Deucravacitinib, an oral, selective tyrosine kinase 2 inhibitor, versus placebo and apremilast in moderate to severe plaque psoriasis: analysis of body surface area involvement in the phase 3 POETYK PSO-1 and PSO-2 trials

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Synopsis

- Tyrosine kinase 2 (TYK2) is an intracellular enzyme that mediates cytokine signaling (eg, interleukin-23, Type 1 interferons) involved in psoriasis pathogenesis[1]
- Deucravacitinib, an oral, selective, allosteric 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[2]
  – Uniquely binds to the TYK2 regulatory domain with high selectivity and inhibits TYK2 via an allosteric mechanism[1] (**Figure 1**)
- The phase 3 POETYK PSO-1 and PSO-2 trials demonstrated that deucravacitinib was superior to placebo and apremilast in patients with moderate to severe plaque psoriasis based on the coprimary endpoints of a ≥75% reduction from baseline in Psoriasis Area and Severity Index (PASI 75) and a 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[3,4]
- Clinical responses were maintained through 52 weeks in patients who received continuous deucravacitinib treatment and were improved in patients who switched from placebo to deucravacitinib at Week 16[5]
- 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[6]

Figure 1. Mechanism of action of deucravacitinib

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

- Responses, including body surface area (BSA) involvement and the composite endpoint BSA × sPGA, were also monitored in both POETYK PSO-1 and PSO-2 to determine deucravacitinib efficacy in multiple endpoints
  – PASI is the standard efficacy outcome for clinical trials but is time consuming and less meaningful for clinicians in everyday practice[8]
  – sPGA is also standard for clinical trials but focuses on plaque qualities and does not include an assessment of BSA involvement[8,9]
  – Together, BSA and BSA × sPGA can be useful proxies for PASI in clinical practice for assessment of disease severity in patients with moderate to severe plaque psoriasis[9]

Objective

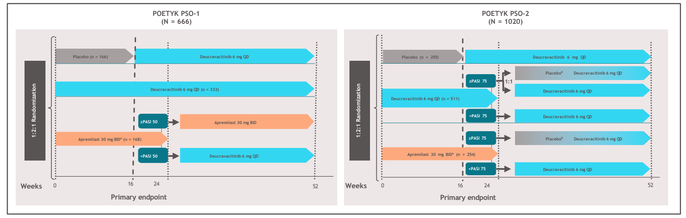
- To evaluate the efficacy of deucravacitinib over 52 weeks based on BSA involvement and BSA × sPGA

Methods

Study designs

- The study designs for POETYK PSO-1 and PSO-2 are illustrated in **Figure 2**
- Patients meeting the following criteria were eligible to enroll in one of the studies:
  – Age ≥18 years
  – Diagnosis of moderate to severe plaque psoriasis
    - Baseline PASI ≥12, sPGA ≥3, and BSA involvement ≥10%
- Patient randomization in POETYK PSO-1 and PSO-2 was stratified by geographic region, body weight, and prior biologic use
- BSA was estimated using the handprint method: the size of the patient's handprint, including fingers and thumb, represented 1% of BSA involvement

Figure 2. POETYK PSO-1 and PSO-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, Psoriasis Area and Severity Index; PASI 50, ≥50% reduction from baseline in PASI; PASI 75, ≥75% reduction from baseline in PASI; QD, once daily.

Outcomes

- The current analysis examined mean percentage change from baseline in BSA and BSA × sPGA
- Response rates for a ≥75% improvement from baseline in BSA × sPGA (BSA × sPGA 75) were also reported
- Efficacy outcomes for Weeks 0–24 were evaluated using the pooled POETYK PSO-1/PSO-2 population
- Maintenance of response through Week 52 was examined in the POETYK PSO-1 population only since it allowed assessment of continuous deucravacitinib treatment without any changes

Statistical methods

- Modified baseline observation carried forward (mBOCF) was used for change from baseline endpoints
  – Baseline observation was carried forward for patients who discontinued due to lack of efficacy or adverse events
  – For patients who discontinued the study treatment for other reasons or had a missing value, the last valid observation was carried forward (including the baseline value as applicable)
- Nonresponder imputation (NRI) was used for BSA × sPGA 75
  – Patients who discontinued the study treatment or study or had missing endpoint data prior to time point of comparison were imputed as nonresponders
- Patients were excluded if data were missing solely due to COVID-19

Results

- A total of 1686 patients were randomized across the POETYK PSO-1 and PSO-2 trials (**Table 1**)
- Mean baseline BSA and BSA × sPGA scores were generally similar in each treatment group in POETYK PSO-1 and PSO-2 (**Table 1**)

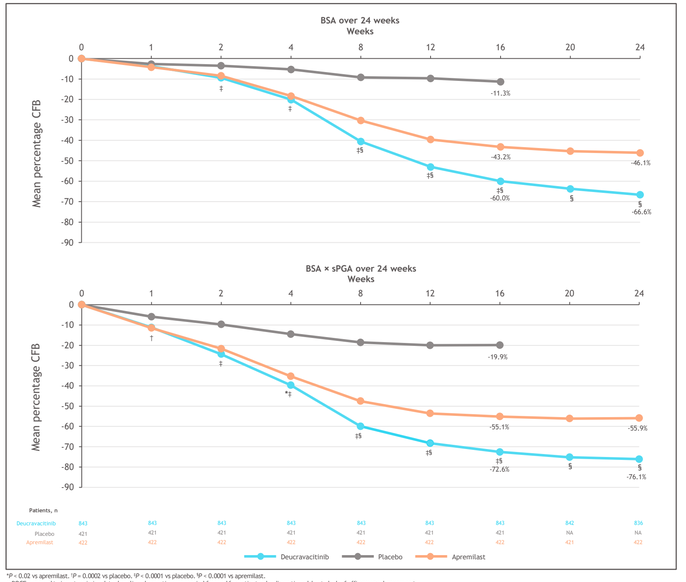
Table 1. Baseline patient demographics and disease characteristics

Parameter	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, mean (SD), y	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, mean (SD), kg	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)
Disease duration, mean (SD), y	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)
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)
BSA × sPGA, mean (SD)	82.1 (57.3)	86.9 (56.1)	85.4 (54.9)	81.1 (56.3)	85.0 (54.6)	92.4 (58.7)
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)
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; BSA × sPGA, body surface area × static Physician's Global Assessment score; DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index; PSSD, Psoriasis Symptoms and Signs Diary.

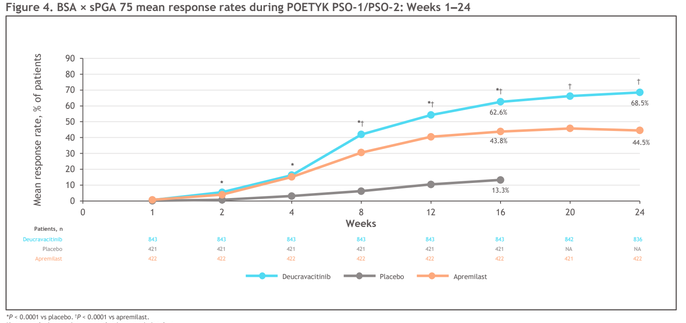
- By Week 16, significantly greater reductions in BSA involvement were observed in patients treated with deucravacitinib (60.0%) vs those treated with placebo (11.3%; $P < 0.0001$) and apremilast (43.2%; $P < 0.0001$) (**Figure 3**)
  – Significantly greater reductions were also observed with deucravacitinib vs apremilast by Week 24 (66.6% vs 46.1%; $P < 0.0001$)
- BSA × sPGA scores followed a similar pattern, with a decrease of 72.6% at Week 16 in deucravacitinib-treated patients vs 19.9% with placebo ($P < 0.0001$) and 55.1% with apremilast ($P < 0.0001$) (**Figure 3**)
  – By Week 24, BSA × sPGA involvement decreased by 76.1% in patients who received deucravacitinib vs 55.9% ($P < 0.0001$) in patients treated with apremilast
- BSA × sPGA 75 response rates were significantly higher in patients treated with deucravacitinib vs those treated with placebo ($P < 0.0001$) and apremilast ($P < 0.0001$) at Week 16 and vs apremilast at Week 24 ($P < 0.0001$) (**Figure 4**)

Figure 3. Mean percentage changes in BSA and BSA × sPGA scores over 24 weeks in POETYK PSO-1 and PSO-2 pooled results



‡P < 0.02 vs apremilast. †P < 0.0002 vs placebo. ††P < 0.0001 vs placebo. §P < 0.0001 vs apremilast.
mBOCF was used to impute missing data; baseline observation was carried forward for patients who discontinued due to lack of efficacy or adverse events.
BSA, body surface area; BSA × sPGA, body surface area × static Physician's Global Assessment score; CFB, change from baseline; mBOCF, modified baseline observation carried forward.

Figure 4. BSA × sPGA 75 mean response rates during POETYK PSO-1/PSO-2: Weeks 1–24

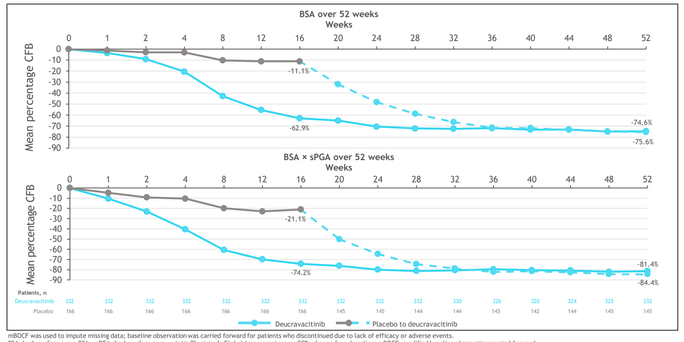


*P < 0.0001 vs placebo. †P < 0.0001 vs apremilast.
Nonresponder imputation was used to impute missing data.
BSA × sPGA 75, ≥75% improvement from baseline in body surface area × static Physician's Global Assessment score.

Weeks 0–52 (POETYK PSO-1 population)

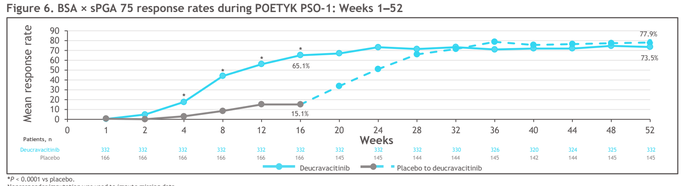
- Findings from POETYK PSO-1 demonstrated maintenance of BSA and BSA × sPGA results in patients who received continuous deucravacitinib treatment, with mean percentage reductions of 74.6% and 81.4%, respectively, from baseline to Week 52 (**Figure 5**)
- Patients who switched from placebo to deucravacitinib at Week 16 had similar mean percentage reductions at Week 52 (BSA, 75.6%; BSA × sPGA, 84.4%) to patients treated continuously with deucravacitinib (**Figure 5**)
- BSA × sPGA 75 responses were maintained through Week 52 in patients who received continuous deucravacitinib treatment and improved in patients who switched from placebo to deucravacitinib at Week 16, with Week 52 response rates that were similar between the groups (**Figure 6**)

Figure 5. Mean change from baseline responses in BSA and BSA × sPGA during POETYK PSO-1: Weeks 0–52



mBOCF was used to impute missing data; baseline observation was carried forward for patients who discontinued due to lack of efficacy or adverse events.
BSA, body surface area; BSA × sPGA, body surface area × static Physician's Global Assessment score; CFB, change from baseline; mBOCF, modified baseline observation carried forward.

Figure 6. BSA × sPGA 75 response rates during POETYK PSO-1: Weeks 1–52



*P < 0.0001 vs placebo.
Nonresponder imputation was used to impute missing data.
BSA × sPGA 75, ≥75% improvement from baseline in body surface area × static Physician's Global Assessment score.

Conclusions

- In the POETYK PSO-1 and PSO-2 trials, deucravacitinib treatment was associated with greater improvements in BSA, BSA × sPGA, and BSA × sPGA 75 over time compared with placebo and apremilast in patients with moderate to severe plaque psoriasis
- Deucravacitinib was associated with long-term improvements in response rates and maintenance of response in patients continuously treated over 52 weeks and in those who switched to deucravacitinib following 16 weeks of placebo

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