

Efficacy of deucravacitinib in plaque psoriasis across a range of body surface area involvement: post hoc analysis of the randomized, double-blinded, placebo-controlled, phase 3b/4 PSORIATYK SCALP trial

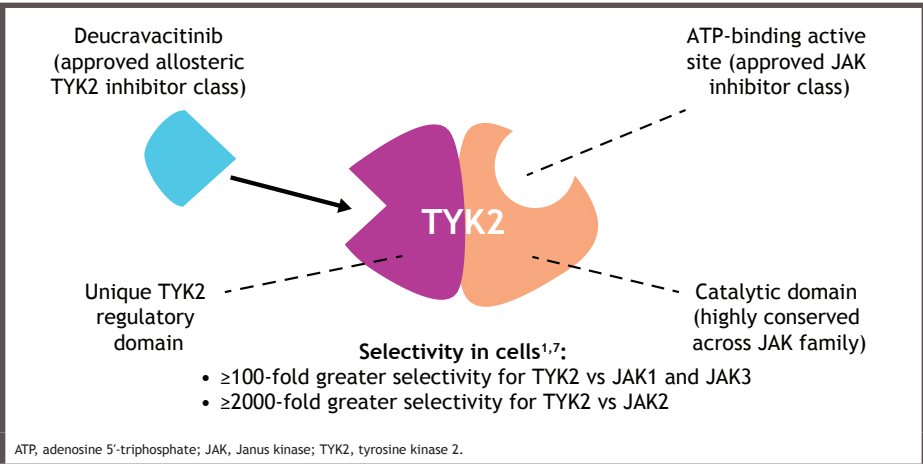
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Synopsis

- 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 pathogenesis¹
- 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 therapy²⁻⁶
- 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



- 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}
- 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 agents¹⁰⁻¹⁶
- 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 an ss-PGA score of 0 (clear) or 1 (almost clear) (ss-PGA 0/1) and ≥90% improvement from baseline in Psoriasis Scalp Severity Index (PSSI) at Week 16¹⁶
- PSORIATYK SCALP (NCT05478499) is an ongoing, 52-week, multicenter, phase 3b/4 trial evaluating deucravacitinib in patients with moderate to severe scalp psoriasis, including those with a range of total body surface area (BSA) involvement (≥3%)
 - Patients in this group are candidates for systemic therapy according to the American Academy of Dermatology/National Psoriasis Foundation and International Psoriasis Council guidelines^{11,14}
 - PSORIATYK SCALP achieved its primary endpoint, with a significantly greater proportion of patients treated with deucravacitinib achieving ss-PGA 0/1 at Week 16 compared with patients receiving placebo; PSORIATYK SCALP also achieved all key secondary endpoints¹⁷

Objective

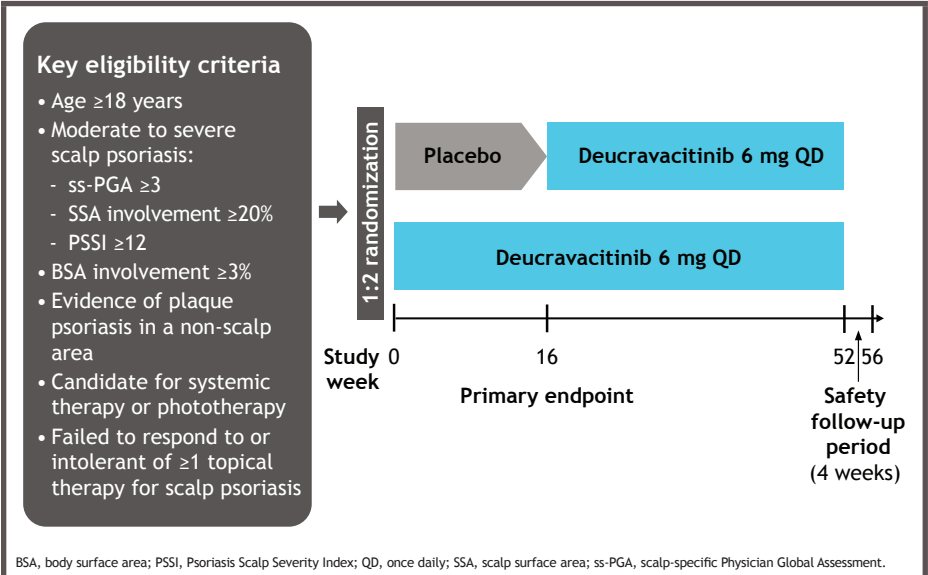
- This PSORIATYK SCALP post hoc analysis evaluated the efficacy of deucravacitinib in improving overall body psoriasis in patients with a range of BSA involvement (≥3%)

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 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



- PSORIATYK SCALP included patients with moderate to severe scalp psoriasis defined by more focused and objective inclusion criteria and less extensive overall body psoriasis (BSA involvement 3%-10%) compared with the phase 3 POETYK PSO-1 and PSO-2 trials

Outcomes

- Static Physician Global Assessment (sPGA) score of 0 (clear) or 1 (almost clear) with ≥2-point reduction from baseline (sPGA 0/1)
 - sPGA×BSA score
 - 75%/90% improvement from baseline in the sPGA×BSA score (sPGA×BSA 75/90)
 - Mean change and mean percentage change from baseline
- Psoriasis Area and Severity Index (PASI)
 - Mean change and mean percentage change from baseline
- Mean change from baseline in whole-body itch numeric rating scale (NRS)

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
- Modified baseline observation carried forward (mBOCF) was used to impute missing data for continuous outcomes; patients who discontinued treatment due to lack of efficacy or adverse events had the baseline observation carried forward for all subsequent analysis weeks after the point of discontinuation, and patients who discontinued treatment due to other reasons or a missing value had the most recent valid observation carried forward

- Adjusted means, 95% CIs, and P values were derived from an analysis of covariance model with treatment and randomization stratification factors as fixed effects and baseline value as a covariate

- All analyses are post hoc and all P values are nominal

Results

Baseline patient demographics and disease characteristics

- Baseline characteristics were similar in the placebo and deucravacitinib groups (Table 1)
 - Mean PASI: 9.4 vs 10.2
 - Mean whole-body itch NRS: 5.8 vs 5.8
- Mean baseline BSA involvement was similar in the placebo and deucravacitinib groups (10.0% vs 10.5%, respectively), and most patients had total BSA involvement in the 3%-10% range (placebo, 74.5%; deucravacitinib, 68.0%)

Table 1. Baseline patient demographics and disease characteristics

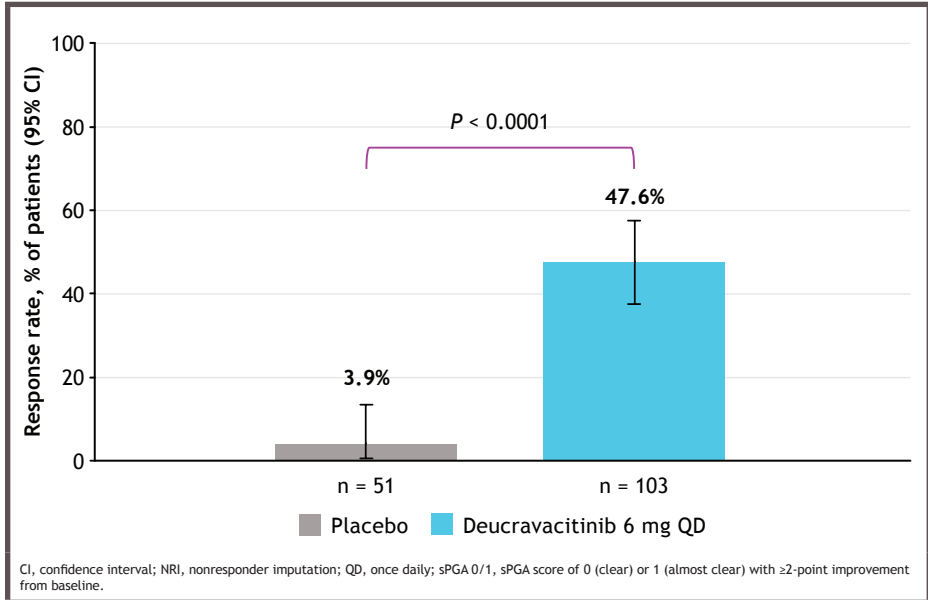
Parameter	Placebo (n = 51)	Deucravacitinib (n = 103)
Age, mean (SD), y	43.2 (13.1)	42.8 (15.7)
Weight, mean (SD), kg	88.2 (27.6)	89.3 (23.8)
Body mass index, mean (SD), kg/m ²	29.2 (7.0)	30.1 (7.1)
Female, n (%)	20 (39.2)	45 (43.7)
Race, n (%)		
White	47 (92.2)	93 (90.3)
Asian	2 (3.9)	3 (2.9)
Black or 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)
Systemic biologic	16 (31.4)	37 (35.9)
Systemic non-biologic	11 (21.6)	17 (16.5)
No prior systemic therapy	24 (47.1)	49 (47.6)
ss-PGA score, n (%)		
3 (moderate)	32 (62.7)	76 (73.8)
4 (severe)	19 (37.3)	27 (26.2)
PSSI score, mean (SD)	32.2 (13.7)	33.5 (12.5)
ss-NRS itching score, mean (SD)	6.4 (1.8)	6.4 (2.3)
sPGA score, 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)		
3%-10%, n (%)	38 (74.5)	70 (68.0)
>10%, n (%)	13 (25.5)	33 (32.0)
PASI, mean (SD)	9.4 (5.6)	10.2 (6.7)
Whole-body itch NRS, mean (SD)	5.8 (2.4)	5.8 (2.8)

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

Efficacy

- At Week 16, a significantly higher proportion of patients receiving deucravacitinib vs placebo achieved sPGA 0/1 (Figure 3)

Figure 3. sPGA 0/1 response rates at Week 16 (NRI)



- Higher sPGA×BSA 75 and 90 response rates (Figure 4) and greater decreases from baseline in sPGA×BSA score (Figure 5) were achieved at Week 16 with deucravacitinib vs placebo

Figure 4. sPGA×BSA 75 and 90 response rates at Week 16 (NRI)

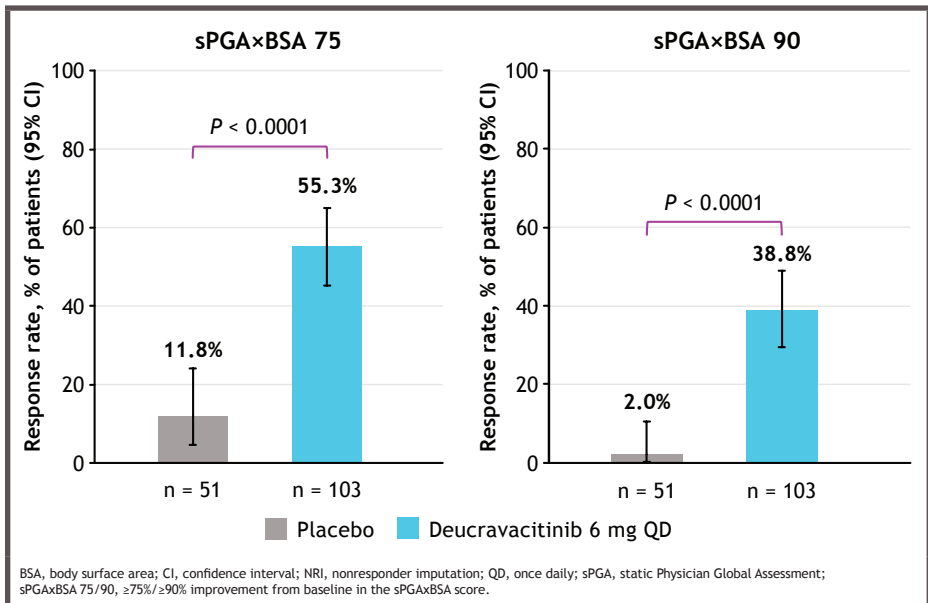
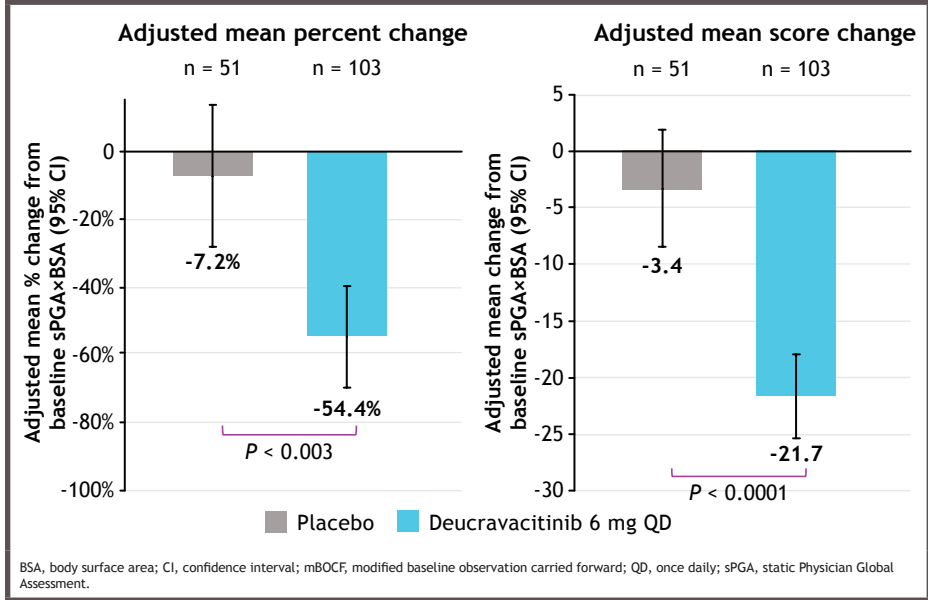


Figure 5. Change from baseline in sPGA×BSA score at Week 16 (mBOCF)



BSA, body surface area; CI, confidence interval; mBOCF, modified baseline observation carried forward; QD, once daily; sPGA, static Physician Global Assessment.

- Patients treated with deucravacitinib had greater decreases from baseline in PASI (Figure 6) and in whole-body itch NRS (Figure 7) score at Week 16 compared with patients who received placebo

Figure 6. Change from baseline in PASI at Week 16 (mBOCF)

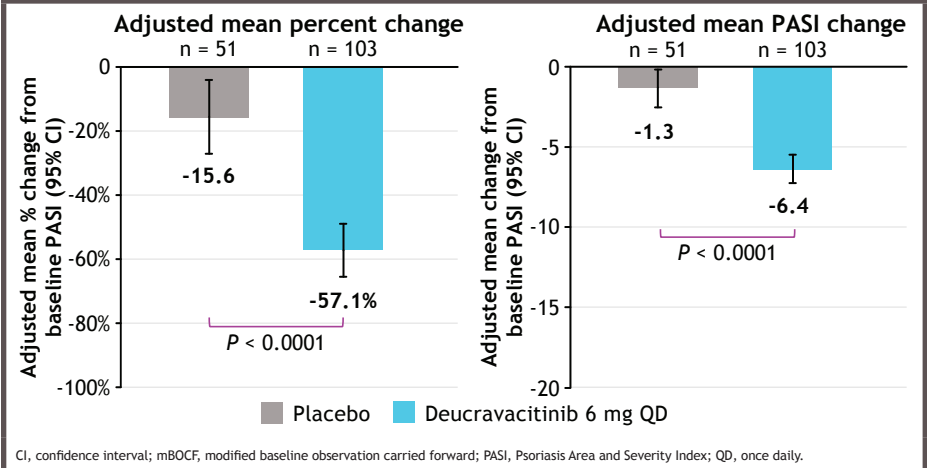
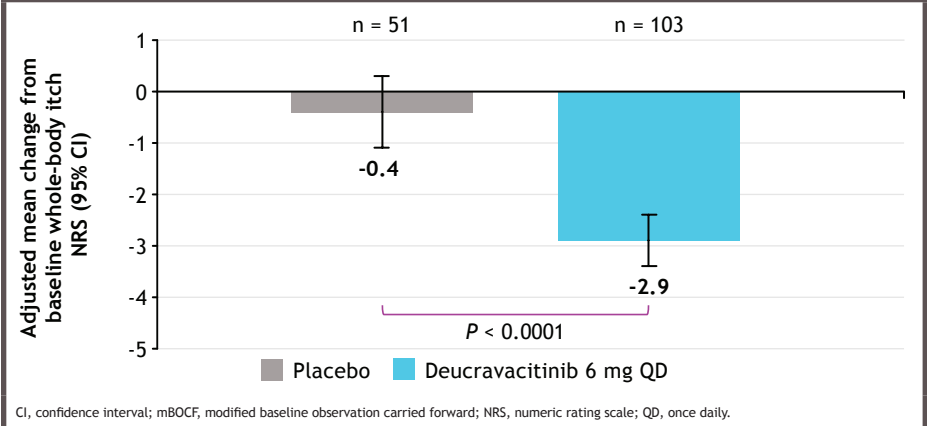


Figure 7. Change from baseline in whole-body itch NRS score at Week 16 (mBOCF)



Conclusions

- In this phase 3b/4 scalp psoriasis-specific trial, deucravacitinib was efficacious in improving overall body plaque psoriasis
- Efficacy rates in overall psoriasis were consistent with those reported in the phase 3 POETYK PSO-1 and PSO-2 trials, despite PSORIATYK SCALP enrolling patients with less extensive overall psoriasis (70% of population had baseline total BSA 3%-10%)^{8,9}

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