Achievement of treat-to-target thresholds for overall psoriasis response with deucravacitinib: post hoc, subgroup analysis of the randomized, double-blind, placebo-controlled phase 3b/4 PSORIATYK SCALP trial

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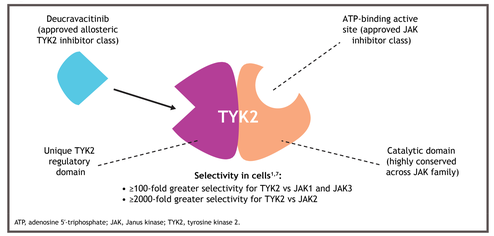
Introduction

- 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[2-6]
- 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.

- Scalp psoriasis, which occurs in up to 80% of patients with psoriasis and is associated with itching, flaking, pain, and bleeding, disproportionately reduces quality of life and is challenging to treat with topical agents[8-14]
- The PSORIATYK SCALP (NCT05478499) trial evaluated deucravacitinib in patients with moderate to severe scalp psoriasis, including those with less extensive overall psoriasis (body surface area [BSA] involvement ≥3%)
  - PSORIATYK SCALP achieved its primary and all key secondary endpoints, with a significantly greater proportion of patients treated with deucravacitinib achieving scalp-specific Physician Global Assessment score of 0 (clear) or 1 (almost clear) (ss-PGA 0/1; 48.5%), ≥90% reduction from baseline in Psoriasis Scalp Severity Index (PSSI 90; 38.8%), static Physician Global Assessment of 0 (clear) or 1 (almost clear) (sPGA 0/1; 51.0%), and a mean decrease from baseline in the scalp-specific numeric rating scale (ss-NRS) itch score (-3.2) at Week 16 compared with patients receiving placebo[13]
- Treatment outcomes for plaque psoriasis based on the absolute Psoriasis Area and Severity Index (PASI) are indicative of patient disease severity status at the time of assessment[16,17]
  - Achieving absolute PASI may be more meaningful to patients and have greater relevance in clinical settings than achieving a set percent reduction from baseline in PASI captured by assessments such as ≥75% reduction from baseline in PASI (PASI 75)[16]
    - Patients with moderate to severe plaque psoriasis may reach PASI 75 relative to their initial disease status but still have significant disease activity and health-related quality-of-life problems[16]
  - Data suggest attainment of an absolute PASI ≤2 correlates with ≥90% reduction from baseline in PASI (PASI 90) and represents meaningful improvements in clinical and health-related quality-of-life outcomes and a relevant treat-to-target measure in the real-world setting[16,17]
  - In addition, absolute PASI ≤3 as a treat-to-target strategy to define clinical remission was recently recommended by a group of psoriasis experts for patients with moderate to severe plaque psoriasis[18]

Objective

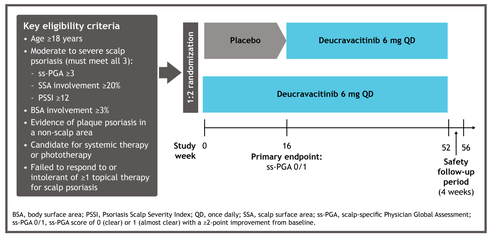
- To evaluate the ability of deucravacitinib treatment to achieve treat-to-target thresholds in subgroups of patients based on baseline BSA involvement (3%-10% vs >10%)

Methods

Study design

- PSORIATYK SCALP is a phase 3b/4, multicenter, randomized, double-blinded, placebo-controlled trial designed to evaluate the efficacy and safety of deucravacitinib in patients with moderate to severe scalp psoriasis (**Figure 2**)
  - Patients were randomized 1:2 to oral placebo or deucravacitinib 6 mg once daily (QD)
    - At Week 16, all patients switched to open-label deucravacitinib 6 mg QD through Week 52
  - Stratification factors were prior use of biologic therapy for psoriasis, psoriatic arthritis, or other inflammatory disease (yes/no) and body weight (≥90 kg/<90 kg)
- PSORIATYK SCALP included patients with moderate to severe scalp psoriasis defined by more focused and objective inclusion criteria (ss-PGA ≥3; scalp surface area [SSA] involvement ≥20%; PSSI ≥12) and including those with less extensive overall body psoriasis (BSA involvement ≥3%) as compared with the POETYK trials[15]

Figure 2. PSORIATYK SCALP study design



BSA, body surface area; PSSI, Psoriasis Scalp Severity Index; QD, once daily; SSA, scalp surface area; ss-PGA, scalp-specific Physician Global Assessment; ss-PGA 0/1, ss-PGA score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline.

Outcomes

- Absolute PASI target thresholds at Week 16:
  - PASI ≤1, ≤2, ≤3, ≤4, and ≤5
- BSA involvement thresholds at Week 16:
  - BSA ≤1% and ≤3%

Analysis populations

- Full analysis set: all patients randomized to study treatment
- BSA subgroups categorized by BSA involvement at baseline: BSA 3%-10% and BSA >10%

Statistical analysis

- Full analysis set
  - Response rates (95% confidence intervals [CIs]) and *P* values for odds ratios were obtained using a stratified Cochran-Mantel-Haenszel test with stratification factors (prior biologic use [yes/no] and body weight [≥90 kg/<90 kg]) per randomization
- Subgroup analyses
  - Response rates (95% CIs) and *P* values for odds ratios were obtained using an unstratified Chi-squared test
- *P* values are nominal
- 95% CIs are based on the Clopper-Pearson (exact binomial) method

Results

Baseline patient demographics and clinical characteristics

- Baseline patient demographics and clinical characteristics were similar with placebo (n = 51) and deucravacitinib (n = 103) (mean PASI, 9.4 vs 10.2; mean BSA involvement, 10.0% vs 10.5%)
- Baseline patient demographics and clinical characteristics were similar between BSA subgroups and in patients who received placebo and deucravacitinib treatment (**Table 1**)

Table 1. Baseline patient demographics and clinical characteristics by baseline BSA involvement of 3%-10% vs >10%

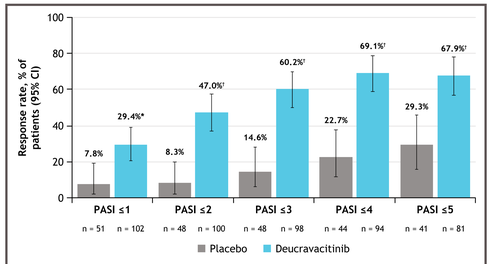
	BSA involvement 3%-10%		BSA involvement >10%	
Parameter	Placebo (n = 38)	Deucravacitinib (n = 70)	Placebo (n = 13)	Deucravacitinib (n = 33)
Age, mean (SD), y	41.8 (13.1)	42.0 (15.2)	47.5 (12.5)	44.3 (16.9)
Weight, mean (SD), kg	86.3 (24.3)	88.7 (25.0)	93.8 (36.2)	90.6 (21.3)
Body mass index, mean (SD), kg/m²	28.7 (6.4)	29.8 (7.3)	30.8 (8.8)	30.6 (6.5)
Female, n (%)	18 (47.4)	33 (47.1)	2 (15.4)	12 (36.4)
Race, n (%)				
White	36 (94.7)	64 (91.4)	11 (84.6)	29 (87.9)
Asian	1 (2.6)	1 (1.4)	1 (7.7)	2 (6.1)
Black or African American	1 (2.6)	3 (4.3)	1 (7.7)	2 (6.1)
Other	0	2 (2.9)	0	0
Psoriasis vulgaris duration, mean (SD), y	11.4 (9.9)	14.4 (10.1)	13.2 (9.6)	19.8 (13.3)
Scalp psoriasis duration, mean (SD), y	12.0 (9.7)	15.4 (11.1)	13.7 (9.8)	18.5 (12.9)
Prior systemic therapy use, n (%)				
Yes	16 (42.1)	35 (50.0)	11 (84.6)	19 (57.6)
Biologic	12 (31.6)	23 (32.9)	4 (30.8)	14 (42.4)
Nonbiologic	4 (10.5)	12 (17.1)	7 (53.8)	5 (15.2)
No	22 (57.9)	35 (50.0)	2 (15.4)	14 (42.4)
ss-PGA score, n (%)				
3 (moderate)	23 (60.5)	56 (80.0)	9 (69.2)	20 (60.6)
4 (severe)	15 (39.5)	14 (20.0)	4 (30.8)	13 (39.4)
PSSI, mean (SD)	32.4 (13.8)	32.1 (11.8)	31.5 (14.0)	36.5 (13.7)
ss-NRS itch score, mean (SD)	6.4 (1.8)	6.3 (2.4)	6.5 (2.0)	6.5 (2.0)
sPGA score, n (%)				
2 (mild)	4 (10.5)	6 (8.6)	0	1 (3.0)
3 (moderate)	31 (81.6)	56 (80.0)	11 (84.6)	25 (75.8)
4 (severe)	3 (7.9)	8 (11.4)	2 (15.4)	7 (21.2)
BSA involvement, mean (SD), %	6.1 (2.1)	5.8 (2.0)	21.5 (8.1)	20.5 (11.5)
PASI, mean (SD)	7.0 (3.1)	6.9 (3.1)	16.5 (5.1)	17.4 (6.6)

BSA, body surface area; PASI, Psoriasis Area and Severity Index; PSSI, Psoriasis Scalp Severity Index; SD, standard deviation; sPGA, static Physician Global Assessment; ss-NRS, scalp-specific numeric rating scale; ss-PGA, scalp-specific Physician Global Assessment.

Absolute PASI thresholds

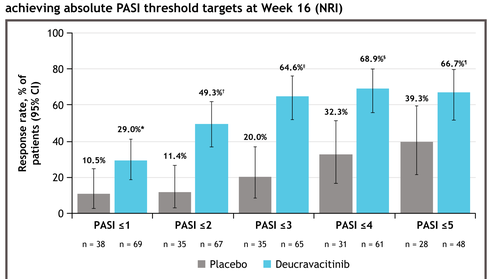
- Higher proportions of patients receiving deucravacitinib vs placebo achieved PASI thresholds ≤1, ≤2, ≤3, ≤4, and ≤5 at Week 16 (**Figure 3**)
- Higher proportions of patients with baseline BSA involvement of 3%-10% (**Figure 4**) and ≥10% (**Figure 5**) receiving deucravacitinib vs placebo achieved PASI thresholds ≤1, ≤2, ≤3, ≤4, and ≤5 at Week 16

Figure 3. Proportion of patients achieving absolute PASI threshold targets at Week 16 (NRI)



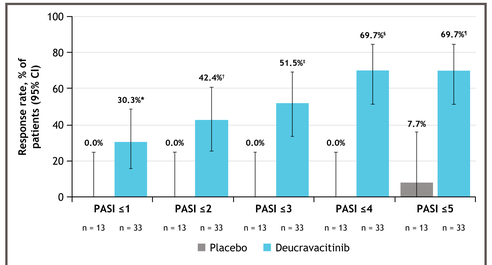
*P = 0.0023; †P < 0.0001 vs placebo. All *P* values are nominal.
Patients were included only if their baseline PASI was greater than the endpoint being evaluated.
CI, confidence interval; NRI, nonresponder imputation; PASI, Psoriasis Area and Severity Index.

Figure 4. Proportion of patients with baseline BSA involvement of 3%-10% achieving absolute PASI threshold targets at Week 16 (NRI)



*P = 0.03; †P = 0.0002; ‡P < 0.0001; §P = 0.0008; ¶P = 0.02 vs placebo. All *P* values are nominal.
Patients were included only if their baseline PASI was greater than the endpoint being evaluated.
BSA, body surface area; CI, confidence interval; NRI, nonresponder imputation; PASI, Psoriasis Area and Severity Index.

Figure 5. Proportion of patients with baseline BSA involvement ≥10% achieving absolute PASI threshold targets at Week 16 (NRI)

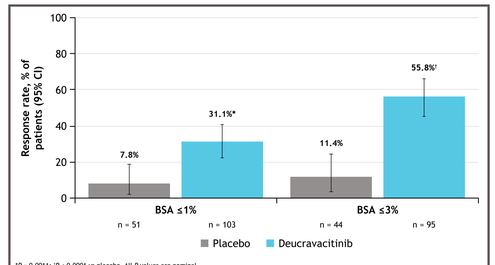


*P = 0.03; †P = 0.005; ‡P = 0.001; §P < 0.0001; ¶P = 0.0002 vs placebo. All *P* values are nominal.
Patients were included only if their baseline PASI was greater than the endpoint being evaluated.
BSA, body surface area; CI, confidence interval; NRI, nonresponder imputation; PASI, Psoriasis Area and Severity Index.

BSA involvement thresholds

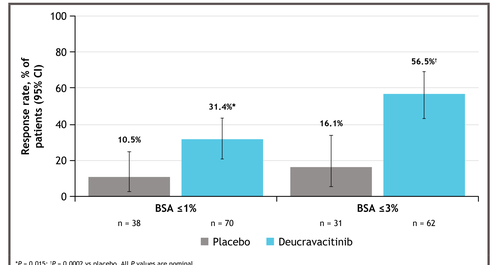
- Higher proportions of patients receiving deucravacitinib vs placebo achieved BSA thresholds ≤1% and ≤3% at Week 16 (**Figure 6**)
- Higher proportions of patients with baseline BSA involvement of 3%-10% (**Figure 7**) and ≥10% (**Figure 8**) receiving deucravacitinib vs placebo achieved BSA thresholds ≤1% and ≤3% at Week 16
- **Figure 9** shows a patient treated with deucravacitinib who achieved a treat-to-target PASI threshold of ≤1 for overall psoriasis response at Week 16

Figure 6. Proportion of patients achieving absolute BSA threshold targets at Week 16 (NRI)



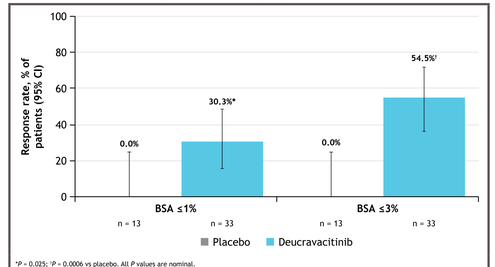
*P = 0.0011; †P < 0.0001 vs placebo. All *P* values are nominal.
Patients were included only if their baseline BSA involvement was greater than the endpoint being evaluated.
BSA, body surface area; CI, confidence interval; NRI, nonresponder imputation.

Figure 7. Proportion of patients with baseline BSA involvement of 3%-10% achieving absolute BSA threshold targets at Week 16 (NRI)



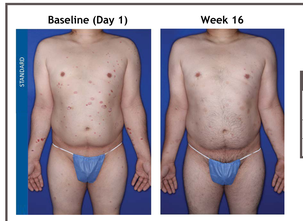
*P = 0.015; †P = 0.0002 vs placebo. All *P* values are nominal.
Patients were included only if their baseline BSA involvement was greater than the endpoint being evaluated.
BSA, body surface area; CI, confidence interval; NRI, nonresponder imputation.

Figure 8. Proportion of patients with baseline BSA involvement ≥10% achieving absolute BSA threshold targets at Week 16 (NRI)



*P = 0.025; †P = 0.0006 vs placebo. All *P* values are nominal.
Patients were included only if their baseline BSA involvement was greater than the endpoint being evaluated.
BSA, body surface area; CI, confidence interval; NRI, nonresponder imputation.

Figure 9. Achievement of treat-to-target PASI threshold of ≤1 for overall psoriasis response with deucravacitinib



	Baseline	Week 16
BSA involvement, %	13	0
PASI	14.6	0
sPGA score	3	0

BSA, body surface area; PASI, Psoriasis Area and Severity Index; sPGA, static Physician Global Assessment.

Conclusions

- Deucravacitinib was more efficacious than placebo in achieving a range of clinically meaningful treat-to-target thresholds for overall body psoriasis in patients with moderate to severe scalp psoriasis in the phase 3b/4 scalp-specific PSORIARTYK SCALP trial
  - A significantly greater proportion of patients treated with deucravacitinib vs placebo achieved treat-to-target PASI thresholds, including PASI ≤2, which correlates with PASI 90
  - Deucravacitinib was also more efficacious than placebo in subgroups of patients based on underlying BSA involvement (3%-10% vs >10%)
- Responses were consistent with those reported in the phase 3 POETYK PSO-1 and PSO-2 trials, despite PSORIATYK SCALP including patients with less extensive overall psoriasis[19]

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