Deucravacitinib, an oral, selective, allosteric tyrosine kinase 2 inhibitor, versus placebo in scalp, nail, and palmoplantar psoriasis: subset analyses of the phase 3 POETYK PSO-1 and POETYK PSO-2 trials

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Introduction

- 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 instead of the catalytic domain of TYK2[2]
    - ≥100-fold greater selectivity for TYK2 vs Janus kinase (JAK) 1/3 and ≥2000-fold greater selectivity for TYK2 vs JAK 2 in cells[2,3]
  - Inhibits TYK2-mediated cytokine signaling involved in psoriasis pathogenesis (eg, interleukin-23, Type I interferons)[2]
- Two 52-week, phase 3 psoriasis trials (POETYK PSO-1 and POETYK PSO-2) previously demonstrated that deucravacitinib was superior to placebo and apremilast at Week 16 based on the coprimary endpoints[4,5]:
  - ≥75% reduction from baseline in Psoriasis Area and Severity Index (PASI 75)
  - Static Physician's Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline (sPGA 0/1)

Objectives

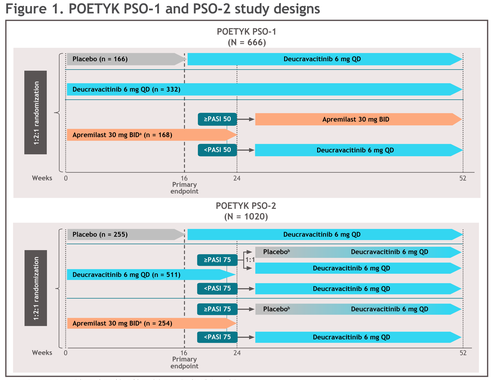
- Efficacy of deucravacitinib vs placebo at Week 16 in patients with moderate to severe involvement at baseline in the pooled POETYK PSO-1 and PSO-2 population of:
  - Scalp
  - Fingernail
  - Palms and soles (palmoplantar psoriasis)
- Efficacy in these high impact areas through Week 52 in POETYK PSO-1 patients:
  - With continuous deucravacitinib treatment from Day 1
  - After switching from placebo to deucravacitinib at Week 16

Methods

Study designs

- The POETYK PSO-1 and PSO-2 study designs are shown in **Figure 1**
- Key eligibility criteria included the following:
  - Age ≥18 years
  - Diagnosis of moderate to severe plaque psoriasis
    - Baseline PASI ≥12, sPGA ≥3, body surface area involvement ≥10%
- Patient randomization was stratified by geographic region, body weight, and prior biologic use

Figure 1. POETYK PSO-1 and PSO-2 study designs



[a]Apremilast was titrated from 10 mg QD to 30 mg BID over the first 5 days of dosing.
[b]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.

Efficacy endpoints

- Moderate to severe scalp psoriasis (scalp-specific PGA [ss-PGA ≥3]) at baseline
  - ss-PGA 0/1
  - ≥90% reduction from baseline in Psoriasis Scalp Severity Index (PSSI 90)
- Moderate to severe fingernail psoriasis (PGA-Fingernails [PGA-F ≥3]) at baseline
  - PGA-F 0/1
- Moderate to severe palmoplantar psoriasis (palmoplantar PGA [pp-PGA ≥3]) at baseline
  - pp-PGA 0/1
  - Palmoplantar PASI (pp-PASI) improvements from baseline

Evaluation time points

- Weeks 0–16 in the pooled POETYK PSO-1 and PSO-2 population
- Weeks 0–52 in POETYK PSO-1 (allowed continuous treatment with deucravacitinib for Weeks 0–52)

Statistical analysis

- None of the statistical comparisons of deucravacitinib vs placebo were multiplicity controlled except for ss-PGA 0/1 vs placebo at Week 16 in POETYK PSO-1

Results

Baseline patient demographics and disease characteristics

- In the pooled POETYK PSO-1 and PSO-2 population (N = 1264) (**Table 1**):
  - 64% (n = 808) had moderate to severe scalp psoriasis
  - 15% (n = 184) had moderate to severe fingernail psoriasis
  - 7% (n = 82) had moderate to severe palmoplantar psoriasis
- Presence of moderate to severe disease in these special areas was balanced overall in the deucravacitinib group vs the placebo group

Table 1. Baseline patient demographics and disease characteristics

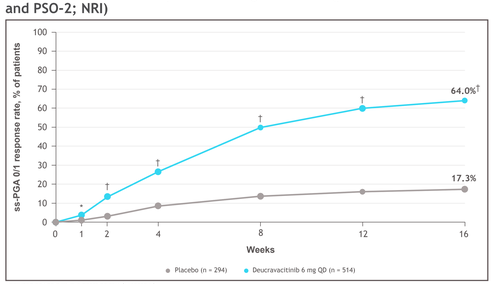
	POETYK PSO-1 and PSO-2	
	Placebo (n = 421)	Deucravacitinib (n = 843)
Age, mean (SD), y	47.5 (13.7)	46.5 (13.5)
Weight, mean (SD), kg	90.6 (21.1)	90.6 (21.9)
Female, n (%)	127 (30.2)	277 (32.9)
Race, n (%)		
White	360 (85.5)	741 (87.9)
Asian	42 (10.0)	83 (9.8)
Other	19 (4.5)	19 (2.3)
Disease duration, mean (SD), y	18.9 (12.9)	18.6 (12.7)
Prior systemic treatment use, n (%)		
Yes	248 (58.9)	474 (56.2)
Nonbiologic (± biologic)	183 (43.5)	326 (38.7)
Biologic	146 (34.7)	295 (35.0)
No	173 (41.1)	369 (43.8)
sPGA, n (%)		
3 (moderate)	345 (81.9)	665 (78.9)
4 (severe)	75 (17.8)	178 (21.1)
PASI, mean (SD)	20.9 (8.6)	21.1 (8.0)
BSA, mean (SD), %	25.3 (16.1)	26.4 (15.8)
ss-PGA ≥3, n (%)	294 (69.8)	514 (61.0)
PGA-F ≥3, n (%)	72 (17.1)	112 (13.3)
pp-PGA ≥3, n (%)	25 (5.9)	57 (6.8)
PSSD symptom score, mean (SD)	50.6 (25.6)	52.1 (25.9)
DLQI, mean (SD)	11.6 (6.7)	11.9 (6.6)

BSA, body surface area; DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index; PGA-F, Physician's Global Assessment-Fingernails; pp-PGA, palmoplantar Physician's Global Assessment; PSSD, Psoriasis Symptoms and Signs Diary; sPGA, static Physician's Global Assessment; ss-PGA, scalp-specific Physician's Global Assessment.

Scalp psoriasis

- In the pooled POETYK PSO-1 and PSO-2 population, significantly more patients receiving deucravacitinib vs placebo achieved ss-PGA 0/1 at Week 16 (**Figure 2**)
  - Efficacy was significantly greater with deucravacitinib vs placebo by Week 1

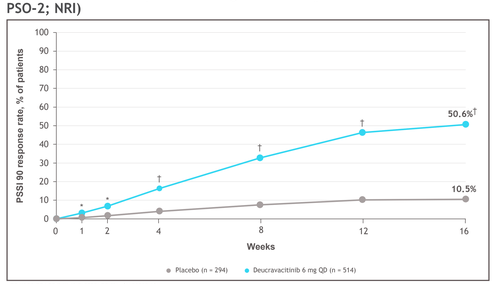
Figure 2. ss-PGA 0/1[a] responses through Week 16 (pooled POETYK PSO-1 and PSO-2; NRI)



[a]Included patients with a baseline ss-PGA score ≥3.
*P < 0.05 vs placebo. †P < 0.0001 vs placebo. NRI was used to impute missing data.
NRI, nonresponder imputation; QD, once daily; ss-PGA 0/1, scalp-specific Physician's Global Assessment score of 0 or 1.

- In the pooled POETYK PSO-1 and PSO-2 population, significantly more patients receiving deucravacitinib vs placebo achieved PSSI 90 at Week 16 (**Figure 3**)
  - Efficacy was significantly greater with deucravacitinib vs placebo by Week 1

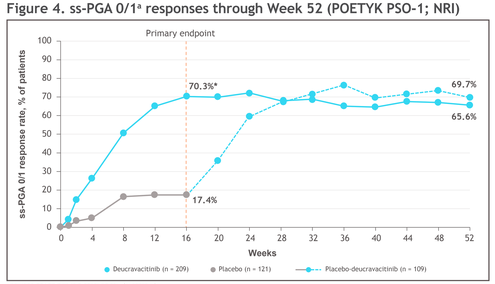
Figure 3. PSSI 90[a] responses through Week 16 (pooled POETYK PSO-1 and PSO-2; NRI)



[a]Included patients with a baseline ss-PGA score ≥3.
*P ≤ 0.05 vs placebo. †P ≤ 0.0001 vs placebo. NRI was used to impute missing data.
NRI, nonresponder imputation; PSSI 90, ≥90% reduction from baseline in Psoriasis Scalp Severity Index; QD, once daily; ss-PGA, scalp-specific Physician's Global Assessment.

- In POETYK PSO-1, ss-PGA 0/1 responses at Week 16 were maintained through Week 52 with continuous deucravacitinib treatment (**Figure 4**)
  - Patients who crossed over from placebo to deucravacitinib at Week 16 achieved comparable ss-PGA 0/1 responses at Week 52 to those who had received continuous deucravacitinib treatment from Day 1

Figure 4. ss-PGA 0/1[a] responses through Week 52 (POETYK PSO-1; NRI)

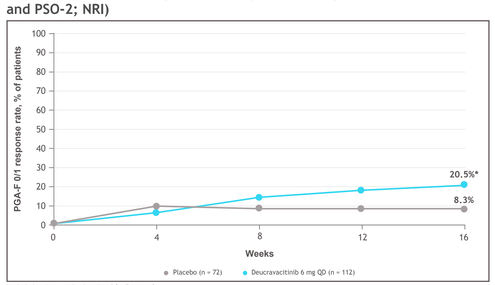


[a]Included patients with a baseline ss-PGA score ≥3.
*P < 0.0001 vs placebo. NRI was used to impute missing data.
NRI, nonresponder imputation; ss-PGA 0/1, scalp-specific Physician's Global Assessment score of 0 or 1.

Fingernail psoriasis

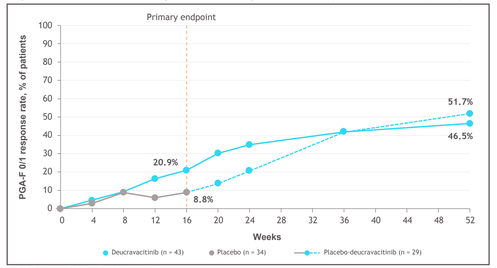
- In the pooled POETYK PSO-1 and PSO-2 population, significantly more patients receiving deucravacitinib vs placebo achieved PGA-F 0/1 at Week 16 (**Figure 5**)
- In POETYK PSO-1, PGA-F 0/1 responses at Week 16 were increased through Week 52 with continuous deucravacitinib treatment (**Figure 6**)
  - Patients who crossed over from placebo to deucravacitinib at Week 16 achieved comparable PGA-F 0/1 responses at Week 52 to those who received continuous deucravacitinib treatment

Figure 5. PGA-F 0/1[a] responses through Week 16 (pooled POETYK PSO-1 and PSO-2; NRI)



[a]Included patients with a baseline PGA-F score ≥3.
*P = 0.0272 vs placebo. NRI was used to impute missing data.
NRI, nonresponder imputation; PGA-F 0/1, Physician's Global Assessment-Fingernails score of 0 or 1; QD, once daily.

Figure 6. PGA-F 0/1[a] responses through Week 52 (POETYK PSO-1; NRI)

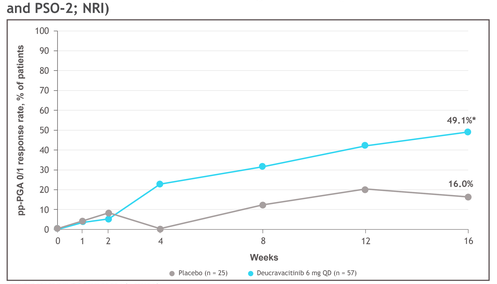


[a]Included patients with a baseline PGA-F score ≥3.
NRI was used to impute missing data.
NRI, nonresponder imputation; PGA-F 0/1, Physician's Global Assessment-Fingernails score of 0 or 1.

Palmoplantar psoriasis

- In the pooled POETYK PSO-1 and PSO-2 population, significantly more patients receiving deucravacitinib vs placebo achieved pp-PGA 0/1 at Week 16 (**Figure 7**)

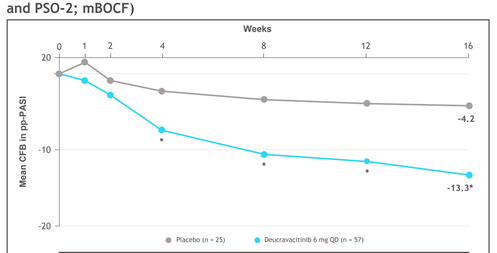
Figure 7. pp-PGA 0/1[a] responses through Week 16 (pooled POETYK PSO-1 and PSO-2; NRI)



[a]Included patients with a baseline pp-PGA score ≥3.
*P = 0.0052 vs placebo. NRI was used to impute missing data.
NRI, nonresponder imputation; pp-PGA 0/1, palmoplantar Physician's Global Assessment score of 0 or 1; QD, once daily.

- In the pooled POETYK PSO-1 and PSO-2 population, mean change from baseline in pp-PASI, adjusted for baseline covariates, was significantly greater with deucravacitinib vs placebo at Week 16 (**Figure 8**)
  - Greater efficacy with deucravacitinib vs placebo was observed as early as Week 4

Figure 8. Mean CFB in pp-PASI[a] through Week 16 (pooled POETYK PSO-1 and PSO-2; mBOCF)



	Placebo (n = 25)	Deucravacitinib (n = 57)
Baseline pp-PASI, mean (SD)	17.5 (12.5)	15.9 (10.9)

[a]Included patients with a baseline pp-PGA score ≥3.
*P ≤ 0.0097 vs placebo. mBOCF was used to impute missing data.
CFB, change from baseline; mBOCF, modified baseline observation carried forward; pp-PASI, palmoplantar Psoriasis Area and Severity Index; pp-PGA, palmoplantar Physician's Global Assessment; QD, once daily.

- In POETYK PSO-1, pp-PGA 0/1 responses at Week 16 were maintained through Week 52 with continuous deucravacitinib treatment (**Table 2**)
  - Patients who crossed over from placebo to deucravacitinib at Week 16 achieved comparable pp-PGA 0/1 responses at Week 52 to those who received continuous deucravacitinib treatment

Table 2. pp-PGA 0/1[a] responses through Week 52 (POETYK PSO-1; NRI)

	pp-PGA 0/1 response rate, %	
Week	Deucravacitinib (n = 18)	Placebo-deucravacitinib (n = 7)
16	55.6	0
24	66.7	42.9
52	55.6	42.9

[a]Included patients with a baseline pp-PGA score ≥3.
NRI was used to impute missing data.
NRI, nonresponder imputation; pp-PGA 0/1, palmoplantar Physician's Global Assessment score of 0 or 1.

Conclusions

- In patients with moderate to severe scalp, fingernail, or palmoplantar psoriasis at baseline in POETYK PSO-1 and PSO-2, deucravacitinib was significantly more efficacious than placebo in improving disease burden in these high impact areas through Week 16
- Clinical responses were maintained or increased in POETYK PSO-1 patients who received continuous deucravacitinib treatment from Day 1 through Week 52
  - Patients who crossed over from placebo to deucravacitinib at Week 16 achieved comparable responses at Week 52 to those who had received continuous deucravacitinib treatment from baseline
- These findings support the use of deucravacitinib, an oral, selective, allosteric TYK2 inhibitor, in patients with moderate to severe scalp, fingernail, or palmoplantar psoriasis

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