Deucravacitinib, an oral, selective tyrosine kinase 2 (TYK2) inhibitor, in moderate to severe plaque psoriasis: 52-week efficacy results from the phase 3 POETYK PSO-1 and PSO-2 trials

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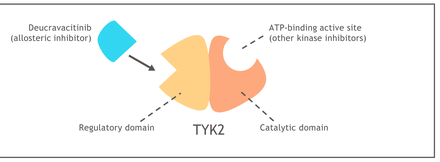
Introduction

- Tyrosine kinase 2 (TYK2) is an intracellular enzyme that mediates signaling of cytokines (interleukin [IL]-23, IL-12, and Type I interferons) involved in psoriasis pathogenesis[1]
- Deucravacitinib is an oral agent that selectively inhibits TYK2 via an allosteric mechanism by uniquely binding to the regulatory domain rather than to the more conserved active domain where Janus kinase (JAK) 1/2/3 inhibitors bind (**Figure 1**)[1]
  - ≥100-fold greater selectivity for TYK2 vs JAK 1/3 and ≥2000-fold greater selectivity for TYK2 vs JAK 2 in cells[1,2]
- In the phase 3 POETYK PSO-1 and PSO-2 trials, deucravacitinib was significantly more efficacious than placebo and apremilast based on the coprimary endpoints of ≥75% reduction from baseline in Psoriasis Area and Severity Index (PASI 75) and static Physician's Global Assessment (sPGA) score of 0/1 at Week 16 and was well tolerated in patients with moderate to severe plaque psoriasis[3]

Figure 1. Mechanism of action of deucravacitinib



ATP, adenosine triphosphate; TYK2, tyrosine kinase 2.

Objective

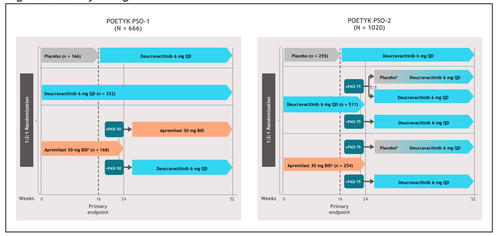
- To evaluate the efficacy of deucravacitinib over 52 weeks in POETYK PSO-1 and PSO-2, including:
  - Efficacy of continuous deucravacitinib treatment and switching from placebo to deucravacitinib at Week 16 through Week 52 (PSO-1)
  - Maintenance of efficacy on continued treatment and durability of response through Week 52 after treatment withdrawal among Week 24 PASI 75 responders (PSO-2)

Methods

Key design elements

- The POETYK PSO-1 and PSO-2 study designs are shown in **Figure 2**
- Key eligibility criteria
  - Adults with moderate to severe plaque psoriasis
  - PASI ≥12, sPGA ≥3, body surface area (BSA) ≥10%
  - Stratified by geographic region, body weight, and prior biologic use
- Coprimary endpoints were the proportion of patients who achieved PASI 75 and sPGA 0/1 responses vs placebo at Week 16

Figure 2. Study designs



*Apremilast was titrated from 10 mg QD to 30 mg BID over the first 5 days of dosing.
†Upon relapse (≥50% loss of Week 24 PASI percentage improvement from baseline), patients were to be switched to deucravacitinib 6 mg QD, BID, twice daily; PASI 50, ≥50% reduction from baseline in Psoriasis Area and Severity Index; PASI 75, ≥75% reduction from baseline in PASI; QD, once daily.

Outcome measures

- PSO-1
  - Efficacy of continuous deucravacitinib treatment through Week 52
    - PASI 75, PASI 90, PASI 100
    - sPGA 0/1, sPGA 0
  - Efficacy of switching from placebo to deucravacitinib treatment at Week 16 through Week 52
    - PASI 75 and sPGA 0/1
    - Percentage change from baseline in PASI
    - Scalp-specific Physician's Global Assessment (ss-PGA) score of 0/1 (clear/almost clear scalp psoriasis)
    - Dermatology Life Quality Index (DLQI) score of 0/1
- PSO-2
  - Maintenance of deucravacitinib response from Week 24 to Week 52 among Week 24 PASI 75 responders
    - PASI 75
    - sPGA 0/1
  - Time to loss of PASI 75 response after deucravacitinib withdrawal among Week 24 PASI 75 responders

Results

Baseline patient demographics and disease characteristics

- Baseline patient demographics and disease characteristics were largely similar across treatment groups in pooled data from the 2 trials (**Table 1**)

Table 1. Baseline patient demographics and disease characteristics

	POETYK PSO-1			POETYK PSO-2		
	Placebo (n = 166)	Deucravacitinib (n = 332)	Apremilast (n = 168)	Placebo (n = 255)	Deucravacitinib (n = 511)	Apremilast (n = 254)
Age, y, mean (SD)	47.9 (14.0)	45.9 (13.7)	44.7 (12.1)	47.3 (13.6)	46.9 (13.4)	46.4 (13.3)
Weight, kg, mean (SD)	89.1 (22.3)	87.9 (21.8)	87.5 (21.1)	91.5 (20.2)	92.3 (21.9)	93.5 (22.2)
Female, n (%)	53 (31.9)	102 (30.7)	58 (34.5)	74 (29.0)	175 (34.2)	97 (38.2)
Race, n (%)						
White	128 (77.1)	267 (80.4)	139 (82.7)	232 (91.0)	474 (92.8)	229 (90.2)
Asian	34 (20.5)	59 (17.8)	28 (16.7)	8 (3.1)	24 (4.7)	12 (4.7)
Other	4 (2.4)	6 (1.8)	1 (0.6)	15 (5.9)	13 (2.5)	13 (5.1)
Disease duration, y, mean (SD)	17.3 (12.8)	17.1 (12.4)	17.7 (11.8)	19.9 (12.8)	19.6 (12.9)	18.9 (12.4)
Prior systemic treatment use, n (%)						
Biologic	63 (38.0)	130 (39.2)	66 (39.3)	83 (32.5)	165 (32.3)	79 (31.1)
No prior systemic therapy	57 (34.3)	132 (39.8)	59 (35.1)	116 (45.5)	237 (46.4)	114 (44.9)
sPGA, n (%)						
3 = moderate	128 (77.1)	257 (77.4)	139 (82.7)	217 (85.1)	408 (79.8)	196 (77.2)
4 = severe	37 (22.3)	75 (22.6)	29 (17.3)	38 (14.9)	103 (20.2)	58 (22.8)
PASI, mean (SD)	20.7 (8.0)	21.8 (8.6)	21.4 (9.0)	21.1 (9.0)	20.7 (7.5)	21.6 (8.4)
DLQI, mean (SD)	11.4 (6.6)	12.0 (6.7)	12.4 (6.8)	11.8 (6.8)	11.8 (6.5)	12.5 (6.7)
BSA, %, mean (SD)	25.3 (16.9)	26.6 (15.9)	26.6 (16.1)	25.3 (15.7)	26.3 (15.8)	28.3 (16.5)
PSSD symptom score, mean (SD)	51.4 (26.8)	51.7 (25.2)	56.2 (25.2)	50.1 (24.8)	52.3 (26.3)	51.9 (25.4)

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

POETYK PSO-1 and PSO-2 patient disposition over 52 weeks

- The patient disposition for both trials over 52 weeks is listed in **Table 2**

Table 2. Disposition of patients over 52 weeks

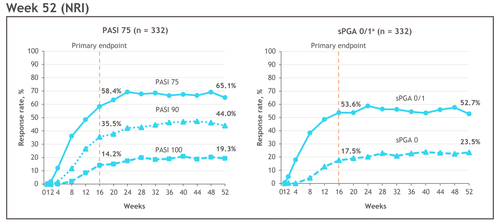
	Patients, n			
Treatment	Week 0	Week 16	Week 24	Week 52
POETYK PSO-1				
Continuous deucravacitinib (Week 0–52)	332	307	302	268
Placebo (Week 0–16) – deucravacitinib (Week 16–52)	165	145	140	129
POETYK PSO-2				
Deucravacitinib (Week 0–16)	510	456[b]		
Week 24 PASI 75 responders – rerandomized to deucravacitinib (Week 24–52)[a]			148	138
Week 24 PASI 75 responders – rerandomized to placebo (Week 24–52)[a]			150	133

[a]142 patients did not achieve PASI 75 response at Week 24 and continued to receive deucravacitinib treatment until Week 52.
[b]An additional 16 patients discontinued deucravacitinib treatment between Weeks 16 and 24.
PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index.

POETYK PSO-1 PASI and sPGA responses

- PASI 75 and sPGA 0/1 responses were maintained from Week 16 to Week 52 in patients who received continuous deucravacitinib treatment (**Figure 3**)
- PASI 90, PASI 100, and sPGA 0 responses (secondary efficacy endpoints) were also maintained through 52 weeks in patients treated with deucravacitinib

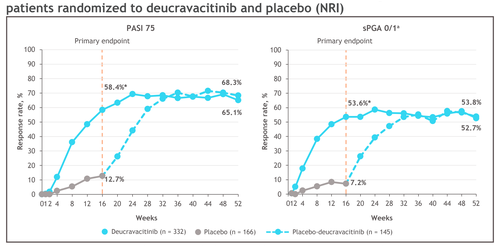
Figure 3. POETYK PSO-1: PASI and sPGA responses with deucravacitinib through Week 52 (NRI)



NRI was used to impute missing data. *sPGA response is defined as a score of 0 or 1, with ≥2-point improvement from baseline.
NRI, nonresponder imputation; PASI, Psoriasis Area and Severity Index; PASI 75, ≥75% reduction from baseline in PASI; PASI 90, ≥90% reduction from baseline in PASI; PASI 100, 100% reduction from baseline in PASI; sPGA 0/1, static Physician's Global Assessment score of 0 or 1.

- Patients who switched from placebo to deucravacitinib at Week 16 demonstrated PASI 75 and sPGA 0/1 responses at Week 52 comparable to those observed in patients who received continuous deucravacitinib treatment from Day 1 (**Figure 4**)

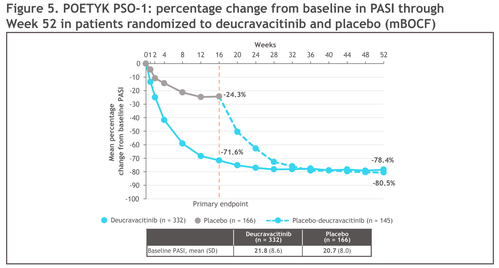
Figure 4. POETYK PSO-1: PASI 75 and sPGA 0/1 responses through Week 52 in patients randomized to deucravacitinib and placebo (NRI)



NRI was used to impute missing data. *sPGA response is defined as a score of 0 or 1, with ≥2-point improvement from baseline.
*P < 0.0001 vs placebo.
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 or 1.

- Patients who switched from placebo to deucravacitinib at Week 16 demonstrated percentage changes from baseline in PASI at Week 52 comparable to those observed in patients who received continuous deucravacitinib treatment from Day 1 (**Figure 5**)

Figure 5. POETYK PSO-1: percentage change from baseline in PASI through Week 52 in patients randomized to deucravacitinib and placebo (mBOCF)

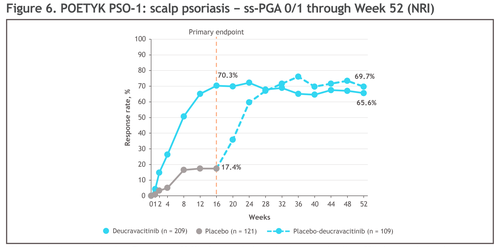


mBOCF was used to impute missing data.
mBOCF, modified baseline observation carried forward; PASI, Psoriasis Area and Severity Index.

POETYK PSO-1 ss-PGA 0/1 through Week 52

- ss-PGA 0/1 responses at Week 16 were maintained through Week 52 with continuous deucravacitinib treatment (**Figure 6**)
  - Patients who switched from placebo to deucravacitinib at Week 16 achieved comparable ss-PGA 0/1 responses at Week 52 to those who received continuous deucravacitinib treatment

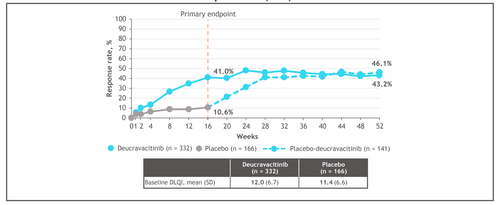
Figure 6. POETYK PSO-1: scalp psoriasis – ss-PGA 0/1 through Week 52 (NRI)



NRI was used to impute missing data. The majority (88.9%) of patients had scalp involvement at baseline; >55% of patients had moderate to severe scalp psoriasis (ss-PGA ≥3) at baseline and were evaluated for ss-PGA 0/1 responses.[4]
NRI, nonresponder imputation; QD, once daily; ss-PGA 0/1, scalp-specific Physician's Global Assessment score of 0 or 1.

- Patients who switched from placebo to deucravacitinib at Week 16 achieved DLQI 0/1 responses at Week 52 comparable to those observed in patients who received continuous deucravacitinib treatment from Day 1 (**Figure 7**)

Figure 7. POETYK PSO-1: DLQI 0/1 response through Week 52 in patients randomized to deucravacitinib and placebo (NRI)

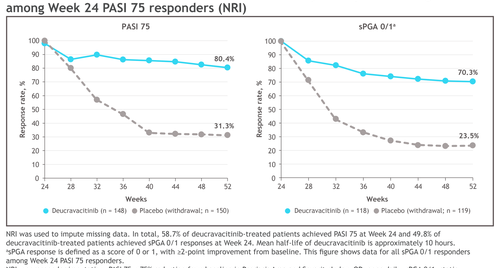


	Deucravacitinib (n = 332)	Placebo (n = 166)
Baseline DLQI, mean (SD)	12.0 (6.7)	11.4 (6.6)

NRI was used to impute missing data. DLQI score of 0 or 1 among patients with a baseline score of 2. DLQI 0/1 is indicative of no impact on a patient's life.
DLQI 0/1, Dermatology Life Quality Index score of 0 or 1; NRI, nonresponder imputation.

- PASI 75 and sPGA 0/1 responses were maintained on continuous treatment through Week 52 in the majority of deucravacitinib-treated patients who achieved PASI 75 at Week 24 (**Figure 8**)
- Median time to loss of PASI 75 response was 12 weeks in the randomized withdrawal arm

Figure 8. POETYK PSO-2: maintenance and durability of response through Week 52 among Week 24 PASI 75 responders (NRI)



NRI was used to impute missing data. In total, 58.7% of deucravacitinib-treated patients achieved PASI 75 at Week 24 and 49.8% of deucravacitinib-treated patients achieved sPGA 0/1 responses at Week 24. Mean half-life of deucravacitinib is approximately 10 hours.
*sPGA response is defined as a score of 0 or 1, with ≥2-point improvement from baseline. This figure shows data for all sPGA 0/1 responders among Week 24 PASI 75 responders.
NRI, nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index; QD, once daily; sPGA 0/1, static Physician's Global Assessment score of 0 or 1.

Conclusions

- In the phase 3 POETYK PSO-1 and PSO-2 trials, deucravacitinib was efficacious through 52 weeks in patients with moderate to severe plaque psoriasis
  - Clinical responses improved through Week 24 and were maintained in patients who received continuous deucravacitinib treatment through Week 52
  - Week 52 responses in patients who switched from placebo to deucravacitinib treatment at Week 16 were comparable to those observed with continuous deucravacitinib treatment from Day 1
- Durable responses were observed after withdrawal of treatment in Week 24 responders
- The results of this 52-week efficacy analysis are consistent with those of the primary analyses of PSO-1 and PSO-2 at Week 16[3]
- Deucravacitinib, a once-daily oral drug, has the potential to become an efficacious and well-tolerated treatment choice for patients with moderate to severe plaque psoriasis

References

1. Burke JR, et al. *Sci Transl Med*. 2019;11:1-16. **2.** Wrobleski ST, et al. *J Med Chem*. 2019;62:8973-8995. **3.** Armstrong A, et al. Presented at the Annual Meeting of the American Academy of Dermatology; April 23-25, 2021. **4.** Blauvelt A, et al. Presented at EADV 30th Congress; 29 September–2 October 2021. Poster P1391.

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