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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Introduction

- Deucravacitinib, an oral, selective, allosteric 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[1,2]
- Recent phase 3 clinical trial results of POETYK PSO-1 demonstrated superior response rates for deucravacitinib vs apremilast at 24 weeks, and deucravacitinib responses were maintained at 52 weeks with continuous treatment[2]
- Calculating the cumulative clinical benefit via 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 vs evaluation based on point-in-time efficacy estimates[3]
- A recent study found that initiating deucravacitinib as the first-line rather than second-line treatment after failure to respond with apremilast may optimize the clinical benefit for patients[4]
- Given different oral treatment pathway options, such as initiating with deucravacitinib or switching to deucravacitinib after failure to respond with apremilast, a need exists to identify those that provide the greatest benefit[5]

Objective

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

Methods

Data source

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

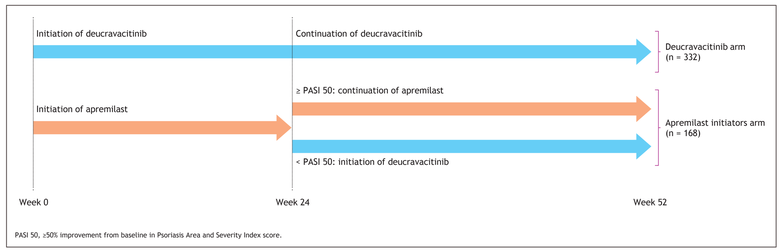
Study design

- 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 (patients with ≥50% improvement from baseline in Psoriasis Area and Severity Index score [PASI 50]) continued with apremilast, while PASI 50 nonresponders crossed over to deucravacitinib
  - Data from the placebo arm of the clinical trial were omitted

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 2 arms of POETYK PSO-1



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

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 ($AUC_{0\text{-}52wk}$) in each arm
  - Clinical response was measured by co-primary efficacy endpoints ≥75% improvement from baseline in PASI score (PASI 75) and sPGA 0/1 (responder status at each time point over 52 weeks)
- Prior biologic and systemic use subgroups were analyzed for each efficacy endpoint
- Total $AUC_{0\text{-}52wk}$ was calculated for each patient 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 P_i denotes the responder status (1 for responder or 0 otherwise) at time point T_i, and i = 0, 1, 2, 3, … 15 represents Weeks 0, 1, 2, 4, and every 4 weeks afterward through Week 52
- Analysis of covariance (ANCOVA) models were used to adjust for each stratification factor (geographic region, prior biologic use, and body weight) and estimate total AUC, 95% CIs, and *P* values for each prior treatment subgroup and outcome
- Adjusted AUC results were standardized as a percentage of the maximum possible benefit (ie, 100% response for all 52 weeks)
- Nonresponder imputation was used for missing data
- Benefit ratios of $AUC_{0\text{-}52wk}$ were calculated for each subgroup, representing the relative cumulative clinical benefit of the 2 treatment pathways in achieving PASI 75 or sPGA 0/1 over the 52-week period

Results

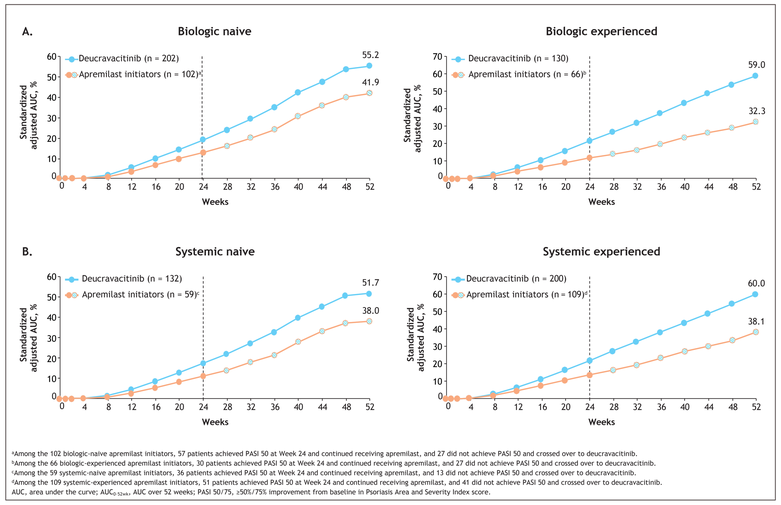
PASI 75

- Among apremilast initiators (n = 168), 87 continued apremilast and 54 switched to deucravacitinib after Week 24 because of inadequate response (< PASI 50)
- Over 52 weeks, patients who initiated with deucravacitinib (n = 332) obtained greater cumulative PASI 75 benefit, regardless of prior treatment, compared with patients who initiated with apremilast (55.2% vs 41.9%, biologic naive; 59.0% vs 32.3%, biologic experienced; 51.7% vs 38.0%, systemic naive; 60.0% vs 38.1%, systemic experienced) (**Figure 2**)
- The benefit ratios of initiating with deucravacitinib vs apremilast were between 1.32 and 1.82 (**Table 1**)
- Regardless of prior treatment, patients who initiated with deucravacitinib vs apremilast spent more time in a state of therapeutic response, as measured by PASI 75

sPGA 0/1

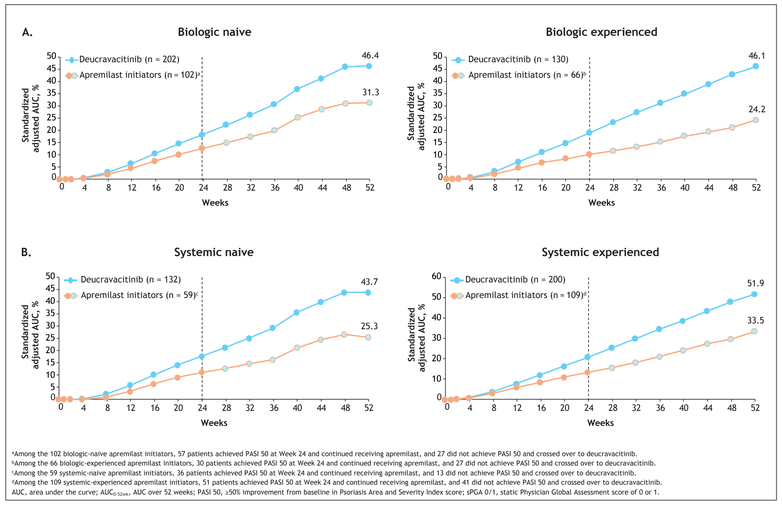
- sPGA 0/1 findings were similar (46.4% vs 31.3%, biologic naive; 46.1% vs 24.2%, biologic experienced; 43.7% vs 25.3%, systemic naive; 51.9% vs 33.5%, systemic experienced) (**Figure 3**)
- The benefit ratios of initiating with deucravacitinib vs apremilast were between 1.48 and 1.90 (**Table 2**)
- Regardless of prior treatment, patients who initiated with deucravacitinib vs apremilast spent more time in a state of therapeutic response, as measured by sPGA 0/1

Figure 2. PASI 75 responder standardized adjusted $AUC_{0\text{-}52wk}$, by (A) prior biologic use and (B) prior systemic treatment use



[a]Among the 102 biologic-naive apremilast initiators, 57 patients achieved PASI 50 at Week 24 and continued receiving apremilast, and 27 did not achieve PASI 50 and crossed over to deucravacitinib.
[b]Among the 66 biologic-experienced apremilast initiators, 30 patients achieved PASI 50 at Week 24 and continued receiving apremilast, and 27 did not achieve PASI 50 and crossed over to deucravacitinib.
[c]Among the 59 systemic-naive apremilast initiators, 36 patients achieved PASI 50 at Week 24 and continued receiving apremilast, and 13 did not achieve PASI 50 and crossed over to deucravacitinib.
[d]Among the 109 systemic-experienced apremilast initiators, 51 patients achieved PASI 50 at Week 24 and continued receiving apremilast, and 41 did not achieve PASI 50 and crossed over to deucravacitinib.
AUC, area under the curve; $AUC_{0\text{-}52wk}$, AUC over 52 weeks; PASI 50/75, ≥50%/75% improvement from baseline in Psoriasis Area and Severity Index score.

Figure 3. sPGA 0/1 responder standardized adjusted $AUC_{0\text{-}52wk}$, by (A) prior biologic use and (B) prior systemic treatment use



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

Table 1. $AUC_{0\text{-}52wk}$ PASI 75, by prior treatment use

Prior treatment/outcomes	Deucravacitinib initiators (n = 332)	Apremilast initiators (n = 168)	Difference in estimate, 95% CI	*P* value	Benefit ratio
Biologic naive	Deucravacitinib initiators (n = 202)	Apremilast initiators (n = 102)[a]			
Adjusted $AUC_{0\text{-}52wk}$	2871	2178	694 (283-1104)	< 0.001	1.32
Standardized adjusted $AUC_{0\text{-}52wk}$ ($AUC_{0\text{-}52wk}$/maximum $AUC_{0\text{-}52wk}$)	55.2%	41.9%			
Biologic experienced	Deucravacitinib initiators (n = 130)	Apremilast initiators (n = 66)[b]			
Adjusted $AUC_{0\text{-}52wk}$	3067	1681	1386 (918-1854)	< 0.001	1.82
Standardized adjusted $AUC_{0\text{-}52wk}$ ($AUC_{0\text{-}52wk}$/maximum $AUC_{0\text{-}52wk}$)	59.0%	32.3%			
Systemic naive	Deucravacitinib initiators (n = 132)	Apremilast initiators (n = 59)[c]			
Adjusted $AUC_{0\text{-}52wk}$	2691	1975	716 (184-1248)	0.009	1.36
Standardized adjusted $AUC_{0\text{-}52wk}$ ($AUC_{0\text{-}52wk}$/maximum $AUC_{0\text{-}52wk}$)	51.7%	38.0%			
Systemic experienced	Deucravacitinib initiators (n = 200)	Apremilast initiators (n = 109)[d]			
Adjusted $AUC_{0\text{-}52wk}$	3119	1983	1136 (755-1517)	< 0.001	1.57
Standardized adjusted $AUC_{0\text{-}52wk}$ ($AUC_{0\text{-}52wk}$/maximum $AUC_{0\text{-}52wk}$)	60.0%	38.1%			

[a]Among the 102 biologic-naive apremilast initiators, 57 patients achieved PASI 50 at Week 24 and continued apremilast; 27 patients did not achieve PASI 50 and crossed over to deucravacitinib at Week 24.
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$AUC_{0\text{-}52wk}$, area under the curve over 52 weeks; CI, confidence interval; PASI 50/75, ≥50%/75% improvement from baseline Psoriasis Area and Severity Index score.

Table 2. $AUC_{0\text{-}52wk}$ sPGA 0/1, by prior treatment use

Prior treatment/outcomes	Deucravacitinib initiators (n = 332)	Apremilast initiators (n = 168)	Difference in estimate, 95% CI	*P* value	Benefit ratio
Biologic naive	Deucravacitinib initiators (n = 202)	Apremilast initiators (n = 102)[a]			
Adjusted $AUC_{0\text{-}52wk}$	2414	1627	787 (372-1207)	< 0.001	1.48
Standardized adjusted $AUC_{0\text{-}52wk}$ ($AUC_{0\text{-}52wk}$/maximum $AUC_{0\text{-}52wk}$)	46.4%	31.3%			
Biologic experienced	Deucravacitinib initiators (n = 130)	Apremilast initiators (n = 66)[b]			
Adjusted $AUC_{0\text{-}52wk}$	2399	1261	1138 (651-1625)	< 0.001	1.90
Standardized adjusted $AUC_{0\text{-}52wk}$ ($AUC_{0\text{-}52wk}$/maximum $AUC_{0\text{-}52wk}$)	46.1%	24.2%			
Systemic naive	Deucravacitinib initiators (n = 132)	Apremilast initiators (n = 59)[c]			
Adjusted $AUC_{0\text{-}52wk}$	2275	1318	957 (416-1498)	< 0.001	1.63
Standardized adjusted $AUC_{0\text{-}52wk}$ ($AUC_{0\text{-}52wk}$/maximum $AUC_{0\text{-}52wk}$)	43.7%	25.3%			
Systemic experienced	Deucravacitinib initiators (n = 200)	Apremilast initiators (n = 109)[d]			
Adjusted $AUC_{0\text{-}52wk}$	2698	1742	956 (567-1346)	< 0.001	1.55
Standardized adjusted $AUC_{0\text{-}52wk}$ ($AUC_{0\text{-}52wk}$/maximum $AUC_{0\text{-}52wk}$)	51.9%	33.5%			

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

Discussion

- 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 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 insight into the cumulative clinical benefit of different treatment pathways
  - The crossover data better reflect real-world treatment patterns with multiple lines of therapy
- Data quality was assured, as the study data from the POETYK PSO-1 trial were reviewed and validated through quality control checks

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 nonresponder imputation, a conservative approach to imputation,[6] but this still may have introduced bias
- The POETYK PSO-1 trial ran from August 2018 to September 2020, with the final participants potentially impacted by the COVID-19 pandemic
  - However, there was no impact on the assessment of the co-primary endpoints, and minimal impact on the assessment of key secondary endpoints

Conclusions

- Initiating treatment with deucravacitinib resulted in greater cumulative clinical benefit over 52 weeks than apremilast for patients with moderate to severe plaque psoriasis
- This greater cumulative clinical benefit was observed, regardless of prior treatment
  - The benefit ratio of initiating with deucravacitinib vs apremilast was between 1.32 and 1.90 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

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Disclosures

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