Deucravacitinib, an oral, selective, allosteric tyrosine kinase 2 inhibitor, in moderate to severe plaque psoriasis: efficacy by baseline body surface area (BSA) involvement and baseline Psoriasis Area and Severity Index (PASI)

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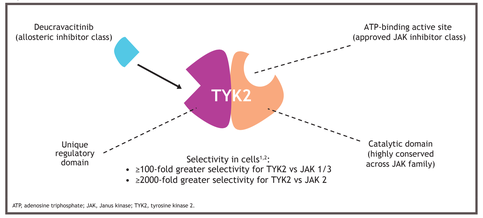
Introduction

- Tyrosine kinase 2 (TYK2) is an intracellular enzyme that mediates signaling of cytokines (interleukin-23 and Type I interferons) involved in psoriasis pathogenesis (**Figure 1**)[1,2]
- Deucravacitinib, an oral, selective, allosteric 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[3]

Figure 1. Mechanism of action of deucravacitinib



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

- In 2 pivotal, multinational phase 3 trials, POETYK PSO-1 (NCT03624127) and PSO-2 (NCT03611751), in patients with moderate to severe plaque psoriasis, deucravacitinib treatment was associated with:
  - Significantly greater response rates for ≥75% reduction from baseline in Psoriasis Area and Severity Index (PASI 75) and static Physician's Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline (sPGA 0/1) at Week 16 vs placebo and apremilast[4,5]
  - Maintenance of clinical efficacy was seen through Week 52 with continuous deucravacitinib treatment[6]

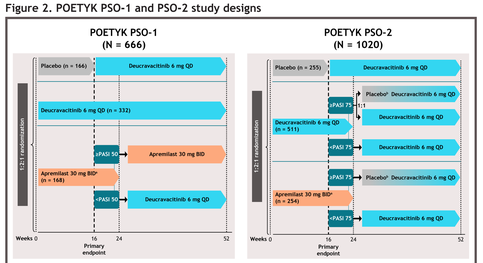
Objective

- To examine the efficacy of deucravacitinib in patients with moderate to severe plaque psoriasis based on baseline body surface area (BSA) involvement and PASI score

Methods

- Adult patients with moderate to severe plaque psoriasis (PASI ≥12, sPGA ≥3, BSA involvement ≥10%) were randomized 1:2:1 to placebo, oral deucravacitinib 6 mg once daily, or apremilast 30 mg twice daily (**Figure 2**)
- Blinded treatment switches occurred at Week 16 and Week 24
  - Patients randomized to placebo crossed over to deucravacitinib at Week 16
  - Patients randomized to apremilast who failed to meet trial-specific efficacy thresholds (≥50% reduction from baseline in PASI [PASI 50] in POETYK PSO-1; PASI 75 in POETYK PSO-2) switched to deucravacitinib at Week 24

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



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. 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. 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/.

*Apremilast was titrated from 10 mg QD to 30 mg BID over the first 5 days of dosing.
†Upon relapse (≥50% loss of Week 24 PASI percentage improvement from baselines), 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.

- Analysis populations:
  - Pooled POETYK PSO-1 and PSO-2: all patients treated with deucravacitinib or apremilast through Week 24 and patients treated with placebo through Week 16
  - Continuous deucravacitinib treatment from baseline: patients in the POETYK PSO-1 trial who received continuous deucravacitinib from Day 1 through Week 52
  - Placebo crossovers: patients in the POETYK PSO-1 trial who crossed over to deucravacitinib treatment at Week 16 through Week 52
- Efficacy was assessed using the achievement of PASI 75 and sPGA 0/1 in the following subgroups using nonresponder imputation (NRI):
  - Baseline BSA involvement: 10%-<15%, 15%-<20%, 20%-<30%, ≥30%
  - Baseline PASI score: 12-<15, ≥15
- Analyses were descriptive; no statistical analyses were performed

Results

Baseline demographics

- Baseline patient demographics were largely comparable across treatment groups and BSA/PASI subgroups in the pooled populations of both trials (**Table 1**) and in the POETYK PSO-1 population alone (**Table 2**)

Table 1. Baseline demographics by baseline BSA involvement and PASI score in the pooled POETYK PSO-1 and PSO-2 population

	Baseline BSA involvement												Baseline PASI score					
	10%-<15%			15%-<20%			20%-<30%			≥30%			12-<15			≥15		
Parameters	Placebo (n = 105)	Deucravacitinib (n = 194)	Apremilast (n = 92)	Placebo (n = 104)	Deucravacitinib (n = 183)	Apremilast (n = 84)	Placebo (n = 92)	Deucravacitinib (n = 198)	Apremilast (n = 101)	Placebo (n = 120)	Deucravacitinib (n = 268)	Apremilast (n = 145)	Placebo (n = 110)	Deucravacitinib (n = 183)	Apremilast (n = 94)	Placebo (n = 310)	Deucravacitinib (n = 660)	Apremilast (n = 328)
Age, mean (SD), y	48.4 (13.8)	46.9 (14.4)	47.0 (12.0)	47.2 (14.5)	47.2 (12.8)	45.5 (12.3)	48.7 (14.0)	45.6 (13.5)	45.2 (13.0)	46.2 (12.8)	46.4 (13.4)	45.5 (13.6)	47.3 (14.4)	47.2 (13.1)	44.9 (12.0)	47.7 (13.5)	46.3 (13.6)	46.0 (13.1)
Weight, mean (SD), kg	88.5 (19.8)	88.7 (22.9)	88.9 (19.1)	89.2 (20.9)	91.1 (22.1)	88.5 (17.7)	92.9 (20.7)	91.9 (22.2)	89.0 (21.7)	91.8 (22.6)	90.5 (20.9)	95.4 (25.3)	91.8 (19.9)	87.0 (21.9)	90.1 (21.4)	90.2 (21.5)	91.5 (21.8)	91.4 (22.1)
BMI, mean (SD), kg/m²	29.7 (6.4)	30.1 (7.0)	30.1 (6.3)	30.1 (6.1)	30.4 (7.2)	30.1 (5.9)	31.3 (6.7)	31.1 (6.9)	30.1 (6.9)	30.3 (7.5)	30.4 (6.6)	32.1 (8.1)	30.5 (6.4)	29.7 (7.3)	30.9 (6.9)	30.3 (6.9)	30.8 (6.7)	30.8 (7.1)
Female, n (%)	38 (36.2)	72 (37.1)	40 (43.5)	34 (32.7)	59 (32.2)	32 (38.1)	30 (32.6)	72 (36.4)	34 (33.7)	25 (20.8)	74 (27.6)	49 (33.8)	34 (30.9)	69 (37.7)	43 (45.7)	93 (30.0)	208 (31.5)	112 (34.1)
Race, n (%)																		
White	87 (82.9)	173 (89.2)	80 (87.0)	92 (88.5)	164 (89.6)	75 (89.3)	82 (89.1)	165 (83.3)	86 (85.1)	99 (82.5)	239 (89.2)	127 (87.6)	97 (88.2)	161 (88.0)	78 (83.0)	263 (84.8)	580 (87.9)	290 (88.4)
Asian	10 (9.5)	17 (8.8)	11 (12.0)	8 (7.7)	15 (8.2)	4 (4.8)	6 (6.5)	26 (13.1)	12 (11.9)	18 (15.0)	25 (9.3)	13 (9.0)	8 (7.3)	19 (10.4)	15 (16.0)	33 (10.6)	64 (9.7)	25 (7.6)
Other	8 (7.6)	4 (2.1)	1 (1.1)	4 (3.8)	4 (2.2)	5 (6.0)	4 (4.3)	7 (3.5)	3 (3.0)	3 (2.5)	4 (1.5)	5 (3.4)	5 (4.5)	3 (1.6)	1 (1.1)	14 (4.5)	16 (2.4)	13 (4.0)

BMI, body mass index; BSA, body surface area; PASI, Psoriasis Area and Severity Index; SD, standard deviation.

Table 2. Baseline demographics by baseline BSA involvement and PASI score in the POETYK PSO-1 population

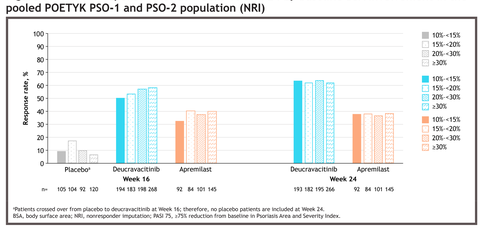
	Baseline BSA involvement								Baseline PASI score			
	10%-<15%		15%-<20%		20%-<30%		≥30%		12-<15		≥15	
Parameters	Placebo-Deucravacitinib (n = 36)	Deucravacitinib (n = 61)	Placebo-Deucravacitinib (n = 36)	Deucravacitinib (n = 73)	Placebo-Deucravacitinib (n = 20)	Deucravacitinib (n = 70)	Placebo-Deucravacitinib (n = 48)	Deucravacitinib (n = 98)	Placebo-Deucravacitinib (n = 40)	Deucravacitinib (n = 64)	Placebo-Deucravacitinib (n = 100)	Deucravacitinib (n = 238)
Age, mean (SD), y	48.0 (14.0)	46.6 (15.1)	51.3 (14.5)	47.6 (13.9)	50.2 (16.3)	43 (13.6)	43.5 (11.9)	46.8 (13.0)	46.3 (14.6)	46.7 (13.4)	48.2 (13.9)	45.9 (14.0)
Weight, mean (SD), kg	89.9 (19.5)	88.2 (22.3)	89.2 (22.4)	88.5 (23.0)	88.8 (22.3)	85.8 (22.4)	86.7 (24.9)	86.9 (20.9)	91.9 (20.5)	84.3 (20.6)	87.1 (23.0)	88.1 (22.3)
BMI, mean (SD), kg/m²	30.1 (6.2)	30.0 (7.1)	30.4 (6.6)	30.1 (8.1)	30.6 (7.8)	29.5 (7.5)	29.2 (8.1)	29.3 (6.0)	30.2 (6.4)	29.3 (8.0)	29.8 (7.5)	29.8 (6.8)
Female, n (%)	12 (33.3)	25 (41.0)	11 (30.6)	24 (32.9)	11 (55.0)	24 (34.3)	12 (25.0)	24 (24.5)	12 (30.0)	27 (42.2)	34 (34.0)	70 (29.4)
Race, n (%)												
White	31 (86.1)	52 (85.2)	28 (77.8)	61 (83.6)	16 (80.0)	50 (71.4)	33 (68.8)	79 (80.6)	34 (85.0)	52 (81.3)	74 (74.0)	190 (79.8)
Asian	5 (13.9)	8 (13.1)	6 (16.7)	11 (15.1)	4 (20.0)	18 (25.7)	14 (29.2)	18 (18.4)	5 (12.5)	12 (18.8)	24 (24.0)	43 (18.1)
Other	0	1 (1.6)	2 (5.6)	1 (1.4)	0	2 (2.9)	1 (2.1)	1 (1.0)	1 (2.5)	0	2 (2.0)	5 (2.1)

BMI, body mass index; BSA, body surface area; PASI, Psoriasis Area and Severity Index; SD, standard deviation.

Efficacy: Pooled POETYK PSO-1/PSO-2 population

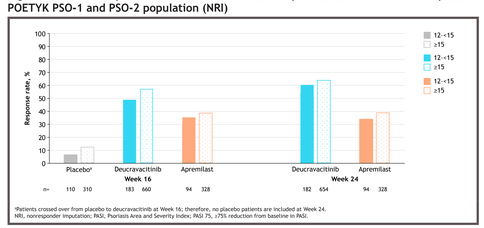
- PASI 75 and sPGA 0/1 response rates were similar across baseline BSA involvement and PASI score subgroups, regardless of treatment type (**Figures 3-6**)
- Patients treated with deucravacitinib achieved numerically higher PASI 75 and sPGA 0/1 vs patients treated with placebo or apremilast at Week 16 and vs apremilast at Week 24, regardless of baseline BSA involvement or PASI score

Figure 3. PASI 75 response rates at Weeks 16 and 24 by baseline BSA involvement in the pooled POETYK PSO-1 and PSO-2 population (NRI)



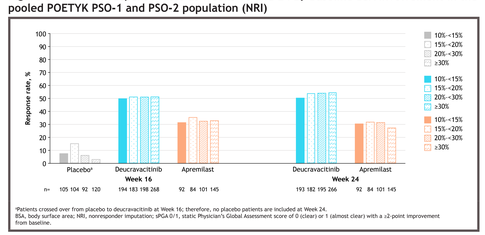
*Patients crossed over from placebo to deucravacitinib at Week 16; therefore, no placebo patients are included at Week 24.
BSA, body surface area; NRI, nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index.

Figure 4. PASI 75 response rates at Weeks 16 and 24 by baseline PASI score in the pooled POETYK PSO-1 and PSO-2 population (NRI)



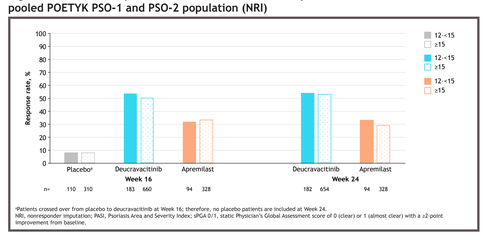
*Patients crossed over from placebo to deucravacitinib at Week 16; therefore, no placebo patients are included at Week 24.
NRI, nonresponder imputation; PASI, Psoriasis Area and Severity Index; PASI 75, ≥75% reduction from baseline in PASI.

Figure 5. sPGA 0/1 response rates at Weeks 16 and 24 by baseline BSA involvement in the pooled POETYK PSO-1 and PSO-2 population (NRI)



*Patients crossed over from placebo to deucravacitinib at Week 16; therefore, no placebo patients are included at Week 24.
BSA, body surface area; NRI, nonresponder imputation; sPGA 0/1, static Physician's Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline.

Figure 6. sPGA 0/1 response rates at Weeks 16 and 24 by baseline PASI score in the pooled POETYK PSO-1 and PSO-2 population (NRI)

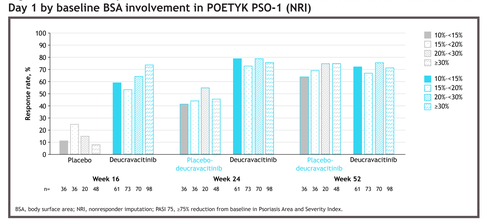


*Patients crossed over from placebo to deucravacitinib at Week 16; therefore, no placebo patients are included at Week 24.
NRI, nonresponder imputation; PASI, Psoriasis Area and Severity Index; sPGA 0/1, static Physician's Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline.

Efficacy: POETYK PSO-1 population

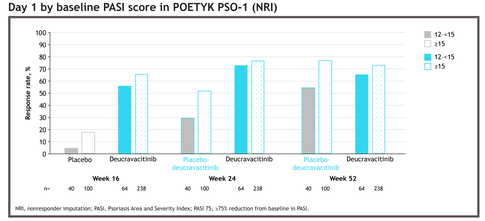
- PASI 75 and sPGA 0/1 response rates were similar across baseline BSA involvement and PASI score subgroups at Weeks 16, 24, and 52 in patients treated with continuous deucravacitinib from Day 1 (**Figures 7-10**)
- By Week 52, patients who crossed over from placebo to deucravacitinib at Week 16 achieved results similar to patients treated continuously with deucravacitinib from Day 1, regardless of baseline BSA involvement or PASI score subgroup

Figure 7. PASI 75 response rates at Weeks 16, 24, and 52 with continuous treatment from Day 1 by baseline BSA involvement in POETYK PSO-1 (NRI)



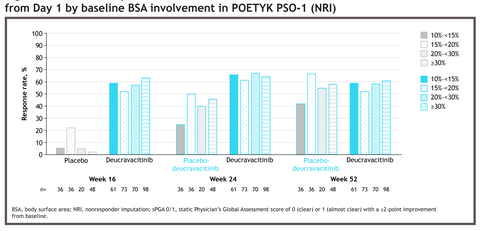
BSA, body surface area; NRI, nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index.

Figure 8. PASI 75 response rates at Weeks 16, 24, and 52 with continuous treatment from Day 1 by baseline PASI score in POETYK PSO-1 (NRI)



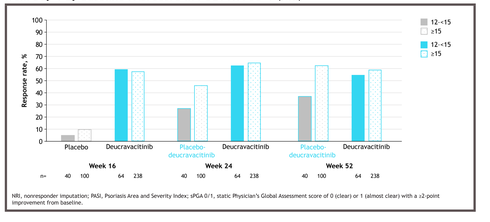
NRI, nonresponder imputation; PASI, Psoriasis Area and Severity Index; PASI 75, ≥75% reduction from baseline in PASI.

Figure 9. sPGA 0/1 response rates at Weeks 16, 24, and 52 with continuous treatment from Day 1 by baseline BSA involvement in POETYK PSO-1 (NRI)



BSA, body surface area; NRI, nonresponder imputation; sPGA 0/1, static Physician's Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline.

Figure 10. sPGA 0/1 response rates at Weeks 16, 24, and 52 with continuous treatment from Day 1 by baseline PASI score in POETYK PSO-1 (NRI)



NRI, nonresponder imputation; PASI, 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.

Conclusions

- Deucravacitinib improved PASI 75 and sPGA 0/1 responses to a similar extent regardless of baseline BSA involvement or PASI score
- Improved efficacy responses were seen by Week 16 with deucravacitinib treatment vs placebo or apremilast
- Responses with deucravacitinib were overall numerically higher at Week 24 vs Week 16
- Responses were maintained through Week 52 in patients receiving continuous deucravacitinib from Day 1 and improved in patients receiving placebo who crossed over to deucravacitinib at Week 16

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