Efficacy of deucravacitinib, an oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor, in scalp psoriasis by baseline Psoriasis Area and Severity Index (PASI) and baseline body surface area (BSA): a subanalysis of the phase 3 clinical trial data

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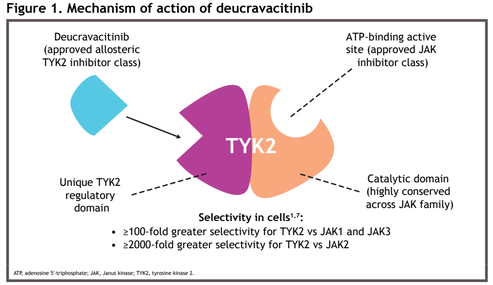
Background

- Tyrosine kinase 2 (TYK2) is an intracellular enzyme that mediates signaling of select inflammatory 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[1,7] (**Figure 1**), 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.

- Deucravacitinib demonstrated a robust efficacy and safety profile in the global phase 3 POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751) trials in patients with moderate to severe plaque psoriasis
  - Deucravacitinib was superior to placebo and apremilast at Week 16, maintained response rates through Week 52, and was well tolerated[8,9]
- Deucravacitinib demonstrated efficacy in scalp psoriasis:
  - In patients with moderate to severe scalp psoriasis (scalp-specific Physician Global Assessment [ss-PGA] score ≥3) at baseline in POETYK PSO-1 and PSO-2, deucravacitinib was superior to placebo based on scalp-specific endpoints (ss-PGA score of 0 [clear] or 1 [almost clear] [ss-PGA 0/1], ≥90% reduction from baseline in Psoriasis Scalp Severity Index [PSSI 90])[10]
  - ss-PGA 0/1 response rates were maintained through Week 52 in patients who continued to receive deucravacitinib[10]
- Efficacy in scalp psoriasis was observed regardless of body weight, body mass index, or type or number of prior psoriasis therapies[10]
  - However, the effect of baseline disease severity overall on deucravacitinib efficacy in scalp psoriasis has not been evaluated

Objective

- To evaluate the effect of baseline disease severity overall on the efficacy of deucravacitinib in scalp psoriasis in the phase 3 POETYK PSO-1 and PSO-2 trials

Methods

POETYK PSO-1 and PSO-2 study designs

- POETYK PSO-1 and PSO-2 were global, 52-week, phase 3, double-blind trials that randomized adults with moderate to severe plaque psoriasis 1:2:1 to oral placebo, deucravacitinib 6 mg once daily (QD), or apremilast 30 mg twice daily[8,9]
  - Placebo patients crossed over to deucravacitinib at Week 16
  - In POETYK PSO-2, deucravacitinib-treated patients who achieved ≥75% reduction from baseline in Psoriasis Area and Severity Index (PASI 75) at Week 24 were rerandomized 1:1 to continue deucravacitinib treatment or switch to placebo

Analysis populations

- Patients with moderate to severe scalp psoriasis at baseline (ss-PGA ≥3) were evaluated in the following populations:
  - Pooled POETYK PSO-1/PSO-2 patients who were treated with deucravacitinib 6 mg QD through Week 24 or who crossed over from placebo to deucravacitinib at Week 16
  - POETYK PSO-1 patients who received continuous deucravacitinib 6 mg QD without change from Day 1 through Week 52 and patients who crossed over from placebo to deucravacitinib at Week 16
- Patients in the 2 populations were stratified by baseline disease severity:
  - Baseline body surface area (BSA) involvement: 10%-≤15% and >15%
  - Baseline PASI score: 12-<15 and ≥15
- Scalp-specific outcomes in the pooled POETYK PSO-1/PSO-2 population through Week 24:
  - ss-PGA 0/1
  - PSSI 90
- Scalp-specific outcomes in the POETYK PSO-1 population through Week 52:
  - ss-PGA 0/1
  - PSSI 90

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

Results

Baseline patient demographics

- Baseline patient demographics were generally similar across the various disease severity subgroups in the pooled POETYK PSO-1/PSO-2 (**Table 1**) and POETYK PSO-1 (**Table 2**) populations

Table 1. Baseline patient demographics (pooled POETYK PSO-1 and PSO-2)

	Baseline BSA involvement				Baseline PASI score			
	Placebo		Deucravacitinib		Placebo		Deucravacitinib	
Parameter	10%-≤15% (n = 95)	>15% (n = 199)	10%-≤15% (n = 147)	>15% (n = 367)	12-<15 (n = 76)	≥15 (n = 218)	12-<15 (n = 96)	≥15 (n = 418)
Age, mean (SD), y	47.3 (14.7)	46.3 (14.3)	45.8 (14.2)	44.0 (13.4)	46.4 (15.5)	46.7 (14.0)	45.5 (13.4)	44.5 (13.7)
Weight, mean (SD), kg	88.5 (21.0)	90.9 (21.6)	89.4 (21.8)	91.6 (22.5)	90.9 (20.7)	89.9 (21.6)	84.5 (20.6)	92.5 (22.4)
Body mass index, mean (SD), kg/m^2	29.8 (6.6)	30.4 (6.9)	29.7 (6.2)	31.0 (7.3)	30.2 (6.7)	30.2 (6.9)	29.0 (7.8)	31.0 (6.8)
Female, n (%)	36 (37.9)	63 (31.7)	51 (34.7)	131 (35.7)	25 (32.9)	74 (33.9)	37 (38.5)	147 (34.7)
Race, n (%)								
White	80 (84.2)	172 (86.4)	133 (90.5)	305 (83.1)	67 (88.2)	185 (84.9)	82 (85.4)	356 (85.2)
Asian	9 (9.5)	21 (10.6)	10 (6.8)	51 (13.9)	6 (7.9)	24 (11.0)	13 (13.5)	48 (11.5)
Other	6 (6.3)	6 (3.0)	4 (2.7)	11 (3.0)	3 (3.9)	9 (4.1)	1 (1.0)	14 (3.4)

BSA, body surface area; PASI, Psoriasis Area and Severity Index; SD, standard deviation.

Table 2. Baseline patient demographics (POETYK PSO-1)

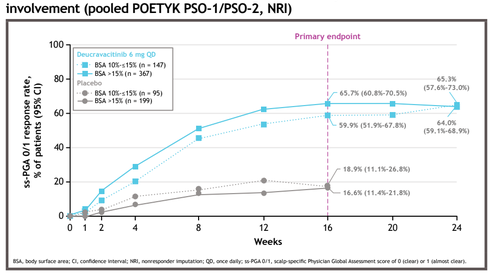
	Baseline BSA involvement				Baseline PASI score			
	Deucravacitinib		Placebo to deucravacitinib		Deucravacitinib		Placebo to deucravacitinib	
Parameter	10%-≤15% (n = 47)	>15% (n = 145)	10%-≤15% (n = 36)	>15% (n = 70)	12-<15 (n = 30)	≥15 (n = 162)	12-<15 (n = 29)	≥15 (n = 77)
Age, mean (SD), y	46.6 (14.9)	43.7 (13.8)	46.3 (14.4)	46.8 (14.9)	42.4 (13.9)	44.7 (14.1)	44.8 (15.0)	47.3 (14.6)
Weight, mean (SD), kg	91.7 (23.3)	87.7 (23.7)	88.3 (20.3)	88.4 (22.5)	85.9 (22.0)	89.2 (23.9)	91.1 (21.7)	87.3 (21.8)
Body mass index, mean (SD), kg/m^2	30.2 (6.4)	30.0 (8.1)	30.2 (6.1)	29.8 (7.1)	30.0 (9.7)	30.1 (7.3)	30.3 (6.8)	29.8 (6.8)
Female, n (%)	14 (29.8)	50 (34.5)	12 (33.3)	24 (34.3)	12 (40.0)	52 (32.1)	9 (31.0)	27 (35.1)
Race, n (%)								
White	41 (87.2)	107 (73.8)	28 (77.8)	53 (75.7)	22 (73.3)	126 (77.8)	24 (82.8)	57 (74.0)
Asian	5 (10.6)	35 (24.1)	6 (16.7)	16 (22.9)	8 (26.7)	32 (19.8)	4 (13.8)	18 (23.4)
Other	1 (2.1)	3 (2.1)	2 (5.6)	1 (1.4)	0	4 (2.5)	1 (3.4)	2 (2.6)

BSA, body surface area; PASI, Psoriasis Area and Severity Index; SD, standard deviation.

ss-PGA 0/1 by baseline BSA involvement

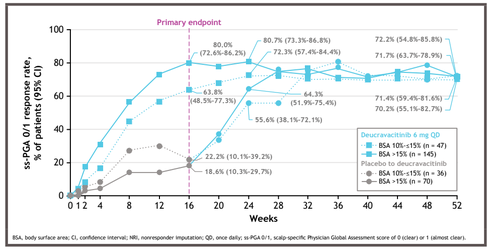
- In the pooled POETYK PSO-1/PSO-2 population, ss-PGA 0/1 response rates were higher with deucravacitinib than with placebo at Week 16 in both baseline BSA involvement subgroups (**Figure 2**)
  - ss-PGA 0/1 response rates were maintained with deucravacitinib in both subgroups through Week 24
- In POETYK PSO-1, ss-PGA 0/1 response rates were maintained in both BSA involvement subgroups through Week 52 among patients who received continuous deucravacitinib treatment from Day 1 (**Figure 3**)
  - Patients who crossed over from placebo to deucravacitinib at Week 16 achieved similar ss-PGA 0/1 response rates at Week 52 compared with those receiving continuous deucravacitinib treatment

Figure 2. ss-PGA 0/1 response rates through Week 24 by baseline BSA involvement (pooled POETYK PSO-1/PSO-2, NRI)



BSA, body surface area; CI, confidence interval; NRI, nonresponder imputation; QD, once daily; ss-PGA 0/1, scalp-specific Physician Global Assessment score of 0 (clear) or 1 (almost clear).

Figure 3. ss-PGA 0/1 response rates through Week 52 by baseline BSA involvement (POETYK PSO-1, NRI)

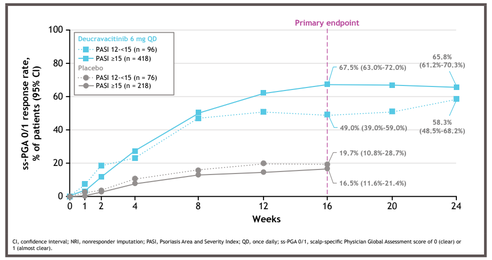


BSA, body surface area; CI, confidence interval; NRI, nonresponder imputation; QD, once daily; ss-PGA 0/1, scalp-specific Physician Global Assessment score of 0 (clear) or 1 (almost clear).

ss-PGA 0/1 by baseline PASI score

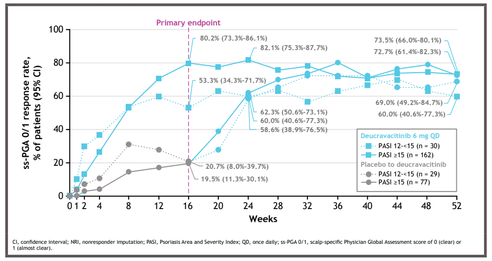
- In the pooled POETYK PSO-1/PSO-2 population, ss-PGA 0/1 response rates were higher with deucravacitinib than with placebo at Week 16 in both baseline PASI score subgroups (**Figure 4**)
  - ss-PGA 0/1 response rates were maintained with deucravacitinib in both subgroups through Week 24
- In POETYK PSO-1, ss-PGA 0/1 response rates were maintained in both PASI score subgroups through Week 52 among patients who received continuous deucravacitinib treatment from Day 1 (**Figure 5**)
  - Patients who crossed over from placebo to deucravacitinib at Week 16 achieved similar ss-PGA 0/1 response rates at Week 52 compared with those receiving continuous deucravacitinib treatment

Figure 4. ss-PGA 0/1 response rates through Week 24 by baseline PASI score (pooled POETYK PSO-1/PSO-2, NRI)



CI, confidence interval; NRI, nonresponder imputation; PASI, Psoriasis Area and Severity Index; QD, once daily; ss-PGA 0/1, scalp-specific Physician Global Assessment score of 0 (clear) or 1 (almost clear).

Figure 5. ss-PGA 0/1 response rates through Week 52 by baseline PASI score (POETYK PSO-1, NRI)

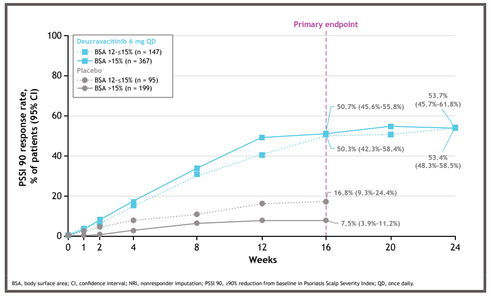


CI, confidence interval; NRI, nonresponder imputation; PASI, Psoriasis Area and Severity Index; QD, once daily; ss-PGA 0/1, scalp-specific Physician Global Assessment score of 0 (clear) or 1 (almost clear).

PSSI 90 by baseline BSA involvement

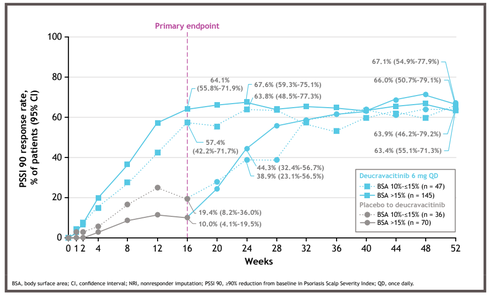
- In the pooled POETYK PSO-1/PSO-2 population, PSSI 90 response rates were higher with deucravacitinib than with placebo at Week 16 in both baseline BSA involvement subgroups (**Figure 6**)
  - PSSI 90 response rates were maintained with deucravacitinib in both subgroups through Week 24
- In POETYK PSO-1, PSSI 90 response rates were maintained in both BSA subgroups through Week 52 among patients who received continuous deucravacitinib treatment from Day 1 (**Figure 7**)
  - Patients who crossed over from placebo to deucravacitinib at Week 16 achieved similar PSSI 90 response rates at Week 52 compared with those receiving continuous deucravacitinib treatment

Figure 6. PSSI 90 response rates through Week 24 by baseline BSA involvement (pooled POETYK PSO-1/PSO-2, NRI)



BSA, body surface area; CI, confidence interval; NRI, nonresponder imputation; PSSI 90, ≥90% reduction from baseline in Psoriasis Scalp Severity Index; QD, once daily.

Figure 7. PSSI 90 response rates through Week 52 by baseline BSA involvement (POETYK PSO-1, NRI)

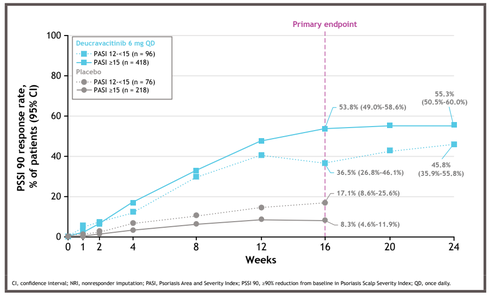


BSA, body surface area; CI, confidence interval; NRI, nonresponder imputation; PSSI 90, ≥90% reduction from baseline in Psoriasis Scalp Severity Index; QD, once daily.

PSSI 90 by baseline PASI score

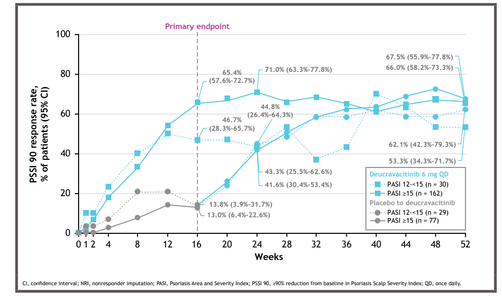
- In the pooled POETYK PSO-1/PSO-2 population, PSSI 90 response rates were higher with deucravacitinib than with placebo at Week 16 in both baseline PASI score subgroups (**Figure 8**)
  - PSSI 90 response rates were maintained with deucravacitinib in both subgroups through Week 24
- In POETYK PSO-1, PSSI 90 response rates were maintained in both PASI subgroups through Week 52 among patients who received continuous deucravacitinib treatment from Day 1 (**Figure 9**)
  - Patients who crossed over from placebo to deucravacitinib at Week 16 achieved similar PSSI 90 response rates at Week 52 compared with those receiving continuous deucravacitinib treatment

Figure 8. PSSI 90 response rates through Week 24 by baseline PASI score (pooled POETYK PSO-1/PSO-2, NRI)



CI, confidence interval; NRI, nonresponder imputation; PASI, Psoriasis Area and Severity Index; PSSI 90, ≥90% reduction from baseline in Psoriasis Scalp Severity Index; QD, once daily.

Figure 9. PSSI 90 response rates through Week 52 by baseline PASI score (POETYK PSO-1, NRI)



CI, confidence interval; NRI, nonresponder imputation; PASI, Psoriasis Area and Severity Index; PSSI 90, ≥90% reduction from baseline in Psoriasis Scalp Severity Index; QD, once daily.

Conclusions

- In POETYK PSO-1 and PSO-2, deucravacitinib improved scalp-specific disease burden regardless of overall baseline disease severity (baseline BSA involvement and PASI score) in patients with moderate to severe plaque psoriasis
  - Higher ss-PGA 0/1 and PSSI 90 response rates were observed at Week 16 in patients receiving deucravacitinib compared with placebo
  - Response rates were maintained through Week 52 in patients receiving continuous deucravacitinib treatment from baseline and were increased through Week 52 in patients crossing over from placebo to deucravacitinib at Week 16
- Patients with higher disease burden (BSA >15%; PASI ≥15) performed numerically better than those with lower disease burden; however, both groups demonstrated improvement relative to placebo and had continued improvement over time
- These findings suggest that deucravacitinib treatment improves scalp-specific disease regardless of baseline disease severity overall in patients with moderate to severe plaque psoriasis
  - Results are consistent with the previous report from POETYK PSO-1 and PSO-2 in which deucravacitinib also improves scalp psoriasis regardless of body weight, body mass index, or use of prior psoriasis therapies[10]

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