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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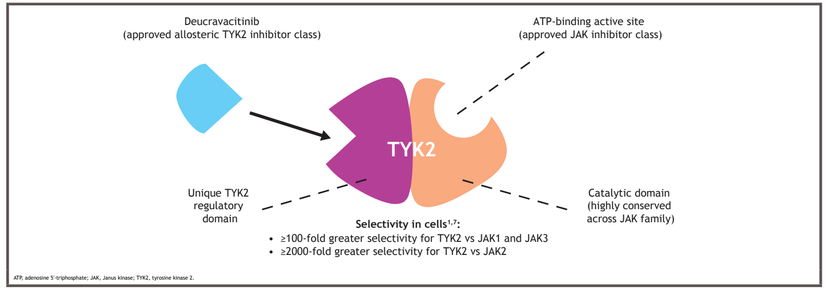
Synopsis

- Tyrosine kinase 2 (TYK2) is an intracellular enzyme that mediates signaling of cytokines (eg, interleukin-23, Type I interferons) that are involved in psoriasis pathogenesis[1]
- Deucravacitinib, an oral, selective, allosteric TYK2 inhibitor, is approved in the US, EU, and other countries for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy[2-6]
- Deucravacitinib uniquely binds to the regulatory domain of TYK2 rather than to the catalytic domain where Janus kinase (JAK) 1,2,3 inhibitors bind[1,7] (**Figure 1**), representing the first in a new class of small molecules
- Deucravacitinib was superior to placebo and apremilast in the global, 52-week, phase 3 POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751) trials in moderate to severe plaque psoriasis[8,9]

Figure 1. Mechanism of action of deucravacitinib



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

Objective

- To evaluate deucravacitinib efficacy by two measures of disease severity at baseline, body surface area (BSA) involvement and Psoriasis Area and Severity Index (PASI) scores

Methods

Study design

- In POETYK PSO-1 and PSO-2, adults with moderate to severe plaque psoriasis (BSA involvement ≥10%; PASI ≥12; static Physician Global Assessment [sPGA] ≥3) were randomized 1:2:1 to oral placebo, deucravacitinib 6 mg once daily, or apremilast 30 mg twice daily[8,9]
- Patients randomized to placebo crossed over to deucravacitinib at Week 16
- Patients randomized to deucravacitinib continued treatment through Week 52
  - Coprimary endpoints were achievement of ≥75% reduction from baseline in PASI (PASI 75) and an sPGA score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline (sPGA 0/1) at Week 16

Analysis populations

- Pooled POETYK PSO-1 and PSO-2
  - All patients treated with deucravacitinib through Week 24 and patients receiving placebo through Week 16
  - Efficacy was evaluated in the pooled population only until Week 24 because of differences in the POETYK PSO-1 and PSO-2 study designs after Week 24
- POETYK PSO-1
  - Continuous deucravacitinib treatment from baseline: patients who received continuous deucravacitinib from Day 1 through Week 52
  - Placebo crossovers: patients receiving placebo who crossed over to deucravacitinib treatment at Week 16 and were treated through Week 52

Efficacy outcomes

- Efficacy was assessed based on achievement of PASI 75, ≥90% reduction from baseline in PASI (PASI 90), 100% reduction from baseline in PASI (PASI 100), sPGA 0/1, and sPGA 0 in the following subgroups:
  - Baseline BSA involvement: 10%-<15%, 15%-<20%, 20%-<30%, ≥30%
  - Baseline PASI score: 12-<15, ≥15
- Nonresponder imputation was used to impute missing data
  - Patients who discontinued treatment prior to Week 16 or have missing Week 16 data for any reason were considered nonresponders

Results

Baseline patient demographics

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

Table 1. Baseline patient 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)	Placebo (n = 104)	Deucravacitinib (n = 183)	Placebo (n = 92)	Deucravacitinib (n = 198)	Placebo (n = 120)	Deucravacitinib (n = 268)	Placebo (n = 110)	Deucravacitinib (n = 183)	Placebo (n = 310)	Deucravacitinib (n = 660)
Age, mean (SD), y	48.4 (13.8)	46.9 (14.4)	47.2 (14.5)	47.2 (12.8)	48.7 (14.0)	45.6 (13.5)	46.2 (12.8)	46.4 (13.4)	47.3 (14.4)	47.2 (13.1)	47.7 (13.5)	46.3 (13.6)
Weight, mean (SD), kg	88.5 (19.8)	88.7 (22.9)	89.2 (20.9)	91.1 (22.1)	92.9 (20.7)	91.9 (22.2)	91.8 (22.6)	90.5 (20.9)	91.8 (19.9)	87.0 (21.9)	90.2 (21.5)	91.5 (21.8)
Body mass index, mean (SD), kg/m²	29.7 (6.4)	30.1 (7.1)	30.1 (6.1)	30.4 (7.2)	31.3 (6.7)	31.1 (6.9)	30.3 (7.5)	30.4 (6.6)	30.5 (6.4)	29.7 (7.3)	30.3 (6.9)	30.8 (6.8)
Female, n (%)	38 (36.2)	72 (37.1)	34 (32.7)	59 (32.2)	30 (32.6)	72 (36.4)	25 (20.8)	74 (27.6)	34 (30.9)	69 (37.7)	93 (30.0)	208 (31.5)
Race, n (%)												
White	87 (82.9)	173 (89.2)	92 (88.5)	164 (89.6)	82 (89.1)	165 (83.3)	99 (82.5)	239 (89.2)	97 (88.2)	161 (88.0)	263 (84.8)	580 (87.9)
Asian	10 (9.5)	17 (8.8)	8 (7.7)	15 (8.2)	6 (6.5)	26 (13.1)	18 (15.0)	25 (9.3)	8 (7.3)	19 (10.4)	33 (10.6)	64 (9.7)
Other	8 (7.6)	4 (2.1)	4 (3.9)	4 (2.2)	4 (4.3)	7 (3.5)	3 (2.5)	4 (1.5)	5 (4.5)	3 (1.6)	14 (4.5)	16 (2.4)

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

Table 2. Baseline patient demographics by baseline BSA involvement and PASI score in the POETYK PSO-1 population treated with continuous deucravacitinib

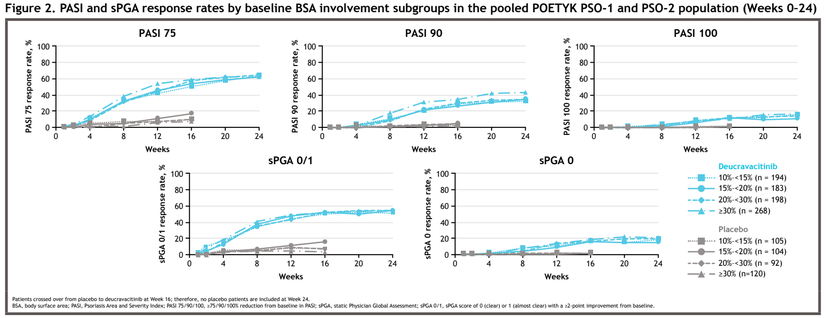
	Baseline BSA involvement				Baseline PASI score	
	10%-<15%	15%-<20%	20%-<30%	≥30%	12-<15	≥15
Parameters	Deucravacitinib (n = 61)	Deucravacitinib (n = 73)	Deucravacitinib (n = 70)	Deucravacitinib (n = 98)	Deucravacitinib (n = 64)	Deucravacitinib (n = 238)
Age, mean (SD), y	46.6 (15.1)	47.6 (13.9)	43 (13.6)	46.8 (13.0)	46.7 (13.4)	45.9 (14.0)
Weight, mean (SD), kg	88.2 (22.3)	88.5 (23.0)	85.8 (22.4)	86.9 (20.9)	84.3 (20.6)	88.1 (22.3)
Body mass index, mean (SD), kg/m²	30.0 (7.1)	30.1 (8.1)	29.5 (7.5)	29.3 (6.0)	29.3 (8.0)	29.8 (6.8)
Female, n (%)	25 (41.0)	24 (32.9)	24 (34.3)	24 (24.5)	27 (42.2)	70 (29.4)
Race, n (%)						
White	52 (85.2)	61 (83.6)	50 (71.4)	79 (80.6)	52 (81.3)	190 (79.8)
Asian	8 (13.1)	11 (15.1)	18 (25.7)	18 (18.4)	12 (18.8)	43 (18.1)
Other	1 (1.6)	1 (1.4)	2 (2.9)	1 (1.0)	0	5 (2.1)

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

Efficacy: pooled POETYK PSO-1 and PSO-2 population

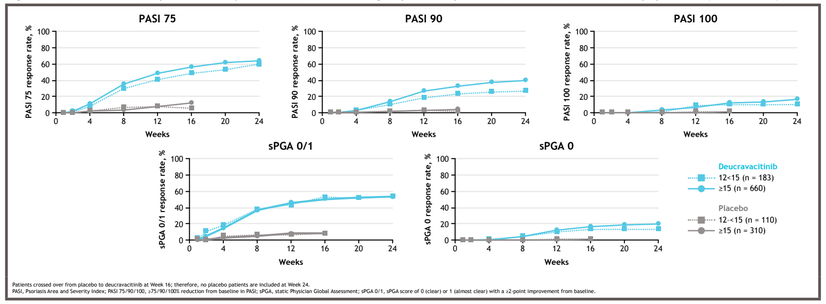
- Patients treated with deucravacitinib achieved numerically higher response rates vs patients receiving placebo at Week 16 regardless of the extent of baseline BSA involvement or PASI score
- PASI 75, PASI 90, PASI 100, sPGA 0/1, and sPGA 0 response rates were similar overall in the different subgroups, with minor numerical differences observed across baseline BSA involvement and PASI score subgroups in each treatment arm through Week 24 (**Figure 2** and **Figure 3**)

Figure 2. PASI and sPGA response rates by baseline BSA involvement subgroups in the pooled POETYK PSO-1 and PSO-2 population (Weeks 0-24)



Patients crossed over from placebo to deucravacitinib at Week 16; therefore, no placebo patients are included at Week 24.
BSA, body surface area; PASI, Psoriasis Area and Severity Index; PASI 75/90/100, ≥75/90/100% reduction from baseline in PASI; sPGA, static Physician Global Assessment; sPGA 0/1, sPGA score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline.

Figure 3. PASI and sPGA response rates by baseline PASI score subgroups in the pooled POETYK PSO-1 and PSO-2 population (Weeks 0-24)

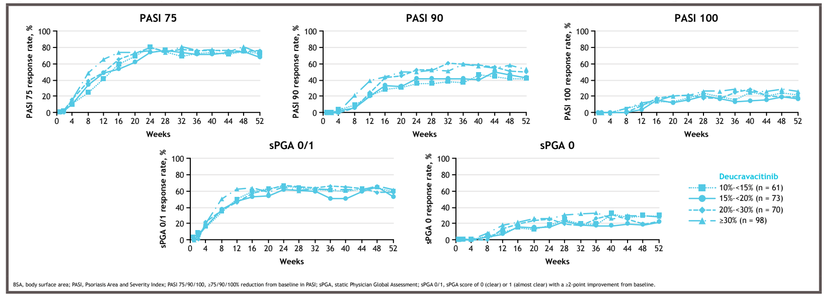


Patients crossed over from placebo to deucravacitinib at Week 16; therefore, no placebo patients are included at Week 24.
PASI, Psoriasis Area and Severity Index; PASI 75/90/100, ≥75/90/100% reduction from baseline in PASI; sPGA, static Physician Global Assessment; sPGA 0/1, sPGA score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline.

Efficacy: POETYK PSO-1 population

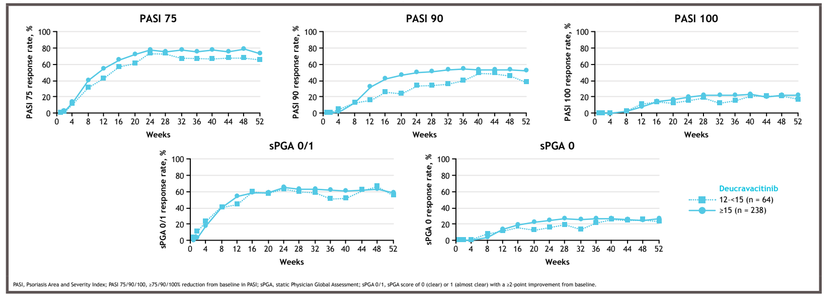
- PASI 75, PASI 90, PASI 100, sPGA 0/1, and sPGA 0 response rates were similar across baseline BSA involvement and PASI score subgroups through Week 52 in patients receiving continuous deucravacitinib treatment from Day 1 (**Figure 4** and **Figure 5**)

Figure 4. PASI and sPGA response rates by baseline BSA involvement subgroups in the POETYK PSO-1 population through Week 52



BSA, body surface area; PASI, Psoriasis Area and Severity Index; PASI 75/90/100, ≥75/90/100% reduction from baseline in PASI; sPGA, static Physician Global Assessment; sPGA 0/1, sPGA score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline.

Figure 5. PASI and sPGA response rates by baseline PASI score subgroups in the POETYK PSO-1 population through Week 52



PASI, Psoriasis Area and Severity Index; PASI 75/90/100, ≥75/90/100% reduction from baseline in PASI; sPGA, static Physician Global Assessment; sPGA 0/1, sPGA score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline.

Conclusions

- Deucravacitinib treatment improved PASI 75/90/100, sPGA 0/1, and sPGA 0 response rates to a comparable extent regardless of baseline BSA involvement or PASI scores in patients in the POETYK PSO-1 and PSO-2 trials
  - Improved efficacy responses were observed at Week 16 with deucravacitinib treatment vs placebo
  - Efficacy responses with deucravacitinib improved from Week 16 to Week 24
  - Efficacy responses were maintained through Week 52 in patients receiving continuous deucravacitinib treatment from baseline (Day 1)

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