSO-1, patients with moderate to severe plaque psoriasis were randomized 2:1:1 to deucravacitinib, placebo, or apremilast.
  - Patients receiving apremilast who did not achieve at least 50% improvement from baseline in Psoriasis Area and Severity Index score (PASI 50) at Week 24 crossed over to deucravacitinib.
  - At Week 52, 46.3% of these patients achieved at least 75% improvement from baseline in PASI score (PASI 75), and 42.6% achieved a static Physician Global Assessment (sPGA) score of 0 or 1 (sPGA 0/1).
  - Patients receiving apremilast who achieved PASI 50 at Week 24 continued with apremilast.
  - Patients who received placebo are not represented in this analysis.

- This study evaluated the cumulative clinical benefit of initiating with deucravacitinib vs apremilast to determine the treatment pathway that provides greater benefit to the patient.
  - The cumulative clinical benefit reflects the total time patients spend in a state of therapeutic response.

- The results of this study indicate that initiating deucravacitinib as a first-line treatment offers greater benefits over time compared with initiating with apremilast.

Objective

- To evaluate the cumulative clinical benefit of initiating with deucravacitinib vs apremilast from baseline to Week 52 based on data from POETYK PSO-1.

Methods

- POETYK PSO-1 was a multicenter, randomized, double-blind, placebo- and active comparator-controlled study.
  - Patients were aged ≥18 years and had moderate to severe plaque psoriasis (PASI score ≥12, sPGA score ≥3, and body surface area involvement ≥10%).
  - Coprimary efficacy endpoints were PASI 75 and sPGA 0/1.
  - Nonresponder imputation was used for missing data.

- This post hoc analysis compared data from 2 arms in 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, PASI 50 responders continued with apremilast while PASI 50 nonresponders crossed over to deucravacitinib.

- Cumulative clinical benefit from randomization to Week 52 was determined by the total area under the curve of clinical response over 52 weeks (AUC_{0-52wk}) in each arm.

- AUC analysis has been employed to evaluate outcomes over time in clinical trials, as the AUC reflects the rapidity and durability, as well as the magnitude, of response.
  - While assessments at discrete time points identify static responses, the AUC approach captures cumulative treatment effects over time.

- This study determined the AUC using data at a patient level (responder status at each time point over 52 weeks).

- Total AUC_{0-52wk} was calculated separately for each efficacy endpoint, using the trapezoidal rule.

- The result was standardized as a percentage of maximum possible AUC_{0-52wk} (0-5200 [% × weeks]) and aggregated to the population level.

- Adjusted AUC comparisons between the 2 treatment arms were based on an analysis of covariance (ANCOVA) model, with the following stratification parameters:
  - Prior use of a biologic treatment (yes/no).
  - Region (United States, China, Japan, rest of the world [ROW]).
  - Body weight (<90 kg, ≥90 kg), in the United States and ROW only.

- Ratios of AUC_{0-52wk} were calculated, representing the relative cumulative clinical benefit of the 2 treatment pathways for achieving PASI 75 or sPGA 0/1 over the 52-week period.
Results

PASI 75
- Standardized average cumulative PASI 75 response over 52 weeks among patients initiating with deucravacitinib was 57.3% compared with 38.2% in patients initiating with apremilast (including 87 patients who continued apremilast after Week 24 and 54 patients who switched to deucravacitinib) (Table 1)
  - Adjusted $AUC_{0-52wk} \% \times \text{weeks}$ was 2978.72 in the deucravacitinib arm and 1988.06 in the apremilast initiators arm
  - The adjusted difference in $AUC_{0-52wk}$ was 990.66 (95% CI, 683.37–1297.95); $P < 0.001$
  - The benefit ratio of initiating with deucravacitinib vs apremilast was 1.50

- Figure 2 displays the standardized adjusted cumulative AUC for PASI 75 over 52 weeks

sPGA 0/1
- Standardized average cumulative sPGA 0/1 response over 52 weeks among patients initiating with deucravacitinib was 50.2% compared with 31.9% in patients initiating with apremilast (Table 2)
  - Adjusted $AUC_{0-52wk} \% \times \text{weeks}$ was 2612.82 in the deucravacitinib arm and 1657.13 in the apremilast initiators arm
  - The adjusted difference in $AUC_{0-52wk}$ was 955.69 (95% CI, 642.22–1269.16); $P < 0.001$
  - The benefit ratio of initiating with deucravacitinib vs apremilast was 1.58

- Figure 3 displays the standardized adjusted cumulative AUC for sPGA 0/1 over 52 weeks

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Table 2. Cumulative clinical benefit measured by sPGA 0/1 response over 52 weeks

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aAmong patients initiating with apremilast, 87 achieved PASI 50 at Week 24 and continued receiving apremilast, and 54 did not achieve PASI 50 and switched to deucravacitinib.

bAUC_{0–52wk}, area under the curve over 52 weeks; CI, confidence interval; sPGA 0/1, static Physician Global Assessment score of 0 or 1.

Figure 3. Standardized adjusted AUC_{0–52wk} : sPGA 0/1

Conclusions

- Initiating with deucravacitinib resulted in greater cumulative benefits over 52 weeks than initiating with apremilast
  - Deucravacitinib initiators spend ≈150% more time in therapeutic response over 1 year compared with apremilast initiators
- Initiating with deucravacitinib as the first line rather than switching to deucravacitinib as the second line after failure to respond with apremilast may optimize the clinical benefit that patients receive

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### Methods

- **Coprimary efficacy endpoints** were PASI 75 and sPGA 0/1.
- Patients receiving apremilast who achieved PASI 50 at Week 24 continued with apremilast; those who did not achieve at least 50% improvement from baseline in Psoriasis Area and Severity Index (PASI) score switched to deucravacitinib.
- Patients receiving apremilast who did not achieve PASI 50 at Week 24 continued with apremilast.

### Results

- Deucravacitinib initiators arm: 50.2% achieved a static Physician Global Assessment (sPGA) score of 0 or 1 (sPGA 0/1) compared with 31.9% in patients initiating with apremilast (Benefit ratio: 1.58).
- Adjusted AUC0–52wk was 2978.72 in the deucravacitinib arm and 1988.06 in the apremilast initiators arm.

### Conclusions

Initiating with deucravacitinib as the first line rather than switching to deucravacitinib as the second line provides greater benefits to the patient.

### References