Deucravacitinib, an oral, allosteric, selective tyrosine kinase 2 inhibitor, in patients with plaque psoriasis who screened positive for psoriatic arthritis in POETYK PSO-1 and POETYK PSO-2: effect on joint pain and peripheral joint disease vs placebo and apremilast

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Background

- Psoriatic arthritis (PsA) is a heterogenous disease often presenting in patients with long-standing psoriasis
  - A large multinational study found 30% of patients with psoriasis had PsA, and as many as 41% of those patients were undiagnosed[1]
- Treatments for PsA should aim to address the dermatologic, musculoskeletal, and psychosocial manifestations of PsA
- Deucravacitinib is a first-in-class, oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor approved in multiple countries for treatment of adults with moderate to severe plaque psoriasis[2-4]
  - Undergoing phase 3 trials for PsA, systemic lupus erythematosus, and Sjögren's syndrome
  - Deucravacitinib has a unique mechanism of action distinct from that of Janus kinase 1,2,3 inhibitors; it selectively binds the TYK2 regulatory domain, locking the enzyme in the inactive state
- In the pivotal phase 3, randomized, controlled POETYK PSO-1 and PSO-2 trials, significantly greater proportions of patients who received deucravacitinib achieved ≥75% reduction from baseline in Psoriasis Area and Severity Index (PASI 75) scores and static Physician Global Assessment (sPGA) scores of 0 (clear) or 1 (almost clear) at Week 16 vs placebo or apremilast[5,6]

Objective

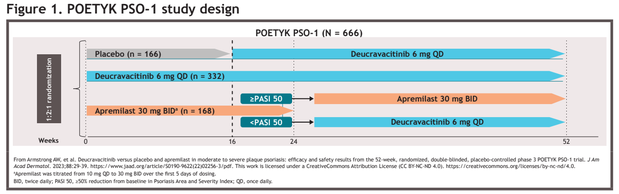
- To compare the effect of deucravacitinib vs placebo and vs apremilast on peripheral joint disease, joint pain, and health-related quality of life (HRQoL) using the 36-item Short Form Health Survey (SF-36) physical component summary (PCS) score at Weeks 16 and 24 in patients from the POETYK PSO-1 and PSO-2 trials who self-reported joint symptoms

Methods

Patients

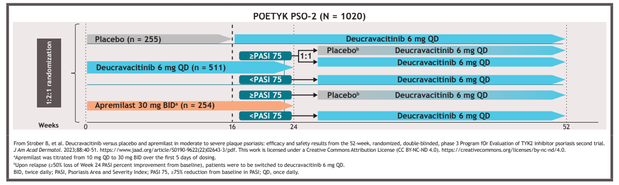
- In POETYK PSO-1 and PSO-2, eligible patients with moderate to severe psoriasis were randomized 1:2:1 to oral placebo, deucravacitinib 6 mg once daily, or apremilast 30 mg twice daily[5,6]
- Blinded treatment switches occurred at Weeks 16 and 24 (**Figure 1** and **Figure 2**)
  - Patients randomized to placebo crossed over to deucravacitinib at Week 16
  - Patients randomized to apremilast who failed to meet trial-specific efficacy thresholds switched to deucravacitinib at Week 24
- Patients with peripheral joint symptoms at baseline completed the self-administered Psoriatic Arthritis Screening and Evaluation (PASE) questionnaire
  - A score of ≥47 on a numeric rating scale has been shown to be associated with PsA vs non-PSA[7]

Figure 1. POETYK PSO-1 study design



From Armstrong AW, et al. Deucravacitinib versus placebo and apremilast in moderate to severe plaque psoriasis: efficacy and safety results from the 52-week, randomized, double-blinded, placebo-controlled phase 3 POETYK PSO-1 trial. *J Am Acad Dermatol*. 2023;88:29-39. https://www.jaad.org/article/S0190-9622(22)02236-3/pdf. This work is licensed under a CreativeCommons Attribution License (CC BY-NC-ND 4.0). https://creativecommons.org/licenses/by-nc-nd/4.0.
[a]Apremilast was titrated from 10 mg QD to 30 mg BID over the first 5 days of dosing.
BID, twice daily; PASI 50, ≥50% reduction from baseline in Psoriasis Area and Severity Index; QD, once daily.

Figure 2. POETYK PSO-2 study design



From Strober B, et al. Deucravacitinib versus placebo and apremilast in moderate to severe plaque psoriasis: efficacy and safety results from the 52-week, randomized, double-blinded, phase 3 Program fOr Evaluation of TYK2 inhibitor psoriasis second trial. *J Am Acad Dermatol*. 2023;88:40-51. https://www.jaad.org/article/S0190-9622(22)02643-3/pdf. This work is licensed under a Creative Commons Attribution License (CC BY-NC-ND 4.0). https://creativecommons.org/licenses/by-nc-nd/4.0.
[a]Apremilast was titrated from 10 mg QD to 30 mg BID over the first 5 days of dosing.
[b]Upon relapse (≥50% loss of Week 24 PASI percent improvement from baseline), patients were to be switched to deucravacitinib 6 mg QD.
BID, twice daily; PASI, Psoriasis Area and Severity Index; PASI 75, ≥75% reduction from baseline in PASI; QD, once daily.

Outcomes

- Peripheral joint pain and joint disease were measured using separate visual analog scales (VAS; range, 0-100; higher scores indicate greater disease burden)[8]
  - Patients were asked to mark on the scale the most joint pain experienced over the previous week and, on a separate scale, how much their joint disease affected them
- HRQoL was measured using SF-36 PCS (score range, 0-50; higher scores indicate better HRQoL)
  - Using a Likert-type scale, the SF-36 measures health dimensions, including limitations in physical activity, role limitations due to physical problems, bodily pain, vitality, general health, social functioning, role limitations due to mental problems, and mental health
- Mean improvement from baseline is reported
  - Treatment differences in proportions, 2-sided *P* values, and 95% confidence intervals (CI) for the treatment differences are reported

Results

- Of the 1686 patients included in the pooled POETYK PSO-1 and PSO-2 populations, this analysis comprised 185 (11%) patients with PASE scores ≥47 (**Table 1**)
- Among all patients with high PASE scores, systemic biologic use (66.7%) and mean PASI score at baseline (23.0) were higher vs the overall population in POETYK PSO-1 (38.9% systemic biologic use, 21.4 baseline PASI score) and POETYK PSO-2 (32.1% systemic biologic use, 21.0 baseline PASI score)

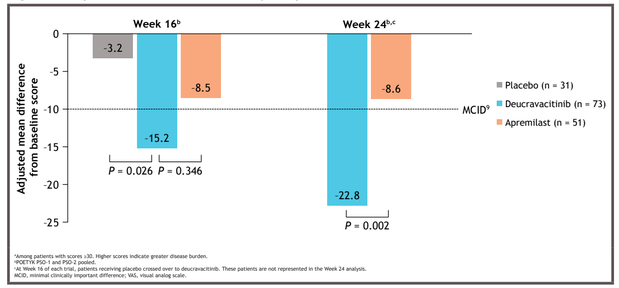
Table 1. Baseline patient demographics and clinical characteristics

Parameter	Placebo (n = 41)	Deucravacitinib (n = 88)	Apremilast (n = 56)
Age, mean, y	53.4	48.0	45.2
Female, n (%)	16 (39.0)	39 (44.3)	31 (55.4)
Body mass index, mean, kg/m²	32.1	33.0	32.9
White, n (%)	39 (95.1)	87 (98.9)	53 (94.6)
Duration of disease, mean, y	25.6	20.9	19.8
PASI score, mean	21.4	23.2	23.6
sPGA score, n (%)			
3 (moderate)	32 (78.0)	68 (77.3)	44 (78.6)
4 (severe)	9 (22.0)	20 (22.7)	12 (21.4)
Joint pain VAS score	71.6	67.4	69.8
Joint disease activity VAS score	64.6	67.3	67.8
SF-36 PCS score	38.3	39.5	38.3
Prior systemic therapy, n (%)	32 (78.0)	68 (77.3)	41 (73.2)
Prior systemic biologic use, n (%)	25 (78.1)	46 (67.6)	23 (56.1)

PASI, Psoriasis Area and Severity Index; SF-36 PCS, 36-Item Short Form Health Survey physical component summary; sPGA, static Physician Global Assessment; VAS, visual analog scale.

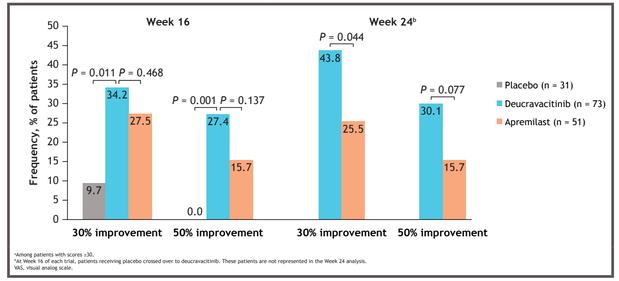
- Joint pain VAS
  - Adjusted mean improvements from baseline were significantly greater for deucravacitinib vs placebo at Week 16 (−15.2 vs −3.2) and vs apremilast at Week 24 (−22.8 vs −8.6) (**Figure 3**)
  - More patients randomized to deucravacitinib achieved 30% and 50% improvement in joint pain VAS at Weeks 16 and 24 vs apremilast (**Figure 4**)

Figure 3. Improvement from baseline in joint pain VAS score[a]



[a]Among patients with scores ≥30. Higher scores indicate greater disease burden.
[b]POETYK PSO-1 and PSO-2 pooled.
[c]At Week 16 of each trial, patients receiving placebo crossed over to deucravacitinib. These patients are not represented in the Week 24 analysis.
MCID, minimal clinically important difference; VAS, visual analog scale.

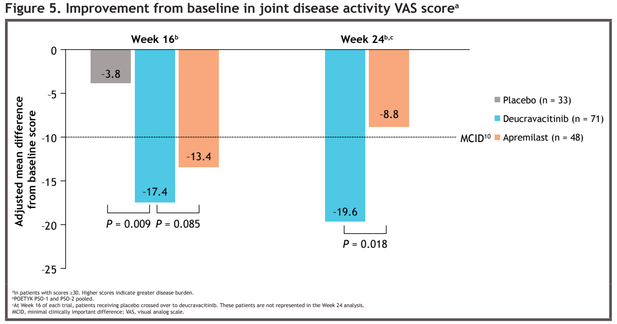
Figure 4. Proportion of patients achieving 30% and 50% improvement in joint pain VAS score[a]



[a]Among patients with scores ≥30.
[b]At Week 16 of each trial, patients receiving placebo crossed over to deucravacitinib. These patients are not represented in the Week 24 analysis.
VAS, visual analog scale.

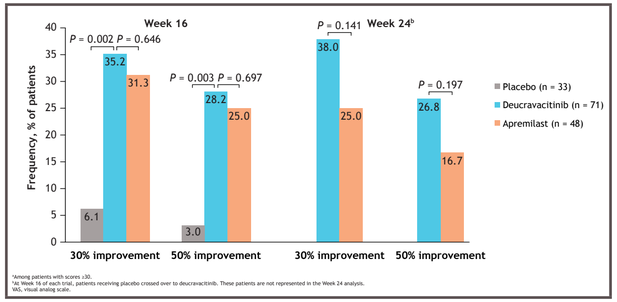
- Joint disease activity VAS
  - Adjusted mean improvements from baseline were significantly greater for deucravacitinib vs placebo at Week 16 (−17.4 vs −3.8) and vs apremilast at Week 24 (−19.6 vs −8.8) (**Figure 5**)
  - More patients randomized to deucravacitinib achieved 30% and 50% improvement in joint disease activity VAS at Weeks 16 and 24 vs apremilast (**Figure 6**)

Figure 5. Improvement from baseline in joint disease activity VAS score[a]



[a]In patients with scores ≥30. Higher scores indicate greater disease burden.
[b]POETYK PSO-1 and PSO-2 pooled.
[c]At Week 16 of each trial, patients receiving placebo crossed over to deucravacitinib. These patients are not represented in the Week 24 analysis.
MCID, minimal clinically important difference; VAS, visual analog scale.

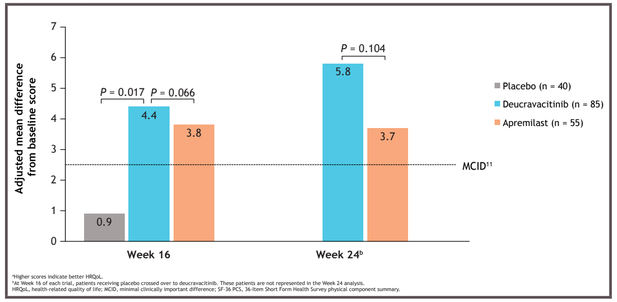
Figure 6. Proportion of patients achieving 30% and 50% improvement in joint disease activity VAS score[a]



[a]Among patients with scores ≥30.
[b]At Week 16 of each trial, patients receiving placebo crossed over to deucravacitinib. These patients are not represented in the Week 24 analysis.
VAS, visual analog scale.

- SF-36 PCS
  - Adjusted mean improvements from baseline were significantly greater for deucravacitinib vs placebo at Week 16 (4.4 vs 0.9) and were numerically greater vs apremilast at Week 24 (5.8 vs 3.7) (**Figure 7**)

Figure 7. Improvement from baseline in SF-36 PCS score[a]



[a]Higher scores indicate better HRQoL.
[b]At Week 16 of each trial, patients receiving placebo crossed over to deucravacitinib. These patients are not represented in the Week 24 analysis.
HRQoL, health-related quality of life; MCID, minimal clinically important difference; SF-36 PCS, 36-Item Short Form Health Survey physical component summary.

Conclusions

- In the POETYK PSO-1 and PSO-2 trials, patients with PASE scores ≥47 reported greater improvements in the impact of joint disease and joint pain with deucravacitinib vs placebo and vs apremilast; greater improvement in SF-36 PCS scores was observed at Week 16 with deucravacitinib vs placebo as well as numerically greater improvement vs apremilast at Week 24
  - The trial was not powered to demonstrate statistical significance in this subgroup; *P* values should be interpreted with caution owing to the small sample size
- Improvements in measures of joint disease and joint pain, as well as SF-36 PCS scores, continued through Week 24

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