Efficacy of deucravacitinib in moderate to severe scalp psoriasis: analysis of complete clearance of scalp disease and symptoms

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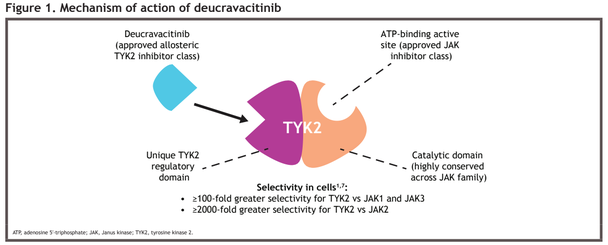
Synopsis

- 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
- 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[8,9]

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[10-16]
- In the POETYK PSO-1 and PSO-2 subpopulation of patients with moderate to severe scalp psoriasis (scalp-specific Physician Global Assessment [ss-PGA] score ≥3 at baseline), deucravacitinib was significantly more efficacious than placebo based on achievement of ss-PGA score of 0 (clear) or 1 (almost clear) (ss-PGA 0/1) and ≥90% improvement from baseline in the Psoriasis Scalp Severity Index (PSSI 90) at Week 16[16]
- PSORIATYK SCALP (NCT05478499) is an ongoing trial evaluating deucravacitinib in patients with moderate to severe scalp psoriasis, including those with a range of total body surface area (BSA) involvement (≥3%)
  - PSORIATYK SCALP achieved its primary and all key secondary endpoints, with significantly greater proportions of patients treated with deucravacitinib achieving ss-PGA 0/1 (48.5%), PSSI 90 (38.8%), static Physician Global Assessment score 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 (all $P < 0.0001$)[17]

Objective

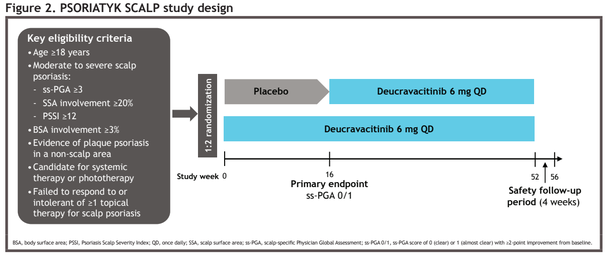
- To evaluate the efficacy of deucravacitinib vs placebo in the achievement of complete clearance of scalp disease and symptoms in this post hoc analysis of the PSORIATYK SCALP trial

Methods

Study designs

- 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 were switched to open-label deucravacitinib 6 mg QD through Week 52
- Stratification factors included in randomization:
  - Prior use of biologic therapy for psoriasis, psoriatic arthritis, or other inflammatory disease (yes/no)
  - Body weight (≥90 kg/<90 kg)

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 ≥2-point improvement from baseline.

- 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 less extensive overall body psoriasis (BSA involvement 3%-10%) compared with the POETYK trials

Outcomes

- ss-PGA 0: the proportion of patients with an ss-PGA score of 0 (clear) with at least a 2-point reduction from baseline
- PSSI 100: the proportion of patients with 100% improvement from baseline in the PSSI
- ss-NRS: patients were asked to describe symptom severity over the prior 24 hours via an 11-point horizontal scale anchored at 0 (no symptoms) and 10 (worst symptom imaginable)
  - ss-NRS itch score of 0: the proportion of patients with an ss-NRS itch score of 0 with a baseline NRS score of at least 1
  - ss-NRS pain score of 0: the proportion of patients with an ss-NRS pain score of 0 with a baseline NRS score of at least 1
  - ss-NRS flaking score of 0: the proportion of patients with an ss-NRS flaking score of 0 with a baseline NRS score of at least 1

Analysis population

- Efficacy was assessed in the full analysis set, which included all patients who were randomized to the study treatment

Statistical analysis

- Efficacy was analyzed after all randomized patients had completed their Week 16 visit or had discontinued treatment prior to Week 16
- Nonresponder imputation (NRI) was used for binary efficacy endpoints for patients who had missing endpoint data
  - 95% confidence intervals (CIs) of the individual response rates were estimated using the exact binomial method
  - *P* values of the odds ratios were obtained using a stratified Cochran-Mantel-Haenszel test with randomization stratification factors
    - Stratification factors included prior biologic use (yes/no) and body weight (≥90 kg/<90 kg) per randomization
- All analyses are post hoc and *P* values are nominal

Results

Baseline patient demographics and clinical characteristics

- Baseline patient demographics and clinical characteristics were similar between the 2 groups (**Table 1**)

Table 1. Baseline patient demographics and clinical characteristics

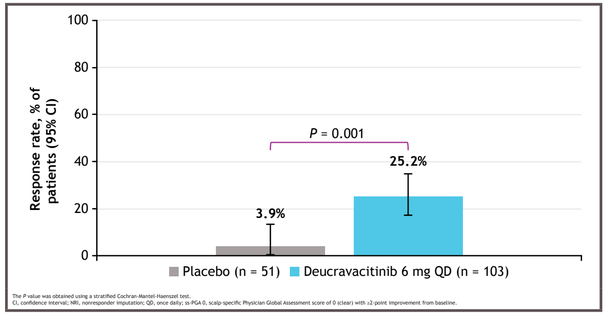
Parameter	Placebo (n = 51)	Deucravacitinib (n = 103)
Age, mean (SD), y	43.2 (13.1)	42.8 (15.7)
Weight, mean (SD), kg	88.3 (27.6)	89.3 (23.8)
Body mass index, mean (SD), kg/m²	29.2 (7.0)	30.1 (7.1)
Female, n (%)	20 (39.2)	45 (43.7)
Race, n (%)		
White	47 (92.2)	93 (90.3)
Asian	2 (3.9)	3 (2.9)
Black or African American	2 (3.9)	5 (4.9)
Other	0	2 (1.9)
Scalp psoriasis duration, mean (SD), y	12.4 (9.6)	16.4 (11.7)
Prior systemic therapy, n (%)		
Yes	27 (52.9)	54 (52.4)
Biologic	16 (31.4)	37 (35.9)
Non-biologic	11 (21.6)	17 (16.5)
No prior systemic therapy	24 (47.1)	49 (47.6)
ss-PGA, n (%)		
3 (moderate)	32 (62.7)	76 (73.8)
4 (severe)	19 (37.3)	27 (26.2)
PSSI, mean (SD)	32.2 (13.7)	33.5 (12.5)
ss-NRS itch score, mean (SD)	6.4 (1.8)	6.4 (2.3)
ss-NRS pain score, mean (SD)	4.5 (3.0)	4.0 (2.8)
ss-NRS flaking score, mean (SD)	6.7 (2.2)	7.0 (2.3)
sPGA, n (%)		
2 (mild)	4 (7.8)	7 (6.8)
3 (moderate)	42 (82.4)	81 (78.6)
4 (severe)	5 (9.8)	15 (14.6)
BSA involvement, mean (SD), %	10.0 (8.1)	10.5 (9.6)
PASI, mean (SD)	9.4 (5.6)	10.2 (6.7)

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.

Efficacy outcomes at Week 16

- At Week 16, a significantly greater proportion of patients treated with deucravacitinib compared with placebo achieved ss-PGA 0 (**Figure 3**)

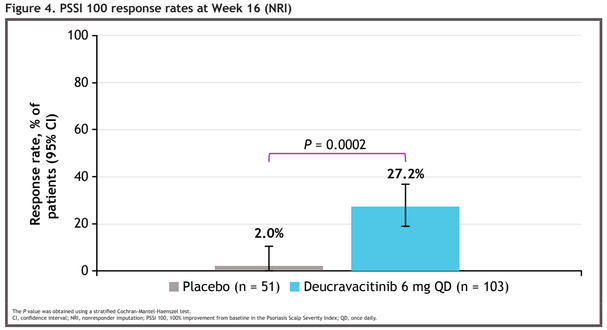
Figure 3. ss-PGA 0 response rates at Week 16 (NRI)



The *P* value was obtained using a stratified Cochran-Mantel-Haenszel test.
CI, confidence interval; NRI, nonresponder imputation; QD, once daily; ss-PGA 0, scalp-specific Physician Global Assessment score of 0 (clear) with ≥2-point improvement from baseline.

- A higher proportion of patients treated with deucravacitinib compared with placebo achieved PSSI 100 at Week 16 (**Figure 4**)

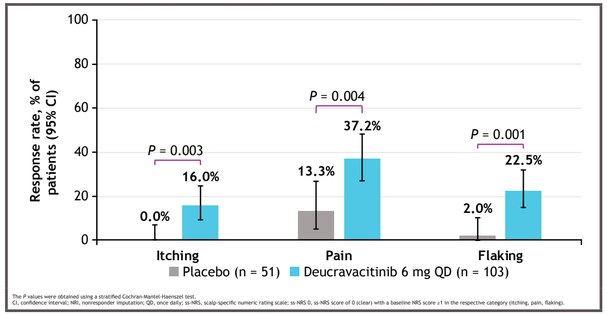
Figure 4. PSSI 100 response rates at Week 16 (NRI)



The *P* value was obtained using a stratified Cochran-Mantel-Haenszel test.
CI, confidence interval; NRI, nonresponder imputation; PSSI 100, 100% improvement from baseline in the Psoriasis Scalp Severity Index; QD, once daily.

- A significantly larger proportion of patients treated with deucravacitinib achieved complete resolution of itching, pain, and flaking compared with placebo (**Figure 5**)

Figure 5. ss-NRS 0 itch, pain, and flaking response rates at Week 16 (NRI)



The *P* values were obtained using a stratified Cochran-Mantel-Haenszel test.
CI, confidence interval; NRI, nonresponder imputation; QD, once daily; ss-NRS, scalp-specific numeric rating scale; ss-NRS 0, ss-NRS score of 0 (clear) with a baseline NRS score ≥1 in the respective category (itching, pain, flaking).

Conclusions

- In addition to achieving primary and all key secondary endpoints,[17] the phase 3b/4 PSORIATYK SCALP trial had greater proportions of patients with complete clearance of signs and symptoms of scalp psoriasis at Week 16 with deucravacitinib treatment vs placebo
  - More than 25% achieved complete scalp clearance
  - Symptom clearance was achieved for itching (16.0%), pain (37.2%), and flaking (22.5%)
- These results support the efficacy of deucravacitinib in patients with moderate to severe scalp psoriasis

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