Deucravacitinib, an oral, selective, allosteric tyrosine kinase 2 inhibitor, in scalp, nail, and palmoplantar psoriasis: subgroup analyses of the phase 3 POETYK PSO-1 and 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)
- Clinical efficacy and overall safety and tolerability were maintained for up to 2 years[6]

Objective

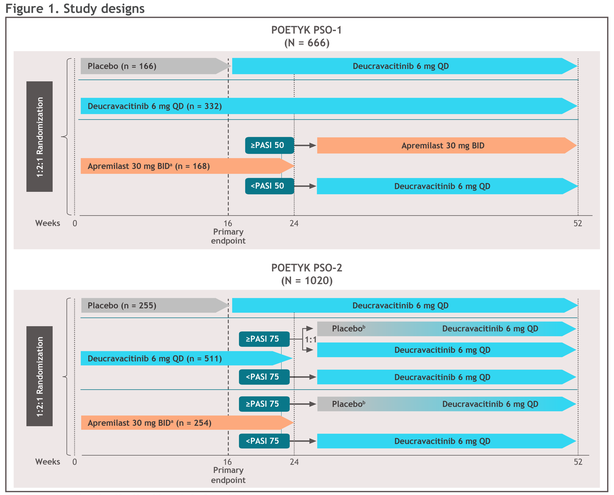
- Evaluate the efficacy of deucravacitinib treatment in patients with moderate to severe scalp, fingernail, and palmoplantar psoriasis

Methods

Study designs

- POETYK PSO-1 (NCT03624127) and PSO-2 (NCT03611751) enrolled adults with moderate to severe plaque psoriasis (PASI ≥12, sPGA ≥3, body surface area involvement ≥10%) (**Figure 1**)

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; 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

- This analysis looked at scalp-, fingernail-, and palmoplantar-specific outcomes in pooled patients from POETYK PSO-1 and PSO-2, including:
  - Scalp-specific PGA score of 0 or 1 (ss-PGA 0/1) and ≥90% reduction from baseline in Psoriasis Scalp Severity Index (PSSI 90) in patients with moderate to severe scalp psoriasis (ss-PGA ≥3) at baseline
  - PGA-Fingernails score of 0 or 1 (PGA-F 0/1) in patients with moderate to severe fingernail psoriasis (PGA-F ≥3) at baseline
  - Palmoplantar PGA score of 0 or 1 (pp-PGA 0/1) and palmoplantar PASI (pp-PASI) response in patients with moderate to severe palmoplantar psoriasis (pp-PGA ≥3) at baseline
- Outcomes in patients randomized to deucravacitinib vs placebo are reported through Week 16, and efficacy in deucravacitinib-treated patients is reported through Week 24
- Outcomes in patients who crossed over from placebo to deucravacitinib at Week 16 are reported from Weeks 16–52

Statistical analysis

- None of the statistical comparisons of deucravacitinib vs placebo were multiplicity controlled

Results

Baseline patient demographics and disease characteristics

- In the pooled POETYK PSO-1 and PSO-2 population (N = 1264; **Table 1**):
  - 63.9% (n = 808) had moderate to severe scalp psoriasis
  - 14.6% (n = 184) had moderate to severe fingernail psoriasis
  - 6.5% (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

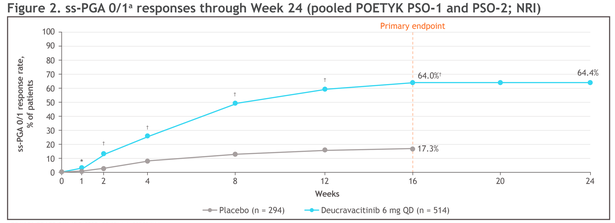
Parameter	POETYK PSO-1 and PSO-2	
	Placebo (n = 421)	Deucravacitinib (n = 843)
Age, mean (SD), y	47.5 (13.7)	46.5 (13.5)
Weight, mean (SD), kg	90.6 (21.1)	90.6 (21.9)
Female, n (%)	127 (30.2)	277 (32.9)
Race, n (%)		
White	360 (85.5)	741 (87.9)
Asian	42 (10.0)	83 (9.8)
Other	19 (4.5)	19 (2.3)
Disease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

- 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
  - ss-PGA 0/1 responses at Week 16 were maintained through Week 24 in deucravacitinib-treated patients

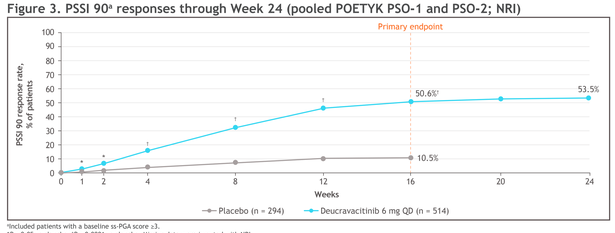
Figure 2. ss-PGA 0/1[a] responses through Week 24 (pooled POETYK PSO-1 and PSO-2; NRI)



[a]Included patients with a baseline ss-PGA score ≥3.
*P < 0.05 vs placebo. †P < 0.0001 vs placebo. 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.

- 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
  - PSSI 90 responses at Week 16 were maintained through Week 24 in deucravacitinib-treated patients

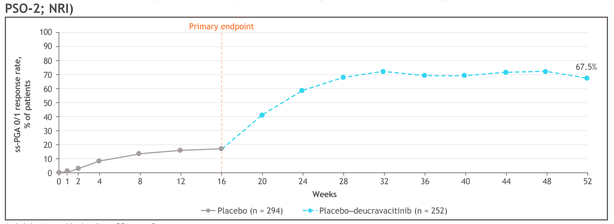
Figure 3. PSSI 90[a] responses through Week 24 (pooled POETYK PSO-1 and PSO-2; NRI)



[a]Included patients with a baseline ss-PGA score ≥3.
*P < 0.05 vs placebo. †P < 0.0001 vs placebo. 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 patients who crossed over from placebo to deucravacitinib at Week 16, 67.5% achieved ss-PGA 0/1 at Week 52 (**Figure 4**) and 62.3% achieved PSSI 90 at Week 52
  - These rates were comparable to Week 24 findings in patients who received continuous deucravacitinib from Day 1

Figure 4. ss-PGA 0/1[a] responses through Week 52 in placebo crossovers (pooled POETYK PSO-1 and PSO-2; NRI)

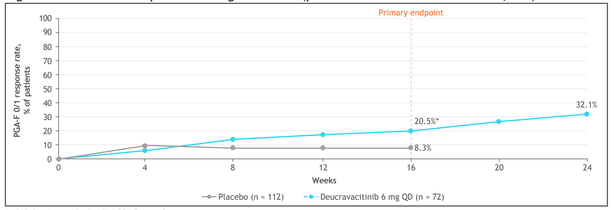


[a]Included patients with a baseline ss-PGA score ≥3.
Missing data were imputed with NRI.
NRI, nonresponder imputation; ss-PGA 0/1, scalp-specific Physician's Global Assessment score of 0 or 1.

Fingernail psoriasis

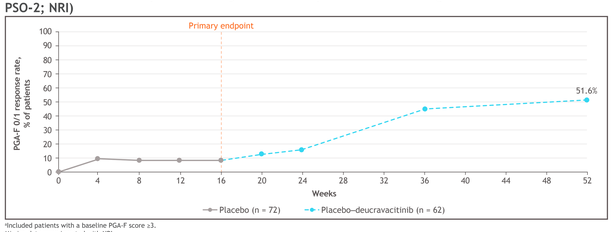
- Significantly more patients receiving deucravacitinib vs placebo achieved PGA-F 0/1 at Week 16 (**Figure 5**)
  - PGA-F 0/1 responses at Week 16 increased through Week 24 in deucravacitinib-treated patients
- In patients who crossed over from placebo to deucravacitinib at Week 16, 51.6% achieved PGA-F 0/1 at Week 52 (**Figure 6**)

Figure 5. PGA-F 0/1[a] responses through Week 24 (pooled POETYK 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 in placebo crossovers (pooled POETYK PSO-1 and PSO-2; NRI)

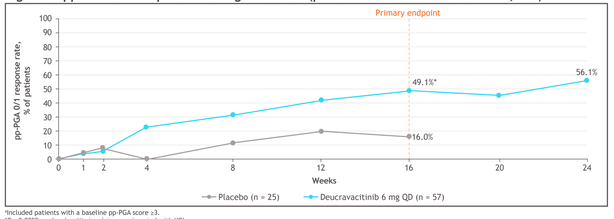


[a]Included patients with a baseline PGA-F score ≥3.
Missing data were imputed with NRI.
NRI, nonresponder imputation; PGA-F 0/1, Physician's Global Assessment-Fingernails score of 0 or 1.

Palmoplantar psoriasis

- Significantly more patients receiving deucravacitinib vs placebo achieved pp-PGA 0/1 at Week 16 (**Figure 7**)
  - pp-PGA 0/1 responses at Week 16 were increased at Week 24 in deucravacitinib-treated patients
- In patients who crossed over from placebo to deucravacitinib at Week 16, 41.2% achieved pp-PGA 0/1 at Week 52

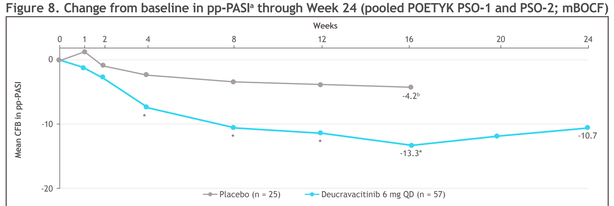
Figure 7. pp-PGA 0/1[a] responses through Week 24 (pooled POETYK PSO-1 and PSO-2; NRI)



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

- 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
  - pp-PASI responses at Week 16 were maintained through Week 24 in deucravacitinib-treated patients

Figure 8. Change from baseline in pp-PASI[a] through Week 24 (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.
[b]Data in placebo crossover patients through Week 52 are currently unavailable.
*P ≤ 0.0097 vs placebo. Missing data were imputed with the mBOCF method.
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.

Conclusions

- In POETYK PSO-1 and PSO-2 patients with moderate to severe scalp, fingernail, or palmoplantar psoriasis at baseline, deucravacitinib was significantly more efficacious than placebo in improving disease burden in these special high impact areas through Week 16, with additional improvements observed in deucravacitinib-treated patients through Week 24
- Patients who crossed over from placebo to deucravacitinib at Week 16 achieved comparable responses at Week 52 to those observed at Week 24 in patients 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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