Deucravacitinib efficacy in palmoplantar and fingernail psoriasis by baseline Psoriasis Area and Severity Index (PASI) and baseline body surface area (BSA) in the phase 3 POETYK PSO-1 and PSO-2 trials

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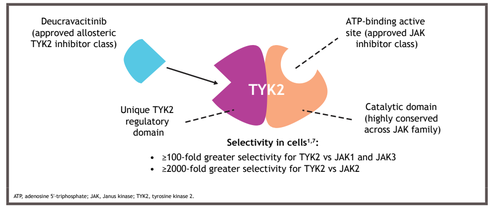
Background

- Tyrosine kinase 2 (TYK2) is an intracellular enzyme that mediates signaling of cytokines (eg, interleukin [IL]-23, IL-12, Type I interferons [IFNs])[1]
  - IL-23 and Type I IFNs are involved in psoriasis pathogenesis[1]
- Deucravacitinib, an oral, selective, allosteric TYK2 inhibitor, is approved in the US, EU, and other countries for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy[2-5]
- Deucravacitinib uniquely binds to the TYK2 regulatory domain rather than to the catalytic domain where Janus kinase (JAK) 1,2,3 inhibitors bind (**Figure 1**),[1,2] driving its selectivity for TYK2 and representing the first in a new class of oral drugs

Figure 1. Mechanism of action of deucravacitinib



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

- The global phase 3 POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751) trials demonstrated that deucravacitinib was superior to placebo and apremilast at Week 16, maintained response rates through Week 52, and was well tolerated with a low rate of discontinuations due to adverse events[6,9]
- Deucravacitinib was also superior to placebo in the hard-to-treat special areas of palmoplantar and fingernail psoriasis in POETYK PSO-1 and PSO-2 and maintained or increased clinical response rates through Week 52 with continuous deucravacitinib treatment from Day 1 in POETYK PSO-1[10]
  - The subsets of patients that were studied had moderate to severe involvement in these areas (palmoplantar psoriasis, palmoplantar Physician Global Assessment [pp-PGA] ≥3; fingernail psoriasis, PGA-Fingernail [PGA-F] ≥3) at baseline
- The impact of overall disease severity on deucravacitinib efficacy in palmoplantar and fingernail psoriasis has not been assessed

Objective

- To evaluate the influence of overall psoriasis severity at baseline on efficacy of deucravacitinib in patients with palmoplantar and fingernail involvement in the phase 3 POETYK PSO-1 and PSO-2 trials in moderate to severe plaque psoriasis

Methods

POETYK PSO-1 and PSO-2 study designs

- In POETYK PSO-1 and PSO-2, eligible patients were randomized 1:2:1 to oral placebo, deucravacitinib 6 mg once daily (QD), or apremilast 30 mg twice daily
- Randomized patients were adults identified as having moderate to severe plaque psoriasis (Psoriasis Area and Severity Index [PASI] ≥12, static Physician Global Assessment [sPGA] ≥3, and body surface area [BSA] involvement ≥10% at baseline)

Analysis populations

- Patients with moderate to severe palmoplantar psoriasis (pp-PGA ≥3) or moderate to severe fingernail psoriasis (PGA-F ≥3)[11,12] in the following study populations:
  - Pooled POETYK PSO-1/PSO-2 patients who were treated with deucravacitinib 6 mg QD through Week 24
  - POETYK PSO-1 patients who received continuous deucravacitinib 6 mg QD treatment from Day 1 through Week 52
  - POETYK PSO-1 patients who were randomized to placebo and crossed over to deucravacitinib at Week 16
- The following subgroups of disease severity of psoriasis at baseline were analyzed:
  - Baseline BSA involvement: 10%-≤15% and >15%
  - Baseline PASI score: 12-<15 and ≥15

Efficacy assessments

- Palmoplantar psoriasis
  - pp-PGA score of 0 (clear) or 1 (almost clear) (pp-PGA 0/1) in patients with a ≥2-point improvement from baseline
  - Change from baseline in palmoplantar PASI (pp-PASI) numeric score (range, 0-72, with a higher score denoting more severe disease)
- Fingernail psoriasis
  - PGA-F score of 0 (clear) or 1 (almost clear) (PGA-F 0/1) in patients with a ≥2-point improvement from baseline
  - Change from baseline in the modified Nail Psoriasis Severity Index (mNAPSI) numeric score (range, 0-130, with a higher score denoting more severe disease)

Evaluation timepoints

- Week 24 for the pooled POETYK PSO-1/PSO-2 analysis population
- Weeks 0-52 for POETYK PSO-1 analysis populations

Statistical analysis

- Nonresponder imputation (NRI) was used for binary endpoints for patients who discontinued early or had missing endpoint data
- Confidence intervals (CIs) were obtained using a stratified Cochran-Mantel-Haenszel test for pooled POETYK PSO-1/PSO-2 with stratification factors for study, and using the Clopper-Pearson method for POETYK PSO-1
- Modified baseline observation carried forward (mBOCF) was used to impute data for continuous endpoints for patients who discontinued study treatment before Week 16 due to lack of efficacy or adverse events
- Change from baseline in pp-PASI and mNAPSI was reported as adjusted mean and 95% CIs from an analysis of covariance model with the baseline value as a covariate

Results

Baseline patient demographics

- The presence of moderate to severe palmoplantar or fingernail involvement was generally balanced across the different BSA and PASI band subgroups of overall disease severity in the pooled POETYK PSO-1/PSO-2 population (**Table 1**) and the POETYK PSO-1 population (**Table 2**)

Table 1. Baseline demographics by baseline BSA involvement and PASI score in patients with moderate to severe palmoplantar or fingernail psoriasis continuously treated with deucravacitinib in the pooled POETYK PSO-1 and PSO-2 population (n = 843)

	pp-PGA ≥3				PGA-F ≥3			
	Baseline BSA involvement		Baseline PASI score		Baseline BSA involvement		Baseline PASI score	
Parameter	10%-≤15% (n = 14)	>15% (n = 43)	12-<15 (n = 8)	≥15 (n = 49)	10%-≤15% (n = 27)	>15% (n = 85)	12-<15 (n = 21)	≥15 (n = 91)
Age, mean (SD), y	49.7 (17.8)	44.8 (10.6)	44.4 (10.5)	46.3 (13.2)	48.7 (11.7)	47.3 (12.0)	48.9 (12.8)	47.3 (11.7)
Weight, mean (SD), kg	92.2 (27.0)	88.4 (24.6)	80.7 (16.5)	90.8 (26.0)	94.8 (22.1)	92.0 (20.0)	91.2 (19.5)	93.0 (20.8)
Body mass index, mean (SD), kg/m²	31.0 (10.0)	29.3 (7.3)	27.4 (6.6)	30.1 (8.2)	30.1 (5.7)	30.2 (6.4)	29.7 (5.2)	30.3 (6.5)
Female, n (%)	6 (42.9)	15 (34.9)	3 (37.5)	18 (36.7)	5 (18.5)	15 (17.6)	6 (28.6)	14 (15.4)
Race, n (%)								
White	13 (92.9)	37 (86.0)	8 (100)	42 (85.7)	23 (85.2)	74 (87.1)	15 (71.4)	82 (90.1)
Asian	1 (7.1)	5 (11.6)	0	6 (12.2)	3 (11.1)	11 (12.9)	5 (23.8)	9 (9.9)
Other	0	1 (2.3)	0	1 (2.0)	1 (3.7)	0	1 (4.8)	0

BSA, body surface area; PASI, Psoriasis Area and Severity Index; PGA-F, Physician Global Assessment-Fingernail; pp-PGA, palmoplantar Physician Global Assessment; SD, standard deviation.

Table 2. Baseline demographics by baseline BSA involvement and PASI score in patients with moderate to severe palmoplantar or fingernail psoriasis continuously treated with deucravacitinib in POETYK PSO-1 (n = 302)

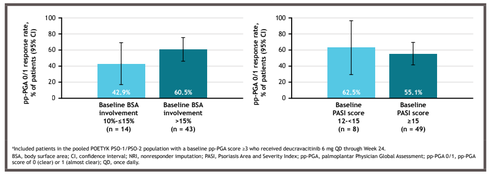
	pp-PGA ≥3				PGA-F ≥3			
	Baseline BSA involvement		Baseline PASI score		Baseline BSA involvement		Baseline PASI score	
Parameter	10%-≤15% (n = 5)	>15% (n = 13)	12-<15 (n = 3)	≥15 (n = 15)	10%-≤15% (n = 9)	>15% (n = 30)	12-<15 (n = 8)	≥15 (n = 31)
Age, mean (SD), y	40.2 (14.9)	42.7 (11.2)	36.7 (7.2)	43.1 (12.5)	46.6 (6.7)	48.1 (11.9)	52.0 (11.3)	46.7 (10.7)
Weight, mean (SD), kg	88.6 (22.1)	77.2 (14.7)	77.7 (18.3)	80.9 (17.5)	94.9 (14.8)	85.3 (17.4)	90.4 (14.2)	86.8 (17.9)
Body mass index, mean (SD), kg/m²	29.6 (7.2)	26.3 (4.1)	26.2 (5.7)	27.4 (5.2)	28.8 (4.4)	28.3 (6.0)	28.5 (3.2)	28.4 (6.1)
Female, n (%)	3 (60.0)	4 (30.8)	1 (33.3)	6 (40.0)	0	5 (16.7)	2 (25.0)	3 (9.7)
Race, n (%)								
White	5 (100)	9 (69.2)	3 (100)	11 (73.3)	7 (77.8)	21 (70.0)	5 (62.5)	23 (74.2)
Asian	0	4 (30.8)	0	4 (26.7)	2 (22.2)	9 (30.0)	3 (37.5)	8 (25.8)
Other	0	0	0	0	0	0	0	0

BSA, body surface area; PASI, Psoriasis Area and Severity Index; PGA-F, Physician Global Assessment-Fingernail; pp-PGA, palmoplantar Physician Global Assessment; SD, standard deviation.

Palmoplantar psoriasis

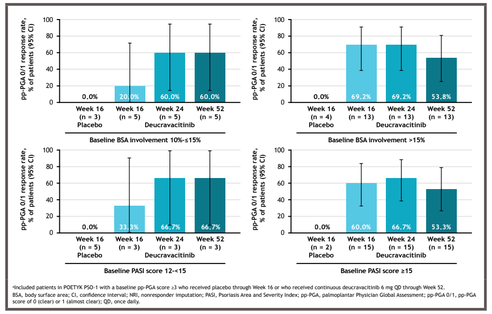
- In the pooled POETYK PSO-1/PSO-2 population and the POETYK PSO-1 population, pp-PGA 0/1 response rates with deucravacitinib treatment were overall similar between the baseline BSA and PASI subgroups of disease severity (**Figure 2** and **Figure 3**) with some minor differences
  - Some subgroups had small sample sizes

Figure 2. pp-PGA 0/1[a] response rates with deucravacitinib treatment at Week 24 by baseline BSA involvement and PASI score (pooled POETYK PSO-1/PSO-2, NRI)



[a]Included patients in the pooled POETYK PSO-1/PSO-2 population with a baseline pp-PGA score ≥3 who received deucravacitinib 6 mg QD through Week 24.
BSA, body surface area; CI, confidence interval; NRI, nonresponder imputation; PASI, Psoriasis Area and Severity Index; pp-PGA, palmoplantar Physician Global Assessment; pp-PGA 0/1, pp-PGA score of 0 (clear) or 1 (almost clear); QD, once daily.

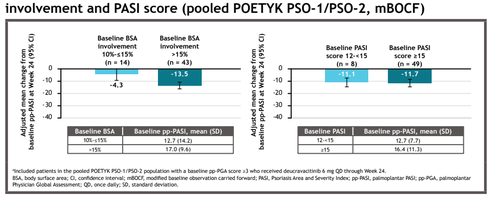
Figure 3. pp-PGA 0/1[a] response rates through Week 52 by baseline BSA involvement and PASI score (POETYK PSO-1, NRI)



[a]Included patients in POETYK PSO-1 with a baseline pp-PGA score ≥3 who received placebo through Week 16 or who received continuous deucravacitinib 6 mg QD through Week 52.
BSA, body surface area; CI, confidence interval; NRI, nonresponder imputation; PASI, Psoriasis Area and Severity Index; pp-PGA, palmoplantar Physician Global Assessment; pp-PGA 0/1, pp-PGA score of 0 (clear) or 1 (almost clear); QD, once daily.

- In the pooled POETYK PSO-1/PSO-2 population, change from baseline in pp-PASI:
  - Tended to increase with greater BSA involvement at baseline (**Figure 4**)
  - Was similar between baseline PASI score subgroups at Week 24 (**Figure 4**)

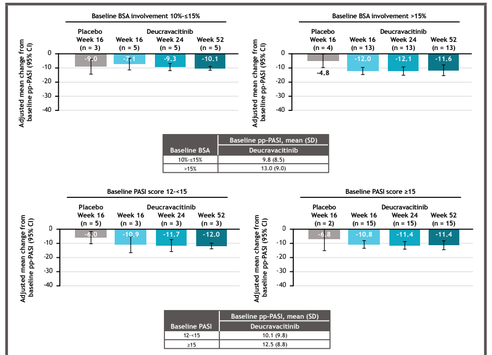
Figure 4. Change from baseline pp-PASI[a] at Week 24 by baseline BSA involvement and PASI score (pooled POETYK PSO-1/PSO-2, mBOCF)



[a]Included patients in the pooled POETYK PSO-1/PSO-2 population with a baseline pp-PGA score ≥3 who received deucravacitinib 6 mg QD through Week 24.
BSA, body surface area; CI, confidence interval; mBOCF, modified baseline observation carried forward; PASI, Psoriasis Area and Severity Index; pp-PASI, palmoplantar PASI; pp-PGA, palmoplantar Physician Global Assessment; QD, once daily; SD, standard deviation.

- Change from baseline in pp-PASI tended to increase over time in the baseline BSA involvement 10%-≤15% subgroup in POETYK PSO-1 (**Figure 5**)
  - Change from baseline was maintained through Week 52 in patients with baseline BSA involvement >15%
- In POETYK PSO-1, change from baseline in pp-PASI was generally maintained through Week 52 in both baseline PASI score subgroups (**Figure 5**)

Figure 5. Change from baseline pp-PASI[a] through Week 52 by baseline BSA involvement and PASI score (POETYK PSO-1, mBOCF)

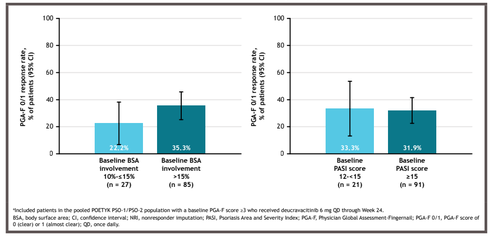


[a]Included patients in POETYK PSO-1 with a baseline pp-PGA score ≥3 who received placebo through Week 16 or who received continuous deucravacitinib 6 mg QD through Week 52.
BSA, body surface area; CI, confidence interval; mBOCF, modified baseline observation carried forward; PASI, Psoriasis Area and Severity Index; pp-PASI, palmoplantar PASI; pp-PGA, palmoplantar Physician Global Assessment; QD, once daily; SD, standard deviation.

Fingernail psoriasis

- In the pooled POETYK PSO-1/PSO-2 population, PGA-F 0/1 response rates were numerically higher for patients with higher baseline BSA involvement and comparable by baseline PASI score (**Figure 6**)

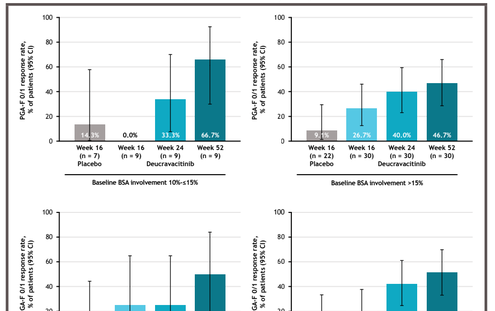
Figure 6. PGA-F 0/1[a] response rates at Week 24 by baseline BSA involvement and PASI score (pooled POETYK PSO-1/PSO-2, NRI)



[a]Included patients in the pooled POETYK PSO-1/PSO-2 population with a baseline PGA-F score ≥3 who received deucravacitinib 6 mg QD through Week 24.
BSA, body surface area; CI, confidence interval; NRI, nonresponder imputation; PASI, Psoriasis Area and Severity Index; PGA-F, Physician Global Assessment-Fingernail; PGA-F 0/1, PGA-F score of 0 (clear) or 1 (almost clear); QD, once daily.

- In POETYK PSO-1, PGA-F 0/1 response rates improved through Week 52 across baseline BSA involvement and PASI score subgroups in patients treated with continuous deucravacitinib from Day 1 (**Figure 7**)

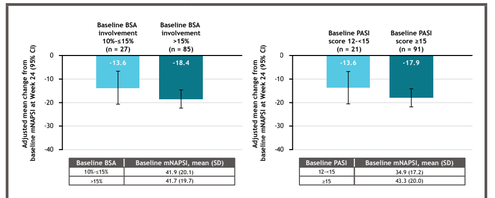
Figure 7. PGA-F 0/1[a] response rates through Week 52 by baseline BSA involvement and PASI score (POETYK PSO-1, NRI)



[a]Included patients in the POETYK PSO-1 population with a baseline PGA-F score ≥3 who received placebo through Week 16 or who received continuous deucravacitinib 6 mg QD through Week 52.
BSA, body surface area; CI, confidence interval; mBOCF, modified baseline observation carried forward; NRI, nonresponder imputation; PASI, Psoriasis Area and Severity Index; PGA-F, Physician Global Assessment-Fingernail; PGA-F 0/1, PGA-F score of 0 (clear) or 1 (almost clear); QD, once daily.

- In the pooled POETYK PSO-1/PSO-2 population, change from baseline in mNAPSI was increased for patients with greater BSA involvement or greater PASI score at baseline (**Figure 8**)

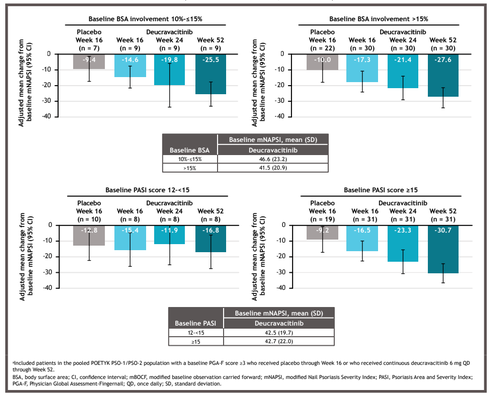
Figure 8. Change from baseline mNAPSI[a] at Week 24 by baseline BSA involvement and PASI score (pooled POETYK PSO-1/PSO-2, mBOCF)



[a]Included patients in the pooled POETYK PSO-1/PSO-2 population with a baseline PGA-F score ≥3 who received deucravacitinib 6 mg QD through Week 24.
BSA, body surface area; CI, confidence interval; mBOCF, modified baseline observation carried forward; mNAPSI, modified Nail Psoriasis Severity Index; PASI, Psoriasis Area and Severity Index; PGA-F, Physician Global Assessment-Fingernail; QD, once daily; SD, standard deviation.

- In the POETYK PSO-1 population, change from baseline in mNAPSI improved through Week 52 regardless of baseline BSA involvement or PASI score (**Figure 9**)

Figure 9. Change from baseline mNAPSI[a] through Week 52 by baseline BSA involvement and PASI score (POETYK PSO-1, mBOCF)



[a]Included patients in the pooled POETYK PSO-1/PSO-2 population with a baseline PGA-F score ≥3 who received placebo through Week 16 or who received continuous deucravacitinib 6 mg QD through Week 52.
BSA, body surface area; CI, confidence interval; mBOCF, modified baseline observation carried forward; mNAPSI, modified Nail Psoriasis Severity Index; PASI, Psoriasis Area and Severity Index; PGA-F, Physician Global Assessment-Fingernail; QD, once daily; SD, standard deviation.

Conclusions

- Deucravacitinib improved disease burden in moderate to severe palmoplantar and fingernail disease regardless of baseline severity of psoriasis by BSA involvement or PASI score in the limited number of patients studied
- Clinical efficacy was maintained or improved through 52 weeks with continuous deucravacitinib treatment
- This analysis further supports the use of deucravacitinib for patients with palmoplantar or fingernail psoriasis regardless of overall disease severity in those hard-to-treat areas

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