Deucravacitinib, an oral, selective, allosteric tyrosine kinase 2 inhibitor, in the phase 3 clinical trials in psoriasis, POETYK PSO-1 and PSO-2: Time to meaningful improvements in itch as assessed by the Psoriasis Symptoms and Signs Diary

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Synopsis

- Itch has been found to be one of the most prevalent and burdensome symptoms for patients with psoriasis, contributing to reduced quality of life[1,2]
- In the phase 3 POETYK PSO-1 and PSO-2 trials,[3,4] patients with moderate to severe plaque psoriasis completed the Psoriasis Symptoms and Signs Diary (PSSD) daily, recording the severity of their symptoms and signs, including itch, over the past 24 hours
- Change from baseline and time to meaningful improvement on the PSSD itch item were evaluated in patients treated with deucravacitinib vs placebo in both POETYK trials
- Patients receiving deucravacitinib experienced greater itch improvement from baseline vs placebo within 2 weeks of treatment in each trial
- About half of patients who received deucravacitinib experienced meaningful improvement in itch within 6 weeks

Objective

- To evaluate change from baseline and time to meaningful improvement on the PSSD itch item for deucravacitinib vs placebo in the phase 3 clinical trials POETYK PSO-1 and PSO-2 in psoriasis

Methods

- In both POETYK PSO-1 and PSO-2,[4] adult patients with moderate to severe plaque psoriasis were randomized 1:2:1 to placebo, deucravacitinib 6 mg once daily, or apremilast 30 mg twice daily
  - At Week 16, patients randomized to placebo crossed over to receive deucravacitinib
- Patients completed the PSSD daily, recording the severity of their psoriasis symptoms and signs, including itch, over the past 24 hours
- Adjusted mean score change from baseline to Week 16 for the PSSD itch item was modeled for deucravacitinib vs placebo
  - An analysis of covariance model used factors for geographic region, body weight, and prior biologic use, and included the baseline value as a covariate
  - Since this was not a pre-specified analysis, reported *P* values are nominal
- Time to ≥2-, ≥3-, and ≥4-point improvements from baseline to Week 16 in itch score were estimated with Kaplan-Meier methods in patients with baseline scores ≥2, ≥3, and ≥4, respectively
  - Improvements of ≥2 points on individual PSSD items (range, 0-10) were previously determined to be meaningful to patients with psoriasis[5]
  - Cox models estimated hazard ratios for these improvements
- Analyses included patients who completed the PSSD itch item at baseline and ≥1 PSSD itch item at a postbaseline visit
- Missing data were imputed with modified baseline observation carried forward methods

Results

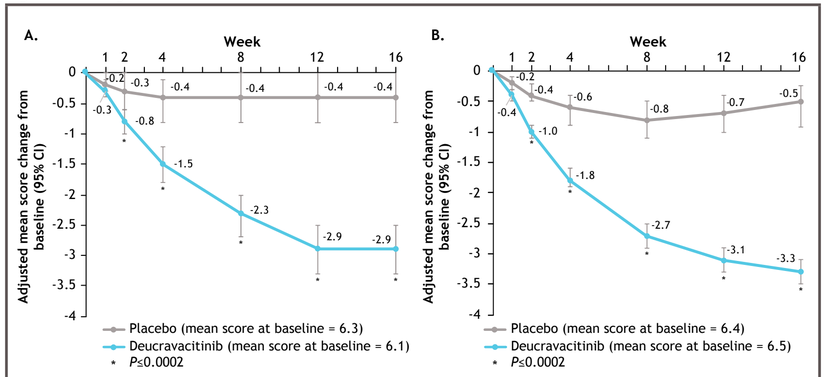
- Mean baseline score for itch on the PSSD was similar across both treatment arms and both POETYK trials (range: 6.1-6.5; **Table**)
- In each trial, greater improvement from baseline in itch score was observed within 2 weeks with deucravacitinib vs placebo (*P*≤0.0002; **Figure 1**)
- In each trial, the median (95% confidence interval [CI]) time to ≥2-point itch improvement was 6.0 (5.0-7.0) weeks for patients receiving deucravacitinib (**Figure 2**)
- The median (95% CI) times to ≥3-point itch improvement for patients receiving deucravacitinib were 9.0 (7.0-11.0) and 9.0 (8.0-11.0) weeks in POETYK PSO-1 and PSO-2, respectively (**Figure 3**)
- The median (95% CI) time to the most stringent ≥4-point improvement threshold for patients receiving deucravacitinib was not reached at Week 16 in POETYK PSO-1, but was 13.0 weeks (10.0-NE) in POETYK PSO-2 (**Figure 4**)
- In each trial, median time to improvement at any of the 3 thresholds was not reached for patients receiving placebo
  - Data were censored at Week 16 owing to placebo crossover to deucravacitinib at this time point
- Patients receiving deucravacitinib were 3 times more likely to achieve ≥2-point improvement in their PSSD itch score by Week 16 than patients receiving placebo (hazard ratio [HR; 95% CI] for improvement: 3.0 [2.1-4.1] in POETYK PSO-1 and 3.4 [2.6-4.5] in POETYK PSO-2 (**Figure 2**)
- HRs for improvement with deucravacitinib vs placebo increased as the threshold for meaningful improvement from baseline increased
  - At ≥3 points, HRs (95% CI) were 4.0 (2.6-6.1) and 4.9 (3.4-6.9) in POETYK PSO-1 and PSO-2, respectively (**Figure 3**)
  - At ≥4 points, HRs (95% CI) were 6.5 (3.4-12.4) and 8.8 (5.1-15.2) in POETYK PSO-1 and PSO-2, respectively (**Figure 4**)

Table. Demographics and baseline clinical characteristics

Characteristic	POETYK PSO-1[3]		POETYK PSO-2[4]	
	Placebo (n = 166)	Deucravacitinib (n = 332)	Placebo (n = 255)	Deucravacitinib (n = 511)
Age, mean (SD), y	47.9 (14.0)	45.9 (13.7)	47.3 (13.6)	46.9 (13.4)
Female, n (%)	53 (31.9)	102 (30.7)	74 (29.0)	175 (34.2)
Weight, mean (SD), kg	89.1 (22.3)	87.9 (21.8)	91.5 (20.2)	92.3 (21.9)
PASI score, mean (SD)	20.7 (8.0)	21.8 (8.6)	21.1 (9.0)	20.7 (7.5)
sPGA score, n (%)				
3	128 (77.1)	257 (77.4)	217 (85.1)	408 (79.8)
4	37 (22.3)	75 (22.6)	38 (14.9)	103 (20.2)
PSSD itch score, n	151	306	239	466
Mean (SD)	6.3 (2.3)	6.1 (2.6)	6.5 (2.5)	6.4 (2.3)
Range	0.0, 10.0	0.0, 10.0	0.0, 10.0	0.0, 10.0
PSSD itch score, n (%)				
≥2	137 (90.7)	292 (95.4)	231 (96.7)	444 (95.3)
≥3	132 (87.4)	277 (90.5)	223 (93.3)	418 (89.7)
≥4	121 (80.1)	253 (82.7)	203 (84.9)	384 (82.4)

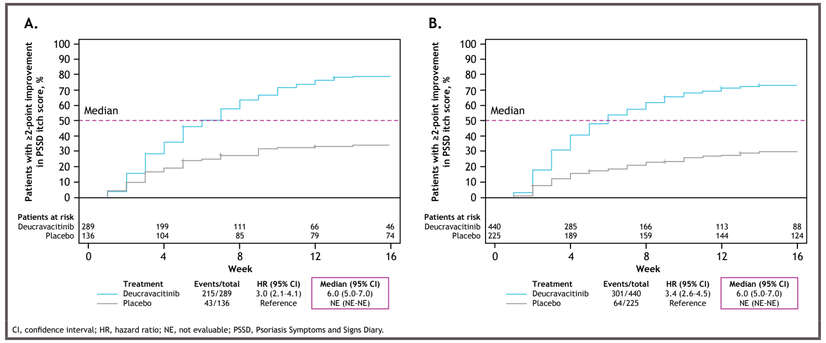
PASI, Psoriasis Area and Severity Index; PSSD, Psoriasis Symptoms and Signs Diary; SD, standard deviation; sPGA, static Physician Global Assessment.

Figure 1. Change from baseline in PSSD itch score[a] in (A) POETYK PSO-1 and (B) POETYK PSO-2



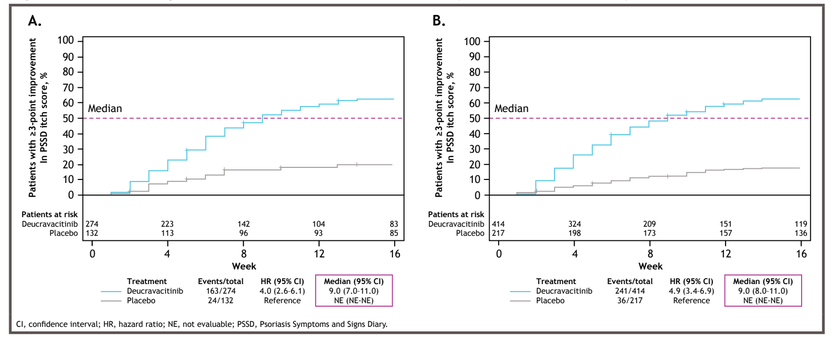
[a]Adjusted means, *P* value, and confidence intervals from an analysis of covariance model with factors for geographic region, body weight, and prior biologic use, and the baseline value as a covariate.
CI, confidence interval; PSSD, Psoriasis Symptoms and Signs Diary.

Figure 2. Time to ≥2-point reduction in PSSD itch score in (A) POETYK PSO-1 and (B) POETYK PSO-2



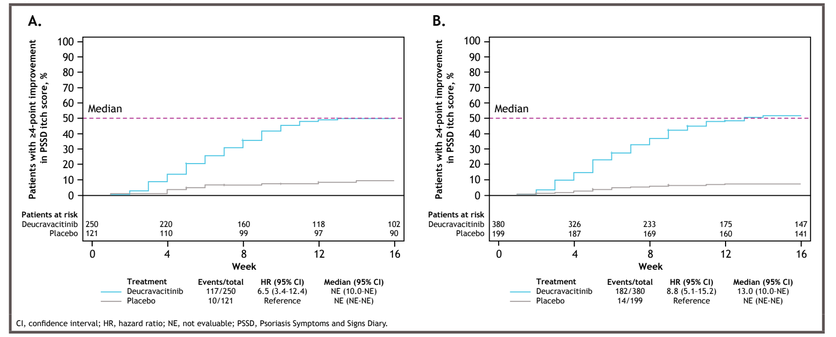
CI, confidence interval; HR, hazard ratio; NE, not evaluable; PSSD, Psoriasis Symptoms and Signs Diary.

Figure 3. Time to ≥3-point reduction in PSSD itch score in A) POETYK PSO-1 and B) POETYK PSO-2



CI, confidence interval; HR, hazard ratio; NE, not evaluable; PSSD, Psoriasis Symptoms and Signs Diary.

Figure 4. Time to ≥4-point reduction in PSSD itch score in A) POETYK PSO-1 and B) POETYK PSO-2



CI, confidence interval; HR, hazard ratio; NE, not evaluable; PSSD, Psoriasis Symptoms and Signs Diary.

Conclusions

- Patients receiving deucravacitinib vs placebo experienced greater improvement from baseline in their itch within 2 weeks of treatment in each trial
- About half of patients receiving deucravacitinib experienced meaningful improvement (≥2-point improvement from baseline) in itch within 6 weeks

References

1. Globe D, et al. *Health Qual Life Outcomes*. 2009;7:62. **2.** Jaworecka K, et al. *Life (Basel)*. 2021;11:623. **3.** Armstrong AW, et al. *J Am Acad Dermatol*. 2023;88:29-39. **4.** Strober B, et al. *J Am Acad Dermatol*. 2023;88:40-51. **5.** Papp KA, et al. *JAMA Dermatol*. Published online December 20, 2023. doi:10.1001/jamadermatol.2023.5058.

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