Efficacy of deucravacitinib over time in psoriasis by baseline total body surface area: post hoc analysis of the randomized, double-blind, placebo-controlled phase 3b/4 PSORIATYK SCALP trial

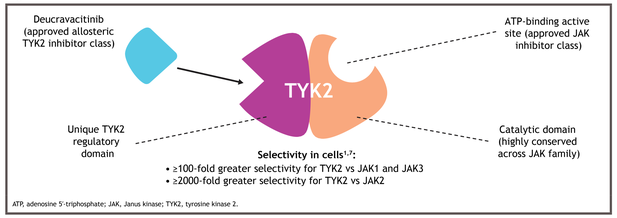
Christopher E. M. Griffiths,[1] Matthias Hoffmann,[2] Andrew Blauvelt,[3] Eugene Balagula,[4] Andrew Napoli,[4] Chun-Yen Cheng,[4] Rachel Dyme,[4] Virginia Hala,[4] Andreas Pinter,[5] Mark Lebwohl[6]

[1]Dermatology Centre, University of Manchester, Manchester, and King's College Hospital and King's College London, London, UK; [2]Private Practice, Witten, Germany; [3]Blauvelt Consulting, Annapolis, MD, USA; [4]Bristol Myers Squibb, Princeton, NJ, USA; [5]University Hospital of Goethe University, Frankfurt am Main, Germany; [6]Icahn School of Medicine at Mount Sinai, New York, NY, USA

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

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[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 agents[10-16]
- Patients with scalp psoriasis have an increased risk of developing psoriatic arthritis[17]
- The PSORIATYK SCALP (NCT05478499) trial evaluated deucravacitinib in patients with moderate to severe scalp psoriasis, including those with more limited overall psoriasis
  - PSORIATYK SCALP achieved its primary endpoint 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 the Psoriasis Scalp Severity Index (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[18]

Objective

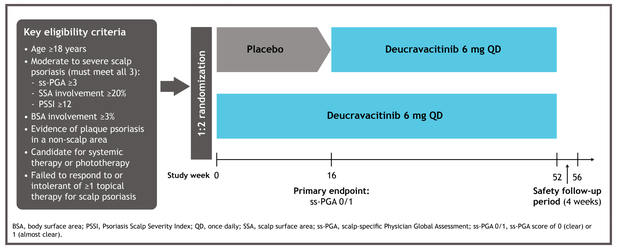
- This post hoc analysis of the PSORIATYK SCALP trial evaluated the efficacy of deucravacitinib in improving overall body psoriasis in patients with moderate to severe scalp psoriasis and more limited overall psoriasis (baseline body surface area [BSA] involvement ≥3%) and in subgroups of patients with total baseline BSA involvement of 3%-10% vs >10%

Methods

Study design

- PSORIATYK SCALP was 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, including those with more limited overall psoriasis (BSA involvement ≥3%)[18] (**Figure 2**)
  - 154 patients were randomized 1:2 to oral placebo (n = 51) or deucravacitinib 6 mg once daily (QD) (n = 103); 90% of patients in each group completed treatment at Week 16
  - At Week 16, all patients were 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 with more limited overall psoriasis as compared with the POETYK trials[18]

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).

Analysis populations

- Full analysis set (BSA involvement ≥3%): all patients randomized to study treatment
- Patients with BSA involvement of 3%-10%
- Patients with BSA involvement >10%

Outcomes

- In each analysis population (Weeks 0-16):
  - Achievement of sPGA 0/1
  - Achievement of ≥75%/≥90% reduction from baseline in the Psoriasis Area and Severity Index (PASI 75/90)
  - Mean percent change from baseline BSA involvement

Statistical analysis

- Efficacy was analyzed after all randomized patients had completed their Week 16 visit or had discontinued treatment prior to Week 16
- BSA subgroups were defined based on categorized BSA involvement at baseline: 3%-10% and >10%
- Nonresponder imputation (NRI) was used for binary efficacy endpoints for patients who had missing endpoint data
  - 95% confidence intervals (CIs) for the individual response rates were estimated using the Clopper-Pearson (exact binomial) method
  - *P* values of the odds ratios were obtained using a stratified Cochran-Mantel-Haenszel test (full analysis set) or an unstratified chi-squared test (BSA subgroups)
- 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 study treatment due to other reasons or a missing value had the most recent valid observation carried forward
  - Adjusted means, 95% CIs, and *P* values for the overall populations were derived from an analysis of covariance model (ANCOVA) with randomization stratification factors (prior biologic use and body weight) as fixed effects and baseline value as a covariate
    - Subgroup ANCOVA values were unstratified
- All analyses are post hoc and all *P* values are nominal

Results

Baseline patient demographics and clinical characteristics

- Baseline patient demographics and clinical characteristics were similar in the placebo and deucravacitinib groups (**Table 1**)
- 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**)
- Patients in the >10% BSA subgroup treated with deucravacitinib had longer disease duration (19.8 years [standard deviation (SD) 13.3] vs 13.2 [SD 9.6]) and were more likely to have had prior biologic therapy (42.4% vs 30.8%) compared with those receiving placebo (**Table 2**)

Table 1. Baseline patient demographics and clinical characteristics: full analysis set (BSA involvement ≥3%)

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)
Psoriasis vulgaris duration, mean (SD), y	11.9 (9.8)	16.1 (11.4)
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)
Nonbiologic	11 (21.6)	17 (16.5)
No	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, 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)
SSA involvement, mean (SD), %	53.0 (24.0)	57.6 (23.1)
BSA involvement, mean (SD), %	10.0 (8.1)	10.5 (9.6)
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)

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

Table 2. Baseline patient demographics and clinical characteristics by baseline BSA involvement: 3%-10% vs >10%

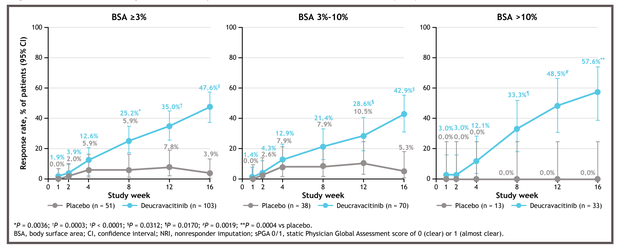
Parameter	Baseline BSA involvement: 3%-10% Placebo (n = 38)	3%-10% Deucravacitinib (n = 70)	>10% Placebo (n = 13)	>10% Deucravacitinib (n = 33)
Age, mean (SD), y	41.8 (13.1)	42.0 (15.2)	47.5 (12.5)	44.3 (16.9)
Weight, mean (SD), kg	86.3 (24.3)	88.7 (25.0)	93.8 (36.2)	90.6 (21.3)
Body mass index, mean (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, 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 (53.9)	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 itching 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)
SSA involvement, mean (SD), %	54.4 (24.4)	53.8 (22.5)	48.8 (23.0)	65.6 (22.7)
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; 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.

sPGA 0/1 response rates, Weeks 0-16 (NRI)

- A greater proportion of patients treated with deucravacitinib achieved sPGA 0/1 compared with patients receiving placebo starting at Week 8 and continuing through Week 16; results were consistent in the analysis of the BSA 3%-10% and >10% subgroups (**Figure 3**)

Figure 3. sPGA 0/1 response rate by BSA involvement, Weeks 0-16 (NRI)

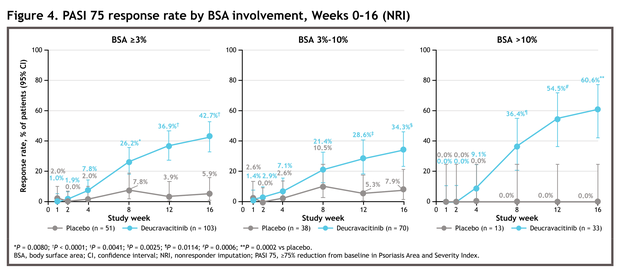


*P = 0.0036; †P = 0.0003; ‡P < 0.0001; §P = 0.0312; ¶P = 0.0170; #P = 0.0019; **P = 0.0004 vs placebo.
BSA, body surface area; CI, confidence interval; NRI, nonresponder imputation; sPGA 0/1, static Physician Global Assessment score of 0 (clear) or 1 (almost clear).

PASI 75 response rates, Weeks 0-16 (NRI)

- A greater proportion of patients treated with deucravacitinib achieved PASI 75 compared with patients receiving placebo starting at Week 8 and continuing through Week 16; results were consistent in the BSA 3%-10% and >10% subgroups (**Figure 4**)

Figure 4. PASI 75 response rate by BSA involvement, Weeks 0-16 (NRI)

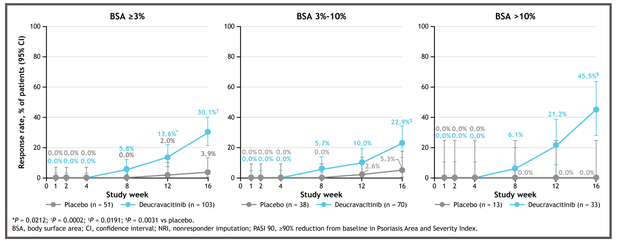


*P = 0.0080; †P > 0.0001; ‡P = 0.0041; §P = 0.0025; ¶P = 0.0114; #P = 0.0006; **P = 0.0002 vs placebo.
BSA, body surface area; CI, confidence interval; NRI, nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index.

PASI 90 response rates, Weeks 0-16 (NRI)

- Higher response rates for PASI 90 were observed in patients treated with deucravacitinib compared with patients receiving placebo through Week 16 in the overall study group and in the BSA 3%-10% and >10% subgroups (**Figure 5**)

Figure 5. PASI 90 response rate by BSA involvement, Weeks 0-16 (NRI)

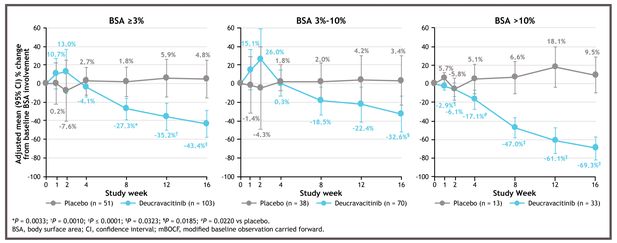


*P = 0.0212; †P = 0.0002; ‡P = 0.0191; §P = 0.0031 vs placebo.
BSA, body surface area; CI, confidence interval; NRI, nonresponder imputation; PASI 90, ≥90% reduction from baseline in Psoriasis Area and Severity Index.

Mean percent change from baseline in BSA involvement, Weeks 0-16 (mBOCF)

- Patients treated with deucravacitinib had greater mean percent change from baseline in BSA score vs placebo overall and by BSA subgroups (**Figure 6**)

Figure 6. Mean percent change in BSA score by BSA involvement, Weeks 0-16 (mBOCF)



*P = 0.0003; †P = 0.0010; ‡P ≤ 0.0001; §P = 0.0323; ¶P = 0.0185; #P = 0.0220 vs placebo.
BSA, body surface area; CI, confidence interval; mBOCF, modified baseline observation carried forward.

Conclusions

- In the phase 3b/4 PSORIATYK SCALP trial, deucravacitinib improved psoriasis through Week 16 compared with placebo across a range of measures, including sPGA 0/1, PASI 75, and PASI 90, in patients with more limited overall psoriasis (BSA involvement ≥3%)
  - Differences in responses in the BSA subgroups were likely driven by the differences in baseline disease severity
- sPGA 0/1 response rates in the full analysis set were consistent with those reported in the phase 3 POETYK PSO-1 and PSO-2 trials, despite PSORIATYK SCALP including patients with more limited overall psoriasis (BSA involvement ≥3%)

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Email: christopher.griffiths@manchester.ac.uk