# Deucravacitinib, an oral, selective, allosteric tyrosine kinase 2 inhibitor, in moderate to severe plaque psoriasis: 52-week efficacy by prior treatment in the phase 3 POETYK PSO-1 trial

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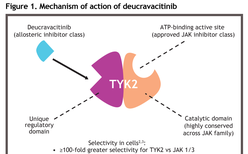
## Synopsis

- Deucravacitinib an oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor, is 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
  - Uniquely binds to the regulatory domain rather than to the catalytic domain where Janus kinase (JAK) 1/2/3 inhibitors bind[1,2] (**Figure 1**)
- In the global, 52-week, phase 3 POETYK PSO-1 trial (NCT03624127), deucravacitinib was significantly more effective than placebo or apremilast in the treatment of moderate to severe plaque psoriasis[3]
  - Clinical responses were maintained through 52 weeks[3]
- Response rates for the coprimary endpoints, ≥75% reduction from baseline in Psoriasis Area and Severity Index (PASI 75) and static Physician's Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline (sPGA 0/1) at Week 16, were superior with deucravacitinib regardless of prior exposure to biologics, systemic nonbiologics, and/or phototherapy[4]
- The 2-year efficacy and safety of deucravacitinib in the POETYK long-term extension trial was consistent with Weeks 0-52 of the POETYK PSO-1 and PSO-2 trials[5]

**Figure 1. Mechanism of action of deucravacitinib**




ATP, adenosine 5'-triphosphate; JAK, Janus kinase; TYK2, tyrosine kinase 2.

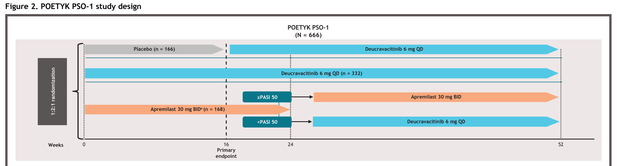
## Objective

- The aim of the current analysis was to evaluate the impact of prior treatment on PASI 75 and sPGA 0/1 responses through Week 52 in patients from POETYK PSO-1 who were randomized to deucravacitinib and in those who crossed over from placebo to deucravacitinib at Week 16

## Methods

- The study design for POETYK PSO-1 is illustrated in **Figure 2**
- Eligible patients were ≥18 years of age with moderate to severe plaque psoriasis (ie, PASI ≥12, sPGA ≥3, body surface area involvement ≥10% at baseline)
- Patients who previously received phototherapy, systemic treatment, and/or biologic treatment were required to complete washout periods ranging from 4 weeks to 6 months before study entry, depending on the treatment
- The current analysis examined PASI 75 and sPGA 0/1 responses through 52 weeks in patients randomized to deucravacitinib and in those who crossed over from placebo to deucravacitinib at Week 16 (placebo crossovers), by prior treatment subgroups:
  - Systemic treatment naive (ie, neither biologic nor nonbiologic systemic treatment)
  - Prior systemic treatment (biologic and/or nonbiologic)
  - Prior oral systemic treatment (nonbiologic only)
  - Biologic treatment naive
  - Biologic treatment experienced
- Nonresponder imputation was used for all reported endpoints

**Figure 2. POETYK PSO-1 study design**




From Armstrong AW, et al. Deucravacitinib versus placebo and apremilast in moderate to severe plaque psoriasis: efficacy and safety results from the 52-week, randomized, double-blinded, placebo-controlled phase 3 POETYK PSO-1 trial. *J Am Acad Dermatol*. 2023;88:29-39. This work is licensed under a Creative Commons Attribution License (CC BY-NC-ND 4.0). https://creativecommons.org/licenses/by-nc-nd/4.0/.

[a]Apremilast was titrated from 10 mg QD to 30 mg BID over the first 5 days of dosing.
BID, twice daily; PASI 50, ≥50% reduction from baseline in Psoriasis Area and Severity Index; QD, once daily.

## Results

- Baseline demographics and disease characteristics for patients randomized to deucravacitinib (n = 332) and to placebo (n = 166) are shown in **Table 1**
  - Prior use of systemic (biologic and nonbiologic), oral systemic, and biologic treatments was generally similar between the groups (**Table 1**)
- At Week 52, PASI 75 response rates were similar in patients randomized to deucravacitinib at baseline and in placebo crossovers (65.1% and 68.3%, respectively) (**Table 2; Figure 3**)
- These findings were consistent across all patient subgroups (**Table 2**), including:
  - Systemic treatment-naive patients and those with prior systemic or oral systemic treatment (**Figure 4**)
  - Patients with and without prior biologic treatment (**Figure 5**)
- At Week 52, sPGA 0/1 response rates were similar in patients randomized to deucravacitinib at baseline and in placebo crossovers (53.8% and 52.7%, respectively) (**Figure 6**)
- These findings were consistent across all patient subgroups (**Table 2**), including:
  - Systemic treatment-naive patients and those with prior systemic or oral systemic treatment (**Figure 7**)
  - Patients with and without prior biologic treatment (**Figure 8**)

**Table 1. Baseline patient demographics and disease characteristics**

| | POETYK PSO-1 | |
|---|---|---|
| Parameter | Placebo (n = 166) | Deucravacitinib (n = 332) |
| **Age, mean (min, max), y** | 47.9 (19, 81) | 45.9 (18, 80) |
| **Weight, mean (min, max), kg** | 89.1 (46.3, 181.6) | 87.9 (36.0, 173.0) |
| **Female, n (%)** | 53 (31.9) | 102 (30.7) |
| **Race, n (%)** | | |
| White | 128 (77.1) | 267 (80.4) |
| Asian | 34 (20.5) | 59 (17.8) |
| Other | 4 (2.4) | 6 (1.8) |
| **Disease duration, mean (min, max), y** | 17.3 (0.9, 62.3) | 17.1 (0.7, 57.8) |
| **sPGA, n (%)** | | |
| 3 (moderate) | 128 (77.1) | 257 (77.4) |
| 4 (severe) | 37 (22.3) | 75 (22.6) |
| **PASI, mean (min, max)** | 20.7 (10.3, 47.7) | 21.8 (12.0, 58.8) |
| **PSSD symptom score, mean (min, max)** | 51.4 (0.3, 100.0) | 51.7 (0.0, 100.0) |
| **DLQI, mean (min, max)** | 11.4 (1.0, 30.0) | 12.0 (0.0, 30.0) |
| **Prior treatment use, n (%)** | | |
| Systemic treatment naive | 57 (34.3) | 132 (39.8) |
| Prior systemic treatment | 109 (65.7) | 200 (60.2) |
| Prior oral systemic treatment | 73 (44.0) | 114 (34.3) |
| Biologic treatment naive | 103 (62.0) | 202 (60.8) |
| Prior biologic treatment | 63 (38.0) | 130 (39.2) |

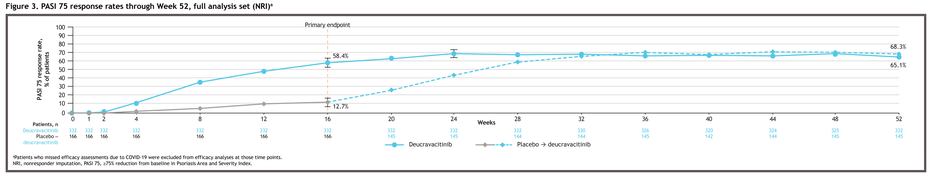
DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index; PSSD, Psoriasis Symptoms and Signs Diary; sPGA, static Physician's Global Assessment.

**Table 2. Summary of Week 52 response rates (NRI)[a]**

| | POETYK PSO-1 | | | |
|---|---|---|---|---|
| | PASI 75 Week 52 response rate, n/N (%) | | sPGA 0/1 Week 52 response rate, n/N (%) | |
| Patients | Placebo→deucravacitinib | Deucravacitinib | Placebo→deucravacitinib | Deucravacitinib |
| **Full analysis set** | 99/145 (68.3) | 216/332 (65.1) | 78/145 (53.8) | 175/332 (52.7) |
| **Systemic treatment naive** | 35/51 (68.6) | 85/132 (64.4) | 26/51 (51.0) | 69/132 (52.3) |
| **Prior systemic treatment** | 64/94 (68.1) | 131/200 (65.5) | 52/94 (55.3) | 106/200 (53.0) |
| **Prior oral systemic treatment** | 45/65 (69.2) | 80/114 (70.2) | 35/65 (53.8) | 65/114 (57.0) |
| **Biologic treatment naive** | 65/90 (72.2) | 136/202 (67.3) | 53/90 (58.9) | 113/202 (55.9) |
| **Prior biologic treatment** | 34/55 (61.8) | 80/130 (61.5) | 25/55 (45.5) | 62/130 (47.7) |

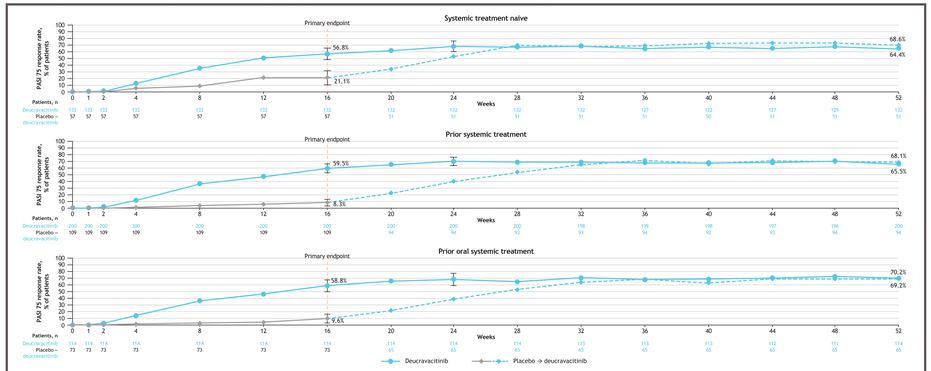
[a]Patients who missed efficacy assessments due to COVID-19 were excluded from efficacy analyses at those time points.
NRI, nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index; sPGA 0/1, static Physician's Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline.

**Figure 3. PASI 75 response rates through Week 52, full analysis set (NRI)[a]**



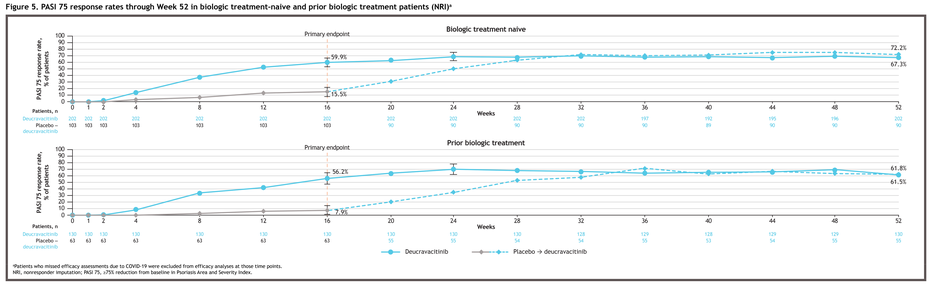

[a]Patients who missed efficacy assessments due to COVID-19 were excluded from efficacy analyses at those time points.
NRI, nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index.

**Figure 4. PASI 75 response rates through Week 52 in systemic treatment-naive, prior systemic treatment, and prior oral systemic treatment patients (NRI)[a]**



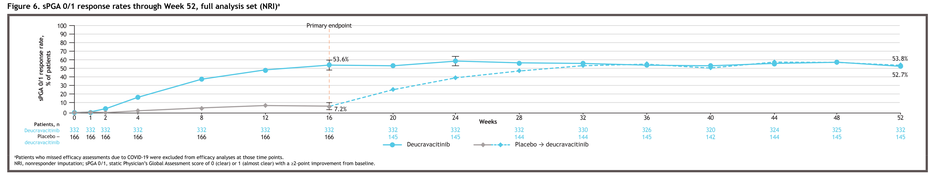

[a]Patients who missed efficacy assessments due to COVID-19 were excluded from efficacy analyses at those time points.
NRI, nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index.

**Figure 5. PASI 75 response rates through Week 52 in biologic treatment-naive and prior biologic treatment patients (NRI)[a]**



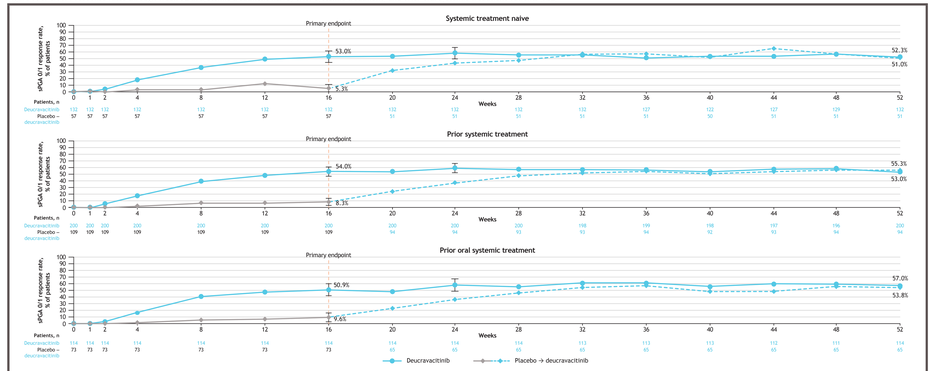

[a]Patients who missed efficacy assessments due to COVID-19 were excluded from efficacy analyses at those time points.
NRI, nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index.

**Figure 6. sPGA 0/1 response rates through Week 52, full analysis set (NRI)[a]**



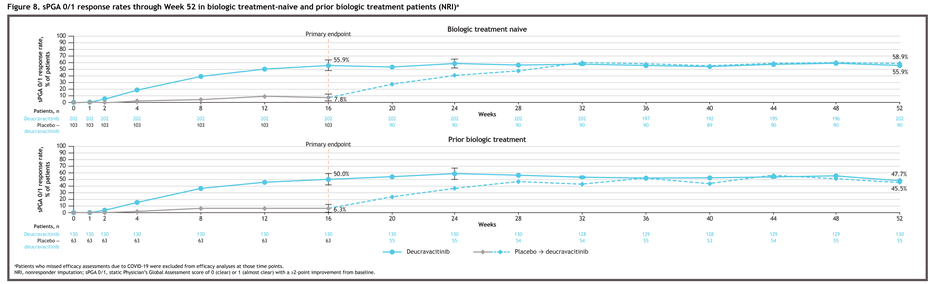

[a]Patients who missed efficacy assessments due to COVID-19 were excluded from efficacy analyses at those time points.
NRI, nonresponder imputation; sPGA 0/1, static Physician's Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline.

**Figure 7. sPGA 0/1 response rates through Week 52 in systemic treatment-naive, prior systemic treatment, and prior oral systemic treatment patients (NRI)[a]**




[a]Patients who missed efficacy assessments due to COVID-19 were excluded from efficacy analyses at those time points.
NRI, nonresponder imputation; sPGA 0/1, static Physician's Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline.

**Figure 8. sPGA 0/1 response rates through Week 52 in biologic treatment-naive and prior biologic treatment patients (NRI)[a]**




[a]Patients who missed efficacy assessments due to COVID-19 were excluded from efficacy analyses at those time points.
NRI, nonresponder imputation; sPGA 0/1, static Physician's Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline.

## Conclusions

- Deucravacitinib-treated patients from the POETYK PSO-1 trial maintained response rates for PASI 75 and sPGA 0/1 through Week 52, regardless of prior treatment exposure to biologic, systemic nonbiologic, and/or oral systemic agents
- Patients who switched from placebo to deucravacitinib at Week 16 also showed robust responses at Week 52 on both endpoints and across subgroups
- These analyses support the efficacy of deucravacitinib in moderate to severe psoriasis regardless of prior treatment history


## References

1. SOTYKTU™ (deucravacitinib) [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; September 2022. 2. Burke JR, et al. *Sci Transl Med*. 2019;11:eaaw1776. 3. Wrobleski ST, et al. *J Med Chem*. 2019;62:8973-8995. 4. Armstrong AW, et al. *J Am Acad Dermatol*. 2023;88:29-39. 5. Warren RB, et al. Presented at the 30th EADV Congress, September 29-October 2, 2021. Late breaker. 6. Warren RB, et al. Presented at the 30th EADV Congress, September 29-October 2, 2021. 7. Warren RB, et al. Presented at the EADV Spring Symposium; May 12-14, 2022.



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