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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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[1]
  - 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[1]
    - 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)[2]
  - 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[3]
- The results of this study indicate that initiating deucravacitinib as a first-line treatment offers greater benefits over time compared with initiating with apremilast

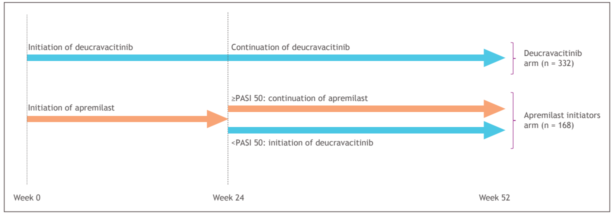
Objective

- 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[1]
  - 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 ($AUC_{0\text{-}52wk}$) 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[3-6]
    - 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 $AUC_{0\text{-}52wk}$ was calculated separately for each efficacy endpoint, using the trapezoidal rule
  - Total $AUC_{0\text{-}52wk} = \sum_{i=0}^{15} \frac{1}{2}(P_i+P_{i+1})(T_{i+1}-T_i)$, where T_i ($i = 0, 1, 2, 3, \ldots, 15$) denotes the time points of Weeks 0, 1, 2, 4, 8, 12, and 16, then every 4 weeks thereafter through Week 52, and P_i denotes the response (yes = 1; no = 0) at each time point, T_i
- The result was standardized as a percentage of maximum possible $AUC_{0\text{-}52wk}$ (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 $AUC_{0\text{-}52wk}$ 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

Figure 1. Study design comparing data from 2 arms of POETYK PSO-1



PASI 50, 50% improvement from baseline in Psoriasis Area and Severity Index score.

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 $AUC_{0\text{-}52wk}$ [% × weeks] was 2978.72 in the deucravacitinib arm and 1988.06 in the apremilast initiators arm
  - The adjusted difference in $AUC_{0\text{-}52wk}$ 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

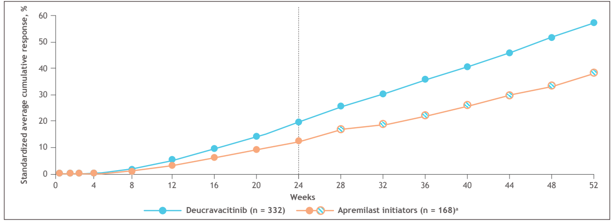
- Standardized average cumulative sPGA 0/1 response over 52 weeks among patients initiating with deucravacitinib was 50.2% compared with 31.9% in patients initiating with apremilast (**Table 2**)
  - Adjusted $AUC_{0\text{-}52wk}$ [% × weeks] was 2612.82 in the deucravacitinib arm and 1657.13 in the apremilast initiators arm
  - The adjusted difference in $AUC_{0\text{-}52wk}$ 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

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

Outcomes	Deucravacitinib, n = 332	Apremilast initiators,[a] n = 168	Difference in estimate (95% CI)	*P* value	Benefit ratio
Adjusted $AUC_{0\text{-}52wk}$, % × weeks	2978.72	1988.06	990.66 (683.37-1297.95)	< 0.001	1.50
Standardized average cumulative response[b]	57.3%	38.2%	–	–	

[a] Among 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.
[b] $AUC_{0\text{-}52wk}$/maximum $AUC_{0\text{-}52wk}$.
$AUC_{0\text{-}52wk}$, area under the curve over 52 weeks; CI, confidence interval; PASI 75, 75% improvement from baseline in Psoriasis Area and Severity Index score.

Figure 2. Standardized adjusted $AUC_{0\text{-}52wk}$: PASI 75



[a] Among 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.
$AUC_{0\text{-}52wk}$, area under the curve over 52 weeks; PASI 50/75, ≥50%/≥75% improvement from baseline in Psoriasis Area and Severity Index score.

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

Outcomes	Deucravacitinib, n = 332	Apremilast initiators,[a] n = 168	Difference in estimate (95% CI)	*P* value	Benefit ratio
Adjusted $AUC_{0\text{-}52wk}$, % × weeks	2612.82	1657.13	955.69 (642.22-1269.16)	< 0.001	1.58
Standardized average cumulative response[b]	50.2%	31.9%	–	–	

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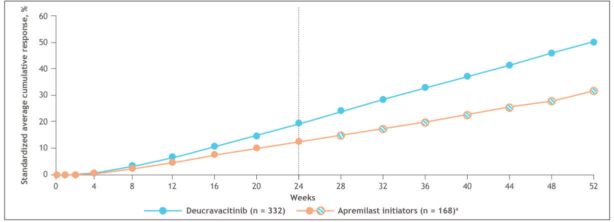

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$AUC_{0\text{-}52wk}$, area under the curve over 52 weeks; PASI 50, ≥50% improvement from baseline in Psoriasis Area and Severity Index score; sPGA, static Physician Global Assessment score of 0 or 1.

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

References

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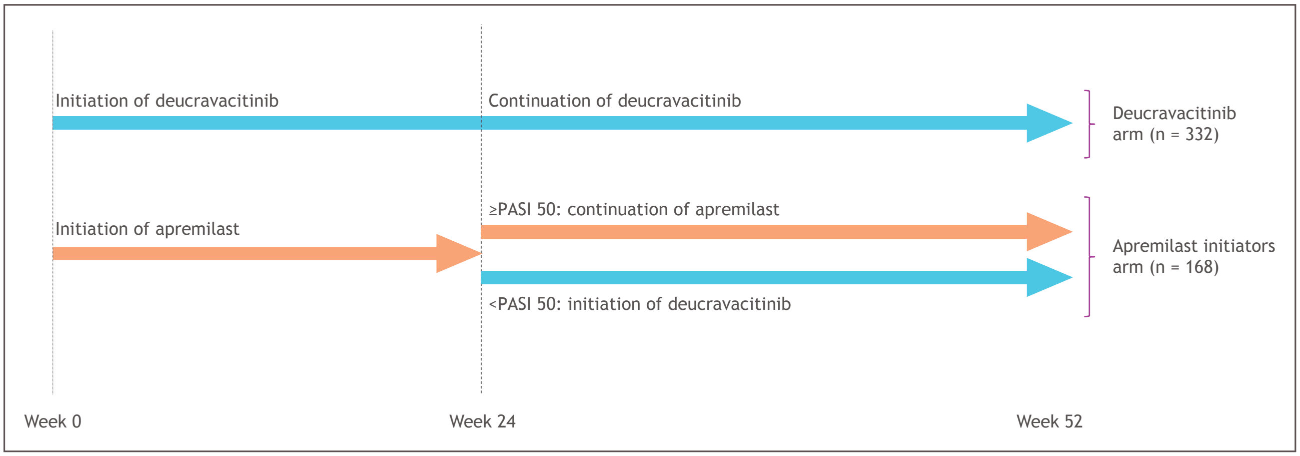

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- **Figure 2** displays the standardized adjusted cumulative AUC for PASI 75 over 52 weeks

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 $\text{AUC}_{0\text{-}52\text{wk}}$ [% × weeks] was 2612.82 in the deucravacitinib arm and 1657.13 in the apremilast initiators arm
  - — The adjusted difference in $\text{AUC}_{0\text{-}52\text{wk}}$ was 955.69 (95% CI, 642.22–1269.16); $P < 0.001$
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Figure 2. Standardized adjusted $\text{AUC}_{0\text{-}52\text{wk}}$: PASI 75

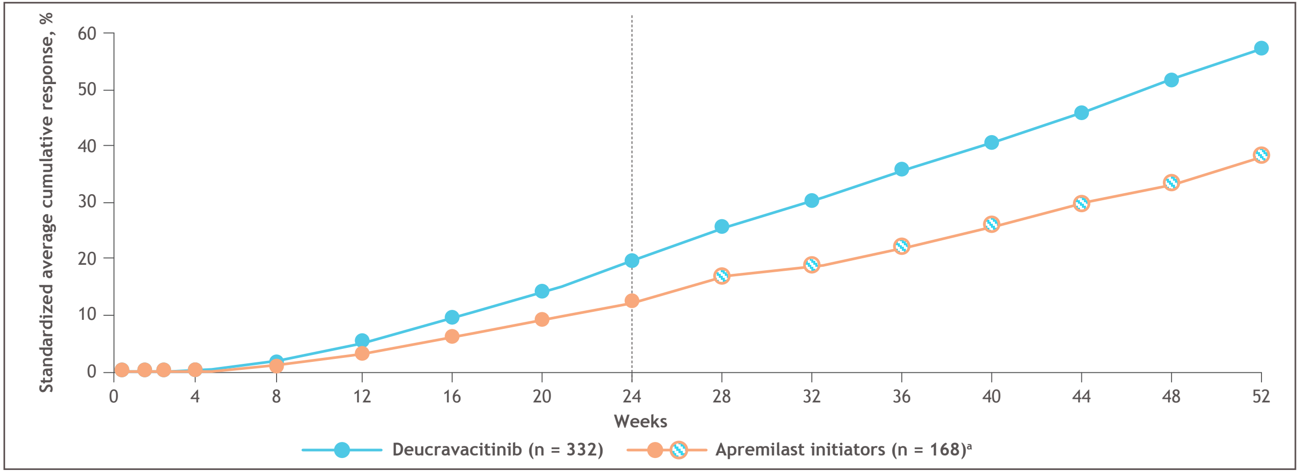

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Table 2. Cumulative clinical benefit measured by sPGA 0/1 response over 52 weeks

Outcomes	Deucravacitinib, n = 332	Apremilast initiators,[a] n = 168	Difference in estimate (95% CI)	*P* value	Benefit ratio
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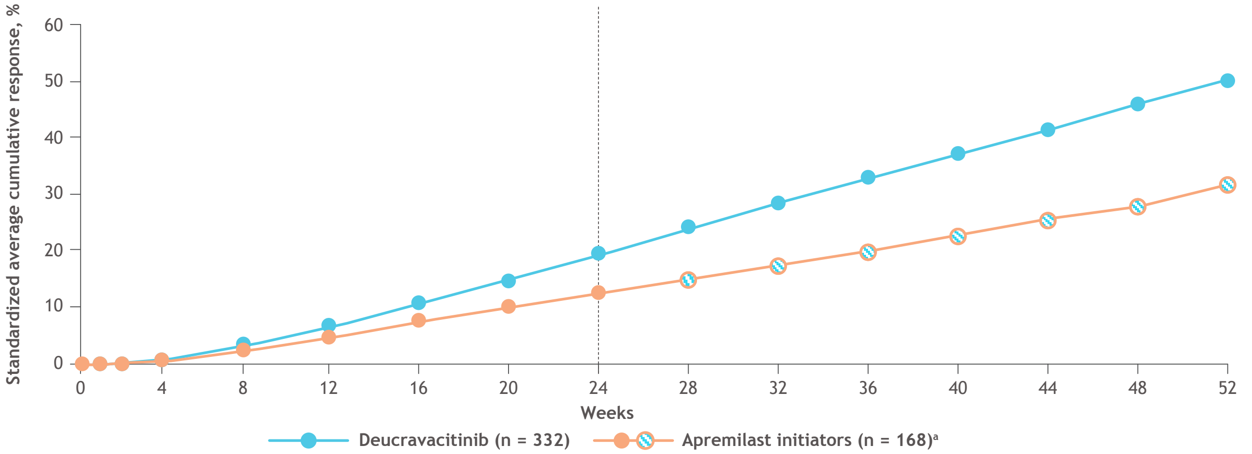
Figure 3. Standardized adjusted $\text{AUC}_{0\text{-}52\text{wk}}$: sPGA 0/1



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