Deucravacitinib, an oral, selective, allosteric tyrosine kinase 2 inhibitor, in moderate to severe plaque psoriasis: efficacy by baseline demographic and disease characteristics in the phase 3 POETYK PSO-1 and PSO-2 trials

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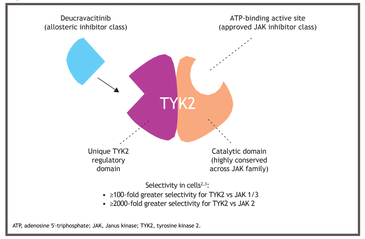
Introduction

- Deucravacitinib, an oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor, is approved in the US and other countries for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy[1]
- Deucravacitinib has a unique mechanism of action distinct from Janus kinase (JAK) 1/2/3 inhibitors[2] (**Figure 1**)
  - Binds to the TYK2 regulatory domain and inhibits TYK2 via an allosteric mechanism[2]
    - ≥100-fold greater selectivity for TYK2 vs JAK 1/3 and ≥2000-fold greater selectivity for TYK2 vs JAK 2 in cells[2,3]
  - Inhibits TYK2-mediated signaling of cytokines involved in psoriasis pathogenesis (eg, interleukin-23 and Type I interferons)[2]
- Deucravacitinib was significantly more efficacious than placebo or apremilast and was well tolerated in patients with moderate to severe plaque psoriasis in the 52-week, phase 3 POETYK PSO-1 (NCT03624127) and PSO-2 (NCT03611751) trials[4,5]

Figure 1. Mechanism of action of deucravacitinib



ATP, adenosine 5′-triphosphate; JAK, Janus kinase; TYK2, tyrosine kinase 2.

Objective

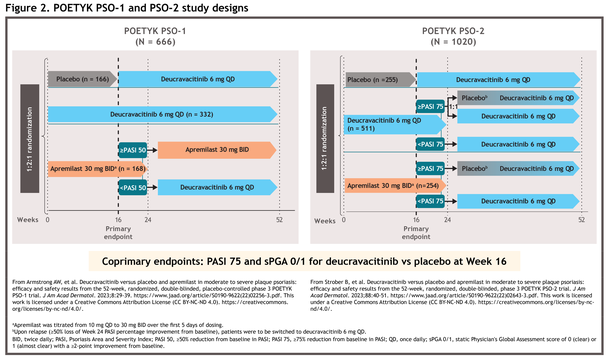
- The current pooled analyses of the POETYK PSO-1 and PSO-2 trials at Weeks 24 and 52 were performed to evaluate the efficacy of deucravacitinib across baseline patient demographics and disease characteristics

Methods

Study designs

- The study designs for POETYK PSO-1 and PSO-2 are summarized in **Figure 2**
- Key eligibility criteria included the following:
  - Age ≥18 years
  - Diagnosis of moderate to severe plaque psoriasis
    - Baseline Psoriasis Area and Severity Index (PASI) ≥12, static Physician's Global Assessment (sPGA) ≥3, and body surface area (BSA) involvement ≥10%
- Patient randomization was stratified by geographic region, body weight, and prior biologic use
- 92.5% of patients in POETYK PSO-1 and 89.4% in POETYK PSO-2 completed 16 weeks of deucravacitinib treatment vs 87.9% and 83.5%, respectively, for placebo and 86.3% and 85.4%, respectively, for apremilast
- All patients were eligible for a long-term extension trial after 52 weeks of treatment

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



Coprimary endpoints: PASI 75 and sPGA 0/1 for deucravacitinib vs placebo at Week 16

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)02256-3.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/.

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 POETYK PSO-2 trial. *J Am Acad Dermatol*. 2023;88:40-51. https://www.jaad.org/article/S0190-9622(22)02043-3.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 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; sPGA 0/1, static Physician's Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline.

Assessments and statistical analyses

- Data from subgroups with the following baseline patient demographics and disease characteristics in POETYK PSO-1 and PSO-2 were pooled and analyzed for the coprimary endpoints (≥75% reduction from baseline in PASI [PASI 75] and sPGA score of 0 [clear] and 1 [almost clear] with a ≥2-point improvement from baseline [sPGA 0/1]) and ≥90% reduction from baseline in PASI (PASI 90) vs apremilast at Week 24
  - Baseline patient demographics: age (<40 y, 40-65 y, ≥65 y); weight (<90 kg, ≥90 kg, body weight deciles); body mass index (BMI; <25 kg/m^2, 25-<30 kg/m^2, 30-<35 kg/m^2, ≥35 kg/m^2); sex; race (White, Asian)
    - Due to a low number of patients in these subgroups, Black or African American, or other races were not analyzed
  - Baseline disease characteristics: PASI (≤20, >20); sPGA score (3 [moderate], 4 [severe]); BSA involvement (10-20%, >20%)
- In patients who received continuous deucravacitinib treatment from Day 1, data were also analyzed at Week 52 (POETYK PSO-1)
- Differences between treatment groups were calculated using a stratified Cochran-Mantel-Haenszel test
- Missing data were imputed using nonresponder imputation

Results

Patients

- Baseline demographics and disease characteristics were largely similar across treatment groups in both trials (**Table 1**)

Table 1. Baseline patient demographics and disease characteristics

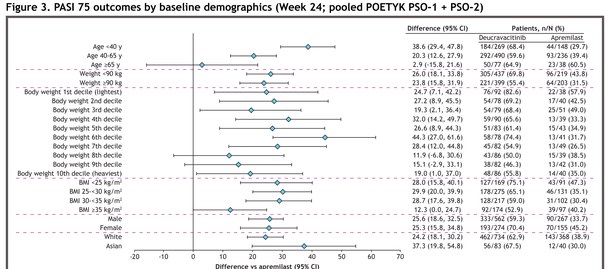
Parameter	Pooled POETYK PSO-1 and PSO-2			
	Placebo (n = 421)	Deucravacitinib (n = 843)	Apremilast (n = 422)	Total (N = 1686)
Age, mean (SD), y	47.5 (13.7)	46.5 (13.5)	45.7 (12.8)	46.6 (13.4)
<65 y, n (%)	370 (87.9)	763 (90.5)	384 (91.0)	1517 (90.0)
≥65 y, n (%)	51 (12.1)	80 (9.5)	38 (9.0)	169 (10.0)
Weight, mean (SD), kg	90.6 (21.1)	90.6 (21.9)	91.1 (22.0)	90.7 (21.7)
Female, n (%)	127 (30.2)	277 (32.9)	155 (36.7)	559 (33.2)
Race, n (%)				
White	360 (85.5)	741 (87.9)	368 (87.2)	1469 (87.1)
Asian	42 (10.0)	83 (9.8)	40 (9.5)	165 (9.8)
Black or African American	12 (2.9)	10 (1.2)	10 (2.4)	32 (1.9)
Other	7 (1.7)	9 (1.1)	4 (0.5)	20 (1.2)
Disease duration, mean (SD), y	18.9 (12.9)	18.6 (12.7)	18.5 (12.1)	18.6 (12.6)
Prior systemic treatment use, n (%)				
Biologic	146 (34.7)	295 (35.0)	145 (34.4)	586 (34.8)
No prior systemic therapy	173 (41.1)	369 (43.8)	173 (41.0)	715 (42.4)
PASI score, mean (SD)	20.9 (8.6)	21.1 (8.0)	21.6 (8.6)	21.2 (8.3)
≤20, n (%)	254 (60.3)	475 (56.3)	241 (57.1)	970 (57.5)
>20, n (%)	167 (39.7)	368 (43.7)	181 (42.9)	716 (42.5)
sPGA, n (%)				
3 (moderate)	345 (81.9)	665 (78.9)	335 (79.4)	1345 (79.8)
4 (severe)	75 (17.8)	178 (21.1)	87 (20.6)	340 (20.2)
BSA involvement, %, mean (SD)	25.3 (16.1)	26.4 (15.8)	27.6 (16.4)	26.4 (16.0)
BSA ≤20%, n (%)	226 (53.7)	421 (49.9)	200 (47.4)	847 (50.2)
BSA >20%, n (%)	195 (46.3)	422 (50.1)	222 (52.6)	839 (49.8)

BSA, body surface area; PASI, Psoriasis Area and Severity Index; SD, standard deviation; sPGA, static Physician's Global Assessment.

Efficacy

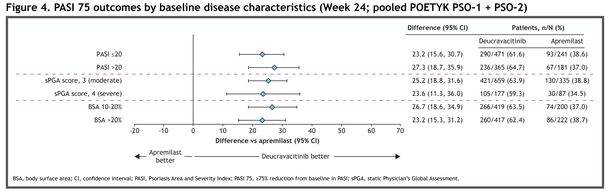
- Analyses of pooled data from POETYK PSO-1 and PSO-2 using PASI 75 (**Figure 3**; **Figure 4**), PASI 90 (**Figure 5**; **Figure 6**), and sPGA 0/1 (**Figure 7**; **Figure 8**) demonstrated a consistent treatment benefit of deucravacitinib (n = 843) vs apremilast (n = 422) across multiple baseline patient demographics and disease characteristics at Week 24
  - Deucravacitinib also demonstrated a consistent treatment benefit vs placebo and apremilast across these characteristics at Week 16[6,7]

Figure 3. PASI 75 outcomes by baseline demographics (Week 24; pooled POETYK PSO-1 + PSO-2)



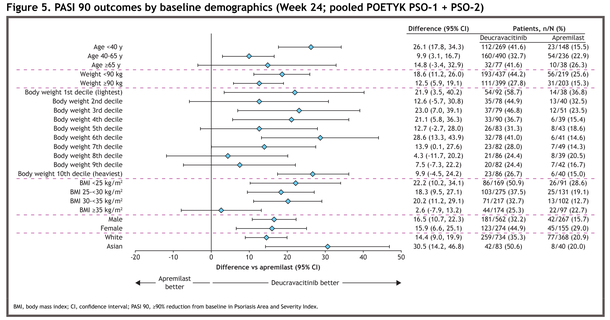
BMI, body mass index; CI, confidence interval; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index.

Figure 4. PASI 75 outcomes by baseline disease characteristics (Week 24; pooled POETYK PSO-1 + PSO-2)



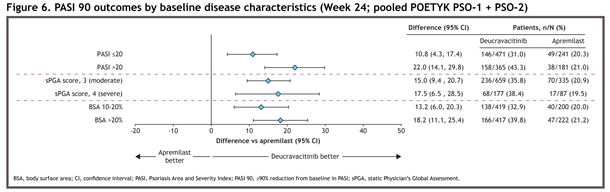
BSA, body surface area; CI, confidence interval; PASI, Psoriasis Area and Severity Index; PASI 75, ≥75% reduction from baseline in PASI; sPGA, static Physician's Global Assessment.

Figure 5. PASI 90 outcomes by baseline demographics (Week 24; pooled POETYK PSO-1 + PSO-2)



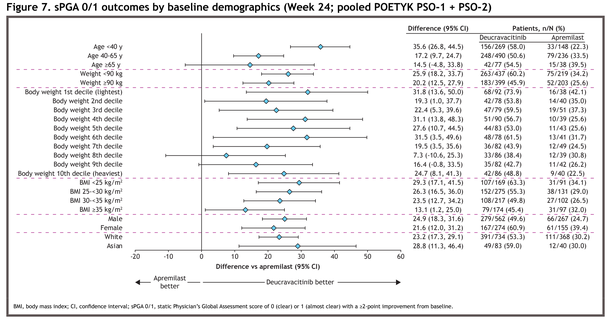
BMI, body mass index; CI, confidence interval; PASI 90, ≥90% reduction from baseline in Psoriasis Area and Severity Index.

Figure 6. PASI 90 outcomes by baseline disease characteristics (Week 24; pooled POETYK PSO-1 + PSO-2)



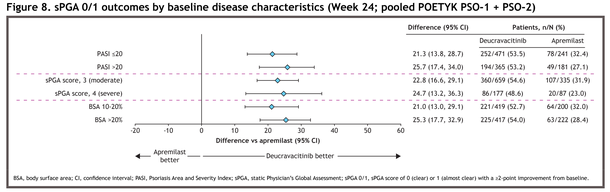
BSA, body surface area; CI, confidence interval; PASI, Psoriasis Area and Severity Index; PASI 90, ≥90% reduction from baseline in PASI; sPGA, static Physician's Global Assessment.

Figure 7. sPGA 0/1 outcomes by baseline demographics (Week 24; pooled POETYK PSO-1 + PSO-2)



BMI, body mass index; CI, confidence interval; sPGA 0/1, static Physician's Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline.

Figure 8. sPGA 0/1 outcomes by baseline disease characteristics (Week 24; pooled POETYK PSO-1 + PSO-2)



BSA, body surface area; CI, confidence interval; PASI, Psoriasis Area and Severity Index; sPGA, static Physician's Global Assessment; sPGA 0/1, sPGA score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline.

- Efficacy was observed through Week 52 in patients who received continuous deucravacitinib treatment in POETYK PSO-1 (n = 332), regardless of baseline demographics or disease severity (**Table 2**; **Table 3**)

Table 2. Week 52 outcomes by baseline demographics (POETYK PSO-1)

Parameter	PASI 75	PASI 90	sPGA 0/1
	Deucravacitinib, n/N (%) (n = 332)	Deucravacitinib, n/N (%) (n = 332)	Deucravacitinib, n/N (%) (n = 332)
Age, y			
<40	71/109 (65.1)	44/109 (40.4)	59/109 (54.1)
40-65	125/197 (63.5)	88/197 (44.7)	101/197 (51.3)
≥65	20/26 (76.9)	14/26 (53.8)	15/26 (57.7)
Weight, kg			
<90	146/200 (73.0)	103/200 (51.5)	121/200 (60.5)
≥90	70/132 (53.0)	43/132 (32.6)	54/132 (40.9)
Body weight categories, decile			
1st decile (lightest)	29/39 (74.4)	26/39 (66.7)	28/39 (71.8)
2nd decile	31/41 (75.6)	25/41 (61.0)	23/41 (56.1)
3rd decile	28/38 (73.7)	19/38 (50.0)	24/38 (63.2)
4th decile	31/41 (75.6)	19/41 (46.3)	22/41 (53.7)
5th decile	21/34 (61.8)	10/34 (29.4)	19/34 (55.9)
6th decile	20/25 (80.0)	14/25 (56.0)	19/25 (76.0)
7th decile	14/24 (58.3)	8/24 (33.3)	12/24 (50.0)
8th decile	14/32 (43.8)	10/32 (31.3)	9/32 (28.1)
9th decile	12/27 (44.4)	6/27 (22.2)	6/27 (22.2)
10th decile (heaviest)	16/31 (51.6)	9/31 (29.0)	13/31 (41.9)
BMI, kg/m^2			
<25	55/78 (70.5)	45/78 (57.7)	46/78 (59.0)
25-<30	89/123 (72.4)	56/123 (45.5)	74/123 (60.2)
30-<35	40/69 (58.0)	25/69 (36.2)	31/69 (44.9)
≥35	32/62 (51.6)	20/62 (32.3)	24/62 (38.7)
Sex			
Male	139/230 (60.4)	82/230 (35.7)	105/230 (45.7)
Female	77/102 (75.5)	64/102 (62.7)	70/102 (68.6)
Race			
White	168/267 (62.9)	115/267 (43.1)	141/267 (52.8)
Asian	45/59 (76.3)	31/59 (52.5)	33/59 (55.9)

BMI, body mass index; PASI 75/90, ≥75%/≥90% reduction from baseline in Psoriasis Area and Severity Index; sPGA 0/1, static Physician's Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline.

Table 3. Week 52 outcomes by baseline disease characteristics (POETYK PSO-1)

Parameter	PASI 75	PASI 90	sPGA 0/1
	Deucravacitinib, n/N (%) (n = 332)	Deucravacitinib, n/N (%) (n = 332)	Deucravacitinib, n/N (%) (n = 332)
PASI score			
≤20	109/177 (61.6)	69/177 (39.0)	85/177 (48.0)
>20	107/155 (69.0)	77/155 (49.7)	90/155 (58.1)
sPGA score			
3 (moderate)	166/257 (64.6)	107/257 (41.6)	137/257 (53.3)
4 (severe)	50/75 (66.7)	39/75 (52.0)	38/75 (50.7)
BSA involvement, %			
10-20%	102/162 (63.0)	61/162 (37.7)	82/162 (50.6)
>20%	114/170 (67.1)	85/170 (50.0)	93/170 (54.7)

BSA, body surface area; PASI, Psoriasis Area and Severity Index; PASI 75/90, ≥75%/≥90% reduction from baseline in PASI; sPGA, static Physician's Global Assessment; sPGA 0/1, sPGA score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline.

Conclusions

- Deucravacitinib is efficacious in adults with moderate to severe plaque psoriasis regardless of baseline patient demographics and disease characteristics
  - Deucravacitinib was more efficacious than apremilast across baseline subgroups at Week 24 in the pooled analysis of POETYK PSO-1 and PSO-2
  - Continuous deucravacitinib treatment was efficacious across baseline subgroups at Week 52 in POETYK PSO-1
- These findings further support deucravacitinib, a once-daily oral drug, as an efficacious therapeutic option for adults with moderate to severe plaque psoriasis regardless of baseline disease characteristics

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- **LS:** Consultant, paid investigator, and/or speaker: AbbVie, Amgen, Anacor, Ascend, Astellas, AstraZeneca, Blaze Bioscience, Boehringer Ingelheim, Botanix, Bristol Myers Squibb, Celgene, Dermira, Eli Lilly, Galderma, Genentech, GlaxoSmithKline, Hexima, Janssen, Leo Pharma, Mayne Pharma, Medimmune, Merck, Merck-Serono, Novartis, Otsuka, Pfizer, Phosphagenics, Photon MD, Regeneron, Roche, Samumed, Sanofi Genzyme, SHR, Sun Pharma ANZ, Trius, UCB, and Zai Lab
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