Deucravacitinib significantly improves symptoms and signs of psoriasis in patients with moderate to severe psoriasis: Results from the phase 3 POETYK PSO-1 and POETYK PSO-2 trials

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Introduction

- Deucravacitinib, an oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor, is approved in the United States and other countries for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy[1]
- Deucravacitinib mediates cytokine signaling involved in the pathogenesis of psoriasis (eg, interleukin [IL]-23, Type I interferons)[2,3]
- In the phase 3 POETYK PSO-1 and POETYK PSO-2 clinical trials, a significantly greater proportion of patients with moderate to severe plaque psoriasis achieved the coprimary endpoints (≥75% reduction from baseline in Psoriasis Area and Severity Index [PASI 75]; static Physician's Global Assessment score of 0 [clear] or 1 [almost clear] with ≥2-point improvement from baseline [sPGA 0/1]) with deucravacitinib treatment vs placebo and vs apremilast over 16 weeks[4,5]
- Patient-reported outcome (PRO) measures help to capture the impact of treatment on the disease aspects, such as pain and itch, which can substantially impact quality of life[6,7]
- The Psoriasis Symptoms and Signs Diary (PSSD) is a validated PRO measure designed to determine the severity of plaque psoriasis based on 11 symptoms and signs, each rated on an 11-point scale from 0 (absent) to 10 (worst)[6]
  - Symptoms: itch, pain, stinging, burning, skin tightness
  - Signs: skin dryness, cracking, scaling, shedding or flaking, redness, bleeding
  - A meaningful within-patient change threshold (MWPCT) of ≥3-5 points for individual items and ≥40 points for summary scores has been previously recommended; however, these thresholds were developed within the context of a clinical trial and are not population specific, warranting further testing
- Findings from the POETYK trials showed that after 16 weeks, deucravacitinib treatment was associated with significantly greater improvements from baseline than placebo or apremilast on the PSSD symptom scores[8]

Objectives

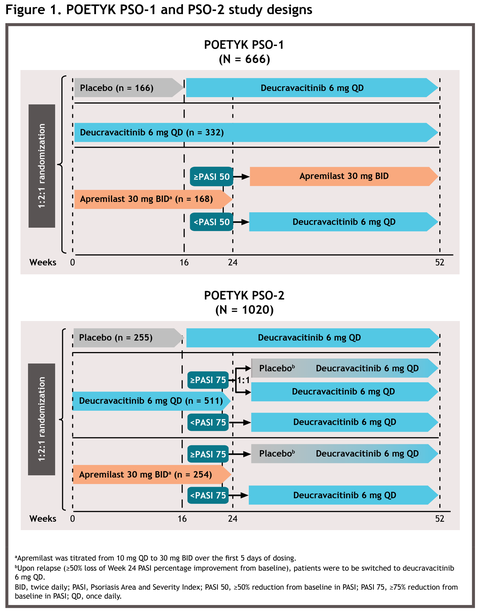
- Derive the MWPCT for each PSSD item using Week 16 data from POETYK PSO-1, with Patient Global Impression (PGI) of Change (PGI-C) and PGI of Severity (PGI-S) as anchors
- Evaluate the efficacy of deucravacitinib on PSSD in the POETYK PSO-1 and PSO-2 trials based on longitudinal patterns of change, MWPCT responder analysis, and assessments of time to and duration of improvement

Methods

Study designs and assessments

- POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751) were phase 3, 52-week, double-blind trials that randomized patients with moderate to severe plaque psoriasis (PASI ≥12, sPGA ≥3, body surface area ≥10%) 1:2:1 to placebo, deucravacitinib 6 mg once daily, or apremilast 30 mg twice daily (**Figure 1**)
- Patients completed the PSSD daily with a 24-hour recall, and weekly scores were calculated as the average of the previous 7 days (≥4 of 7 days required)
  - Symptom score is the average of 5 items (itch, pain, stinging, burning, skin tightness) multiplied by 10
  - Sign score is the average of 6 items (skin dryness, cracking, scaling, shedding or flaking, redness, bleeding) multiplied by 10
- Baseline changes in individual symptoms and signs were compared between deucravacitinib- and placebo-treated patients over Weeks 0-16 (end of placebo treatment) using a pairwise *t* test; baseline changes were also reported for patients who received continuous deucravacitinib treatment from Day 1 through Week 52 in POETYK PSO-1 and through Week 24 in POETYK PSO-2 (**Figure 1**)

Figure 1. POETYK PSO-1 and PSO-2 study designs



*Apremilast was titrated from 10 mg QD to 30 mg BID over the first 5 days of dosing.
^bUpon relapse (≥50% loss of Week 24 PASI percentage improvement from baseline), patients were to be switched to deucravacitinib 6 mg QD.
BID, twice daily; PASI, Psoriasis Area and Severity Index; PASI 50, ≥50% reduction from baseline in PASI; PASI 75, ≥75% reduction from baseline in PASI; QD, once daily.

Determination of MWPCT

- MWPCTs are valuable for assessing the benefits of an intervention from the patient perspective, and anchor-based methods using PGI scales are typically recommended[9]
- Anchor-based MWPCT derivation was conducted using combined Week 16 data from all 3 treatment groups in POETYK PSO-1
- PGI-C and PGI-S were used as anchors to estimate MWPCTs via a multistep process
  1. Polyserial correlation coefficients were calculated between changes in PSSD scores and changes in anchor variables to ensure that a sufficient correlation exists before proceeding to step 2
  2. Where adequate correlation (>0.40) was observed, within-group change scores were examined regarding standardized effect size (>0.50), paired *t* test for change from baseline ($P < 0.05$), and confidence intervals (CIs) associated with the no change and improved/worsened groups
  3. Results were triangulated across anchors to determine estimated MWPCTs, with higher priority given to the change in PGI-S, as it is less sensitive to recall bias

Responder analysis, time to improvement, and duration of improvement

- Responder analyses evaluating the proportion of patients achieving the MWPCT as well as the proportion with complete resolution (ie, score = 0) were conducted to determine the efficacy of deucravacitinib on the individual PSSD symptoms and signs
  - Hazard ratios and 95% CIs were used to assess the efficacy of deucravacitinib by comparing results with the placebo group
- A Kaplan-Meier analysis was used to determine time to improvement, defined as the number of weeks between baseline and the first improvement ≥ MWPCT or attainment of a score of 0, with no subsequent worsening at the next 2 consecutive visits
  - If no improvement was observed within the first 16 weeks, time to improvement was censored at the individual's last PRO assessment or Week 16, whichever was earlier
  - Patients with baseline scores less than the MWPCT (no "room to improve") were considered to have had the event at baseline
- In patients achieving a meaningful improvement during the first 16 weeks, duration of improvement was assessed
  - The end of the improvement period was defined as the time of worsening to below the MWPCT relative to baseline or, if an individual's score did not worsen, the time of the last PRO visit or the end of the analysis period, whichever was earlier

Results

Patients

- This analysis included 1148 patients from POETYK PSO-1 (deucravacitinib, n = 303; placebo, n = 150) and POETYK PSO-2 (deucravacitinib, n = 462; placebo, n = 233)
- Baseline scores on PSSD items were similar across treatment groups and studies (**Table 1**)

Table 1. Baseline PSSD scores

Mean (SD) score	POETYK PSO-1		POETYK PSO-2	
	Placebo (n = 150)	Deucravacitinib (n = 303)	Placebo (n = 233)	Deucravacitinib (n = 462)
PSSD symptoms	51.57 (26.74)	51.59 (25.07)	50.16 (24.81)	52.04 (26.23)
Itch	6.15 (2.59)	6.26 (2.33)	6.43 (2.27)	6.45 (2.47)
Pain	4.63 (3.08)	4.80 (2.95)	4.46 (2.99)	4.70 (3.16)
Stinging	4.60 (3.04)	4.44 (3.06)	4.28 (2.90)	4.43 (3.16)
Burning	4.62 (3.03)	4.69 (2.96)	4.51 (2.88)	4.65 (3.08)
Skin tightness	5.79 (2.65)	5.59 (2.49)	5.40 (2.66)	5.79 (2.57)
PSSD signs	55.70 (23.02)	55.19 (21.75)	55.82 (21.14)	57.45 (22.02)
Skin dryness	6.34 (2.39)	6.32 (2.19)	6.44 (2.21)	6.63 (2.24)
Cracking	5.39 (2.73)	5.24 (2.65)	5.22 (2.72)	5.34 (2.83)
Scaling	6.24 (2.36)	6.13 (2.29)	6.38 (2.19)	6.55 (2.25)
Shedding or flaking	6.27 (2.38)	6.27 (2.36)	6.40 (2.31)	6.58 (2.25)
Redness	5.87 (2.52)	5.95 (2.38)	5.80 (2.42)	5.98 (2.44)
Bleeding	3.30 (2.94)	3.20 (2.90)	3.25 (2.81)	3.39 (3.03)

PSSD, Psoriasis Symptoms and Signs Diary; SD, standard deviation.

Longitudinal change from baseline on PSSD symptoms and signs

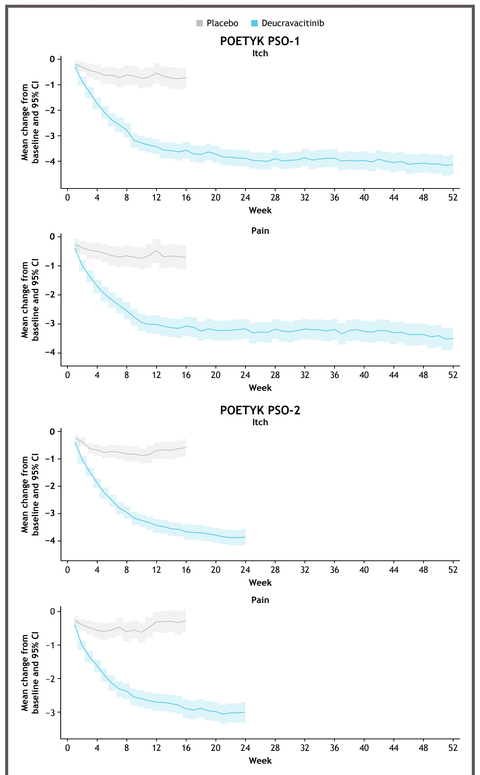
- Significantly greater mean improvements were observed with deucravacitinib vs placebo from baseline to Week 16 on individual PSSD items ($P < 0.0001$ for all), and improvements in the deucravacitinib group were maintained or improved through Week 52 and Week 24 in POETYK PSO-1 and PSO-2, respectively (**Table 2**)
- Longitudinal analysis of the most clinically relevant symptoms, itch and pain, showed statistical separation of deucravacitinib from placebo as early as Week 1 and no later than Week 2, which was maintained through Week 16 (**Figure 2**)
  - Similar findings were observed across all other PSSD items

Table 2. Change from baseline in PSSD symptoms and signs

Mean (SD) change from baseline	POETYK PSO-1			POETYK PSO-2		
	Placebo (n = 150)	Deucravacitinib (n = 303)		Placebo (n = 233)	Deucravacitinib (n = 462)	
	Week 16	Week 16	Week 52	Week 16	Week 16	Week 24
PSSD symptoms	-7.00 (21.58)	-32.07 (24.12)*	-36.22 (25.88)	-3.73 (20.14)*	-31.82 (25.71)	-33.31 (25.80)
Itch	-0.72 (2.29)	-3.57 (2.61)*	-4.13 (2.82)	-0.59 (2.18)*	-3.67 (2.72)	-3.86 (2.76)
Pain	-0.71 (2.27)	-3.07 (2.67)*	-3.50 (2.77)	-0.28 (2.28)*	-2.90 (2.80)	-3.00 (2.89)
Stinging	-0.57 (2.24)	-2.81 (2.76)*	-3.14 (2.98)	-0.16 (2.23)*	-2.77 (2.86)	-2.89 (2.91)
Burning	-0.64 (2.26)	-3.15 (2.69)*	-3.51 (2.90)	-0.33 (2.35)*	-2.99 (2.90)	-3.12 (2.90)
Skin tightness	-0.87 (2.38)	-3.43 (2.60)*	-3.83 (2.87)	-0.50 (2.17)*	-3.59 (2.78)	-3.78 (2.78)
PSSD signs	-8.16 (21.53)	-34.41 (23.32)*	-37.82 (24.80)	-6.81 (17.86)*	-35.45 (24.13)	-37.43 (24.14)
Skin dryness	-0.88 (2.34)	-3.81 (2.55)*	-4.29 (2.74)	-0.76 (2.00)*	-3.97 (2.66)	-4.19 (2.67)
Cracking	-0.94 (2.60)	-3.50 (2.68)*	-3.80 (2.94)	-0.66 (2.29)*	-3.31 (2.71)	-3.61 (2.81)
Scaling	-0.92 (2.38)	-3.64 (2.63)*	-3.97 (2.79)	-0.65 (2.02)*	-3.94 (2.69)	-4.17 (2.71)
Shedding or flaking	-0.87 (2.31)	-3.82 (2.76)*	-4.25 (2.81)	-0.73 (2.02)*	-4.07 (2.73)	-4.35 (2.73)
Redness	-0.68 (2.35)	-3.59 (2.46)*	-3.93 (2.69)	-0.68 (2.13)*	-3.60 (2.69)	-3.80 (2.73)
Bleeding	-0.60 (2.10)	-2.29 (2.49)*	-2.46 (2.78)	-0.64 (1.99)*	-2.30 (2.69)	-2.35 (2.69)

*$P < 0.0001$ vs placebo at Week 16.
PSSD, Psoriasis Symptoms and Signs Diary; SD, standard deviation.

Figure 2. Longitudinal change from baseline in itch and pain



CI, confidence interval.

Determination of MWPCT

- Both PGI-C and PGI-S were sufficiently correlated (>0.40) with all PSSD items except for bleeding (**Table 3**)
- Using the PGI-S anchor, substantial separation was observed between the 95% CIs for the patients with no change vs the patients with ≥1-point improvement
- For all symptoms and signs, MWPCT was determined to be 2 points

Table 3. Correlation of PSSD symptoms and signs with anchor variables

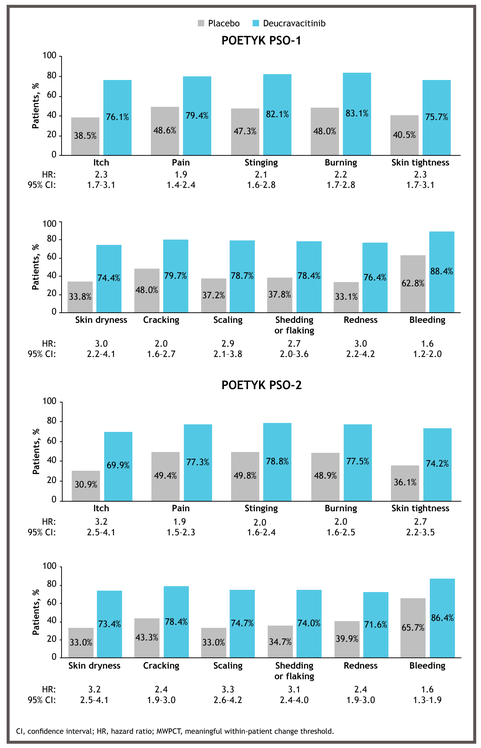
	POETYK PSO-1	
	PGI-C (n = 609)	PGI-S (n = 609)
PSSD symptoms		
Itch	0.599	0.612
Pain	0.450	0.478
Stinging	0.437	0.451
Burning	0.460	0.480
Skin tightness	0.548	0.568
PSSD signs		
Skin dryness	0.617	0.617
Cracking	0.520	0.532
Scaling	0.599	0.600
Shedding or flaking	0.618	0.600
Redness	0.569	0.553
Bleeding	0.374	0.375

PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity; PSSD, Psoriasis Symptoms and Signs Diary.

Responder analysis, time to improvement, and duration of improvement

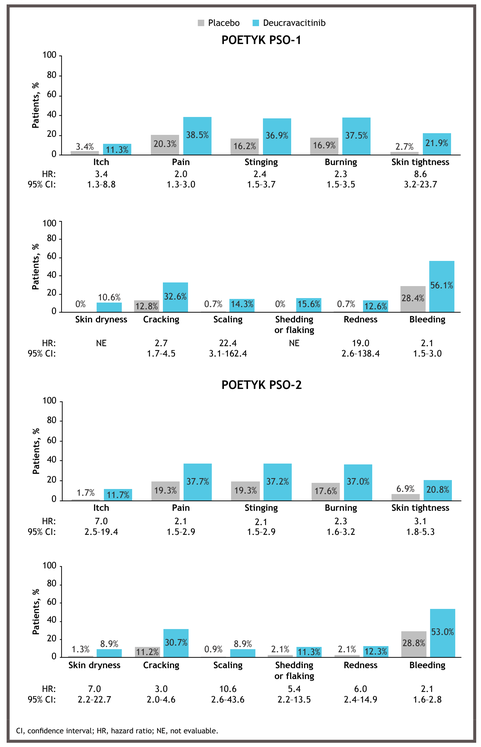
- Responder analyses showed that patients were significantly more likely to achieve MWPCT in PSSD symptoms and signs over 16 weeks with deucravacitinib vs placebo (**Figure 3**)
  - Median time to achieving MWPCT ranged from 2-6 weeks with deucravacitinib and was not reached with placebo
- Deucravacitinib-treated patients were also more likely to achieve complete resolution of PSSD symptoms and signs than placebo patients (**Figure 4**)
  - However, few patients achieved complete resolution over 16 weeks, and median time to improvement was not achieved in either treatment group
- In a small number of deucravacitinib-treated patients with complete resolution of itch (ie, score of 0) in the first 16 weeks of POETYK PSO-1 (n = 34), 13 (38.2%) maintained complete resolution through Week 52 (**Figure 5**)
- Duration of improvement could not be determined for most other PSSD symptoms and signs in either treatment group up to Week 16 (data not shown)

Figure 3. Proportion of patients achieving an MWPCT ≥2 (MWPCT responders) at Week 16



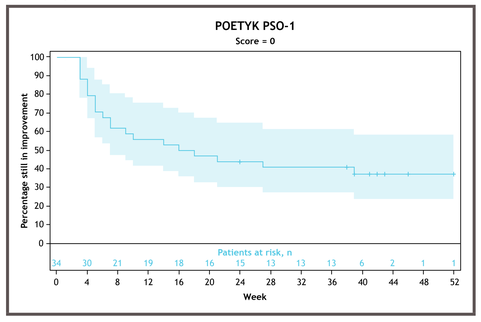
CI, confidence interval; HR, hazard ratio; MWPCT, meaningful within-patient change threshold.

Figure 4. Proportion of patients achieving a score of 0 at Week 16



CI, confidence interval; HR, hazard ratio; NE, not evaluable.

Figure 5. Duration of improvement in deucravacitinib-treated patients with complete resolution of itch in the first 16 weeks of POETYK PSO-1



Conclusions

- Deucravacitinib treatment was associated with rapid and sustained improvement in all PSSD symptoms and signs
- MWPCT analysis indicated that an improvement of ≥2 points from baseline was appropriate for evaluating individual patient responses on PSSD symptoms and signs
- Responder analyses showed significantly greater proportions of patients achieved an MWPCT with deucravacitinib than with placebo across all PSSD symptoms and signs
- Overall, these findings further support the benefits of deucravacitinib treatment in patients with moderate to severe plaque psoriasis

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