Deucravacitinib, an oral, selective 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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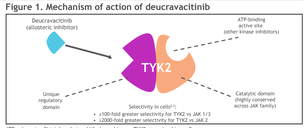
Synopsis

- 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[1]
  - Uniquely binds to the regulatory domain rather than to the catalytic domain where Janus kinase 1/2/3 inhibitors bind[1-3] (**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[4]
  - Clinical responses were maintained through 52 weeks[5]
- 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[7]

Figure 1. Mechanism of action of deucravacitinib



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

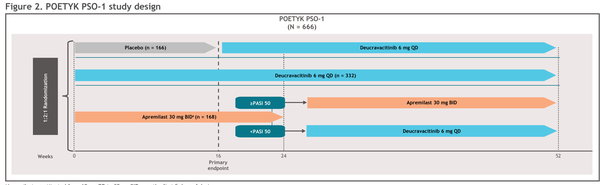
Objective

- 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



[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

Parameter	POETYK PSO-1	
	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)

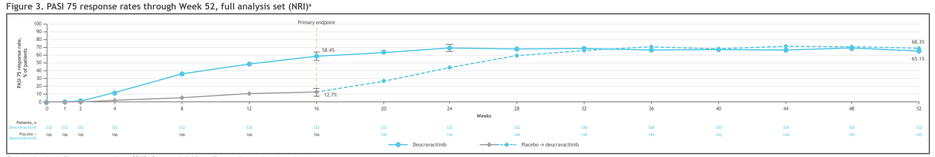
DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index; PSSD, Psoriasis Symptoms and Signs Diary; sPGA, static Physician's Global Assessment.

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

Patients	POETYK PSO-1			
	PASI 75 Week 52 response rate, n/N (%)		sPGA 0/1 Week 52 response rate, n/N (%)	
	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)

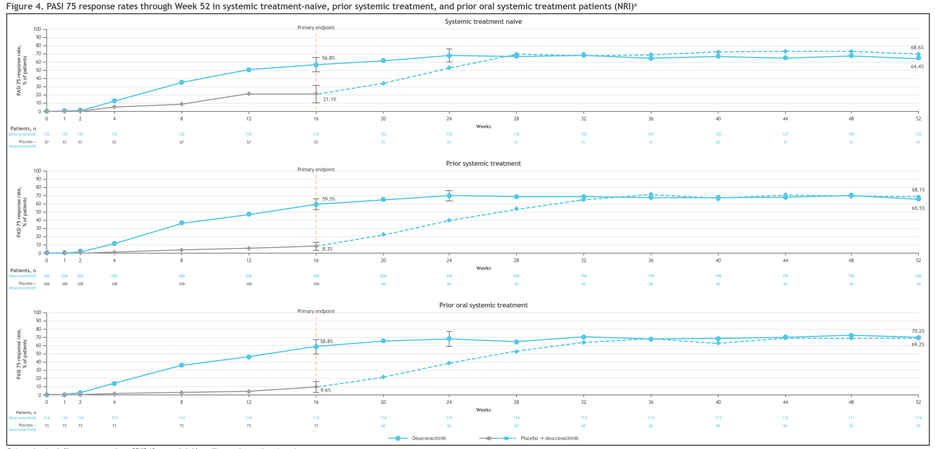
[a]Patients who missed efficacy assessments due to COVID-19 were excluded from efficacy analyses at those time points.
NRI, nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index; sPGA 0/1, static Physician's Global Assessment score of 0 (clear) or 1 (almost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

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



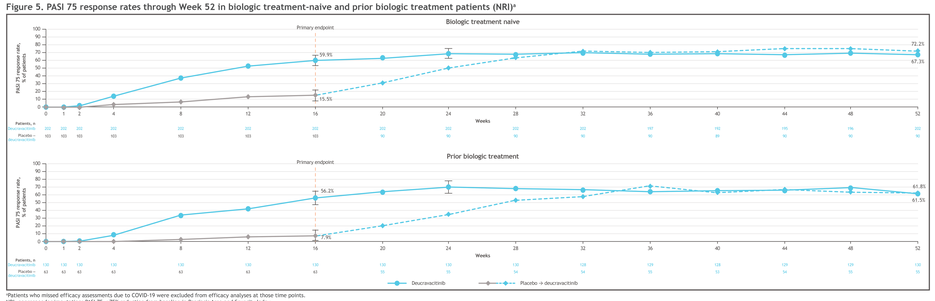
[a]Patients who missed efficacy assessments due to COVID-19 were excluded from efficacy analyses at those time points.
NRI, nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index.

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



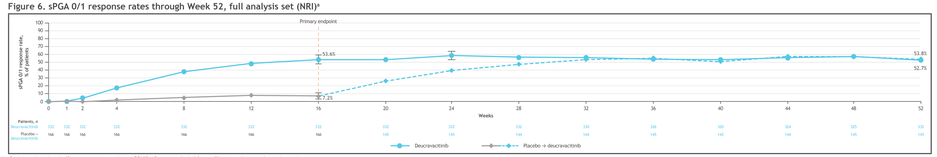
[a]Patients who missed efficacy assessments due to COVID-19 were excluded from efficacy analyses at those time points.
NRI, nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index.

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



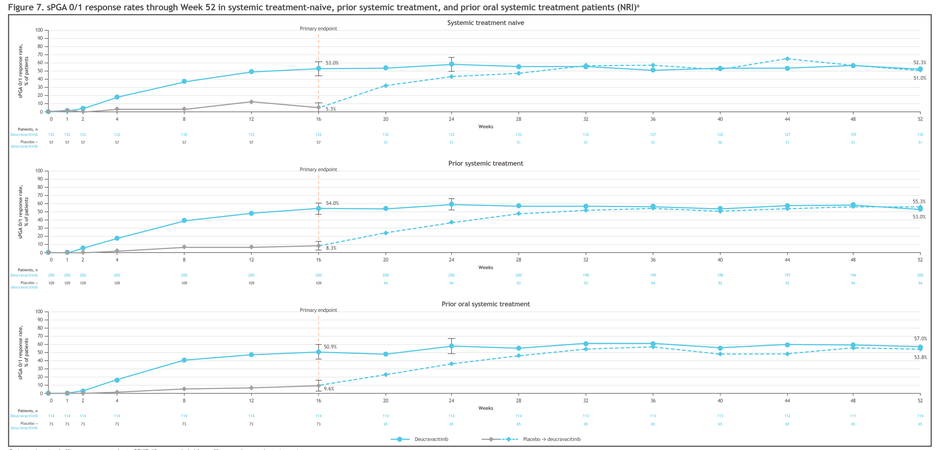
[a]Patients who missed efficacy assessments due to COVID-19 were excluded from efficacy analyses at those time points.
NRI, nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index.

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



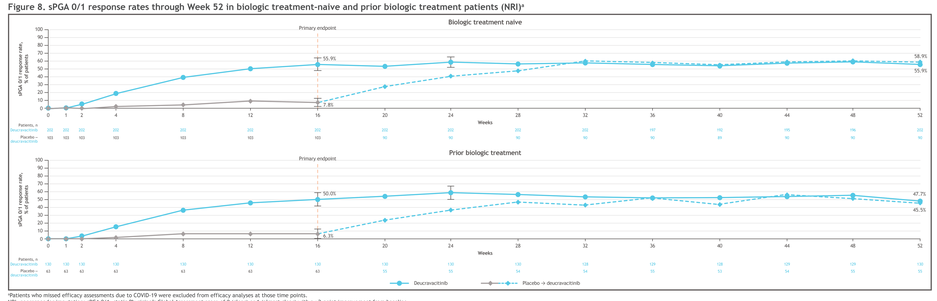
[a]Patients who missed efficacy assessments due to COVID-19 were excluded from efficacy analyses at those time points.
NRI, nonresponder imputation; sPGA 0/1, static Physician's Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline.

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

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1. SOTYKTU™ (deucravacitinib) [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; September 2022. **2.** Burke JR, et al. *Sci Transl Med*. 2019;11:eaaw1736. **3.** Wrobleski ST, et al. *J Med Chem*. 2019;62:8973-8995. **4.** Armstrong AW, et al. *J Am Acad Dermatol*. 2022;S0190-9622(22)02256-3. doi: 10.1016/j.jaad.2022.07.002. Online ahead of print. **5.** Warren RB, et al. Presented at the European Academy of Dermatology and Venereology (EADV) 30th Congress, September 29–October 2, 2021. Late breaker. **6.** Warren RB, et al. Presented at the European Academy of Dermatology and Venereology (EADV) 30th 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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