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

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Synopsis

- Deucravacitinib
  - Oral, selective tyrosine kinase 2 (TYK2) inhibitor that acts via an allosteric mechanism by uniquely binding to the regulatory domain instead of the catalytic domain of TYK2[1]
    - ≥100-fold greater selectivity for TYK2 vs Janus kinase (JAK) 1/3 and ≥2000-fold greater selectivity for TYK2 vs JAK 2 in cells[1,2]
  - Inhibits TYK2-mediated cytokine signaling involved in psoriasis pathogenesis (eg, interleukin-23, Type I interferons)[1]
- 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[3]:
  - ≥75% reduction from baseline in Psoriasis Area and Severity Index (PASI 75)
  - A static Physician's Global Assessment score of 0 or 1 (sPGA 0/1; clear or almost clear skin)

Objectives

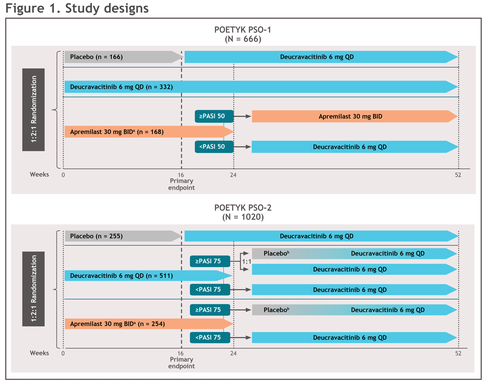
- Efficacy of deucravacitinib vs placebo at Week 16 in patients with moderate to severe involvement at baseline in the pooled PSO-1 and PSO-2 population of:
  - Scalp
  - Fingernail
  - Palms and soles (palmoplantar psoriasis)
- Efficacy in these high impact areas through Week 52 in PSO-1 patients:
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

Methods

Study designs

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

Figure 1. 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; INSI, 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 PSO-1 and PSO-2 population
- Weeks 0–52 in PSO-1 (allowed continuous treatment with deucravacitinib for Weeks 0–52)

Statistical analysis

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

Results

Baseline patient demographics and disease characteristics

- In the pooled 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 vs placebo group

Table 1. Baseline patient demographics and disease characteristics

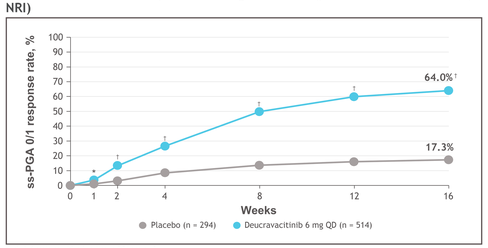
	POETYK PSO-1 and PSO-2	
	Placebo (n = 421)	Deucravacitinib (n = 843)
Age, mean (SD), y	47.5 (13.7)	46.5 (13.5)
Weight, mean (SD), kg	90.6 (21.1)	90.6 (21.9)
Female, n (%)	127 (30.2)	277 (32.9)
Race, n (%)		
White	360 (85.5)	741 (87.9)
Asian	42 (10.0)	83 (9.8)
Other	19 (4.5)	19 (2.3)
Disease duration, 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 prior systemic therapy	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 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

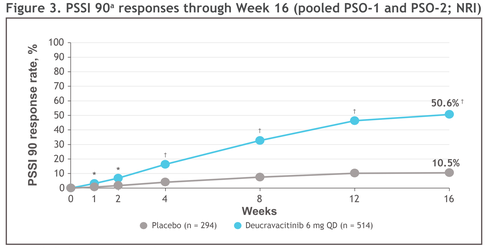
Figure 2. ss-PGA 0/1[a] responses through Week 16 (pooled PSO-1 and PSO-2; NRI)



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

- In the pooled 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

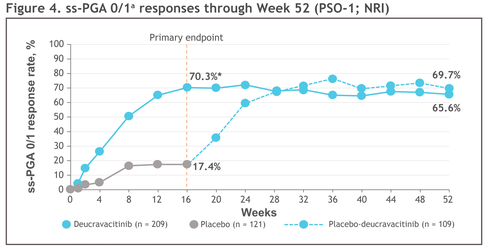
Figure 3. PSSI 90[a] responses through Week 16 (pooled PSO-1 and PSO-2; NRI)



[a]Included patients with a baseline ss-PGA score ≥3.
*P < 0.05 vs placebo. †P < 0.0001 vs placebo. Missing data were imputed with NRI.
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 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 (PSO-1; NRI)

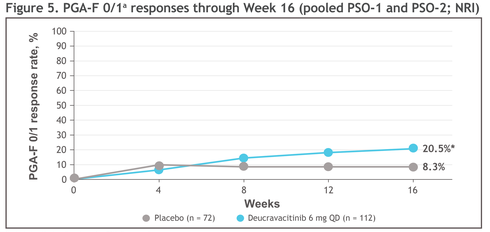


[a]Included patients with a baseline ss-PGA score ≥3.
*P < 0.0001 vs placebo. Missing data were imputed with NRI.
NRI, nonresponder imputation; ss-PGA 0/1, scalp-specific Physician's Global Assessment score of 0 or 1.

Fingernail psoriasis

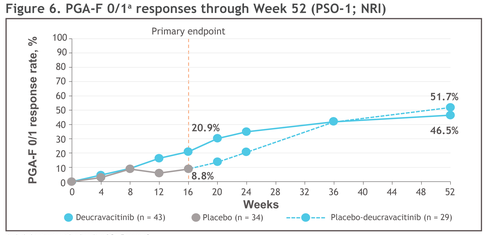
- In the pooled PSO-1 and PSO-2 population, significantly more patients receiving deucravacitinib vs placebo achieved PGA-F 0/1 at Week 16 (**Figure 5**)
- In PSO-1, PGA-F 0/1 responses at Week 16 were increased through Week 52 with continuous deucravacitinib treatment (**Figure 6**)
  - Patients who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



[a]Included patients with a baseline PGA-F score ≥3.
*P = 0.0272 vs placebo. Missing data were imputed with NRI.
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 (PSO-1; NRI)

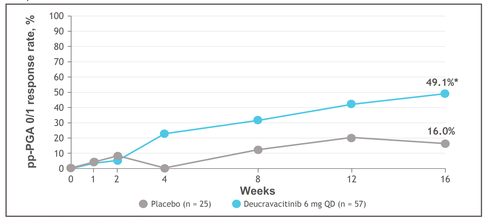


[a]Included patients with a baseline PGA-F score ≥3.
Missing data were imputed with NRI.
NRI, nonresponder imputation; PGA-F 0/1, Physician's Global Assessment-Fingernails score of 0 or 1.

Palmoplantar psoriasis

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

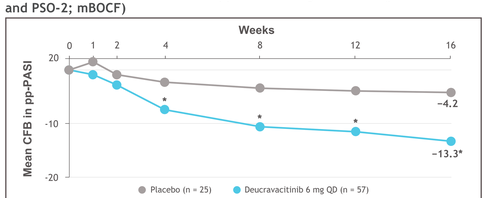
Figure 7. pp-PGA 0/1[a] responses through Week 16 (pooled PSO-1 and PSO-2; NRI)



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

- In the pooled 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. Change from baseline in pp-PASI[a] through Week 16 (pooled 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. Missing data were imputed with the modified baseline observation carried forward method.
CFB, change from baseline; mBOCF, modified baseline observation carried forward; pp-PASI, palmoplantar Psoriasis Area and Severity Index; QD, once daily.

- In 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 (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.
Missing data were imputed with NRI.
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 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 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 TYK2 inhibitor, in patients with moderate to severe scalp, fingernail, or palmoplantar 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.

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