Deucravacitinib in moderate plaque psoriasis: efficacy in the phase 3 POETYK PSO-1 and PSO-2 trials

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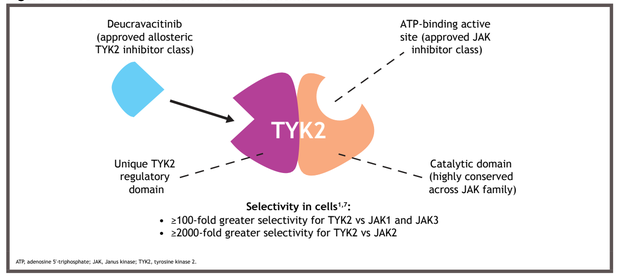
Synopsis

- Tyrosine kinase 2 (TYK2) is an intracellular enzyme that mediates signaling of cytokines (eg, interleukin [IL]-23, IL-12, and Type I interferons [IFNs])[1]
  - IL-23 and Type I IFNs 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 the catalytic domain where Janus kinase (JAK) 1,2,3 inhibitors bind[1,7] (**Figure 1**), driving its selectivity and representing the first in a new class of oral drugs

Figure 1. Mechanism of action of deucravacitinib



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

- Deucravacitinib demonstrated a robust efficacy profile in the global phase 3 POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751) trials in adults with moderate to severe plaque psoriasis[8-10]
  - Deucravacitinib was superior to placebo and apremilast at Week 16 and to apremilast at Week 24 and showed maintenance of response through Week 52
  - Deucravacitinib was well tolerated with a low rate of discontinuations due to adverse events[8,9]
- However, the efficacy of deucravacitinib has not been exclusively studied in patients in POETYK PSO-1 and PSO-2 who met the criteria for plaque psoriasis of moderate severity
- In the real-world setting, up to 36% of patients with plaque psoriasis of moderate severity are undertreated with conventional systemic therapies, which may lead to unsatisfactory skin clearance in these patients[11-14]

Objectives

- This analysis evaluated the clinical efficacy of deucravacitinib 6 mg once daily (QD) through Week 52 in patients with plaque psoriasis of moderate severity at baseline in both trials

Methods

POETYK PSO-1 and PSO-2 study designs

- Adults with moderate to severe plaque psoriasis (Psoriasis Area and Severity Index [PASI] ≥12, static Physician Global Assessment [sPGA] ≥3, and body surface area [BSA] involvement ≥10% at baseline) were randomized
- Patients were stratified by geographic region, body weight, and prior biologic use
- Any patients receiving placebo crossed over to deucravacitinib at Week 16
- Patients randomized to deucravacitinib continued treatment through Week 52 without change in POETYK PSO-1
- Coprimary endpoints were the proportion of patients who achieved ≥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) vs placebo at Week 16
- In this analysis, data from the subgroup of deucravacitinib-treated patients meeting criteria for plaque psoriasis of moderate severity (defined as an sPGA of 3 and BSA involvement of 10%–≤15%)[14] at baseline were evaluated for efficacy vs placebo in the following treatment arms:
  - Deucravacitinib through Week 24 and placebo through Week 16 in the POETYK PSO-1 and PSO-2 trials (pooled data)
  - Deucravacitinib through Week 52 in the POETYK PSO-1 trial
  - Placebo to deucravacitinib crossovers through Week 52 in the POETYK PSO-1 trial
- Efficacy evaluations were based on the following outcomes:
  - PASI 75
  - ≥90% reduction from baseline in PASI (PASI 90)
  - Change from baseline PASI
  - sPGA 0/1

Statistical analysis

- Descriptive statistics were used to summarize data; means and standard deviations (SDs) are presented for continuous variables and frequency counts and percentages are presented for categorical variables
- Missing responder data were imputed with nonresponder imputation (NRI), and missing change from baseline data were imputed with modified baseline observation carried forward (mBOCF)

Results

- Baseline demographics and disease characteristics of patients with moderate psoriasis were generally similar across treatment groups in the moderate psoriasis subgroup and the entire study population with moderate to severe psoriasis (**Table 1**)

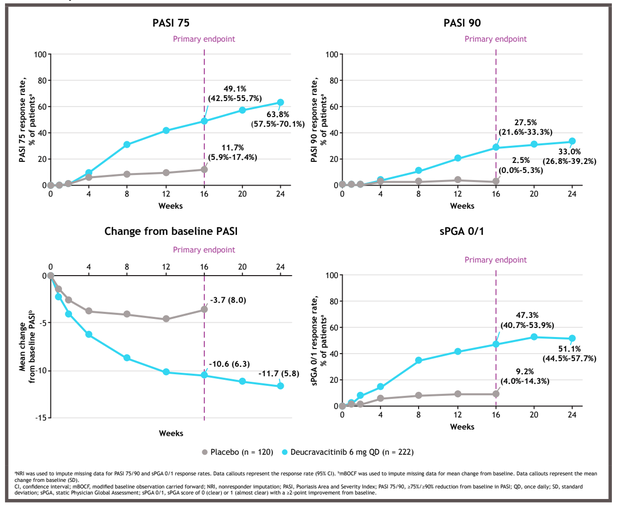
Table 1. Baseline demographics and disease characteristics in patients with moderate psoriasis

Parameter	Pooled POETYK PSO-1 and PSO-2			POETYK PSO-1		
	Moderate psoriasis		Moderate to severe psoriasis	Moderate psoriasis		Moderate to severe psoriasis
	Placebo (n = 120)	Deucravacitinib (n = 222)	Total (N = 1686[a])	Continuous deucravacitinib (n = 74)	Placebo to deucravacitinib (n = 43)	Total (N = 666[a])
Age, mean (SD), y	48.5 (14.0)	47.9 (14.2)	46.6 (13.4)	49.1 (15.1)	48.2 (13.7)	46.1 (13.4)
Weight, mean (SD), kg	88.5 (20.0)	87.5 (22.9)	90.7 (21.7)	88.0 (23.2)	88.1 (19.9)	88.1 (21.7)
Female, n (%)	46 (38.3)	78 (35.1)	559 (33.2)	30 (40.5)	17 (39.5)	213 (32.0)
Race, n (%)						
White	101 (84.2)	199 (89.6)	1469 (87.1)	64 (86.5)	36 (83.7)	534 (80.2)
Asian	10 (8.3)	19 (8.6)	165 (9.8)	10 (13.5)	5 (11.6)	121 (18.2)
Black or African American	6 (5.0)	2 (0.9)	32 (1.9)	0	1 (2.3)	6 (0.9)
Other	3 (2.5)	2 (0.9)	20 (1.2)	0	1 (2.3)	5 (0.8)
Age at disease onset, mean (SD), y	31.5 (14.7)[c]	29.7 (16.2)	28.8 (14.9)	33.6 (17.4)	31.3 (15.4)	29.6 (14.6)
Disease duration, mean (SD), y	18.0 (14.0)[c]	19.0 (14.7)	18.6 (12.6)	16.3 (13.4)	17.8 (15.2)	17.3 (12.3)
PASI, mean (SD)	15.4 (3.3)	16.0 (3.5)	21.2 (8.3)	16.5 (4.4)	15.1 (3.4)	21.4 (8.6)
BSA involvement, mean (SD), %	12.6 (1.7)	12.9 (1.7)	26.4 (16.0)	13.0 (1.7)	12.7 (1.9)	26.3 (16.2)
Prior systemic treatment use, n (%)	62 (51.7)	122 (55.0)	971 (57.6)	41 (55.4)	25 (58.1)	418 (62.8)
Biologic	42 (35.0)	71 (32.0)	586 (34.8)	28 (37.8)	19 (44.2)	259 (38.9)
Non-biologic	20 (16.7)	51 (23.0)	692 (41.0)	13 (17.6)	6 (14.0)	159 (23.9)

[a]A total of 1686 patients were randomized 1:2:1 to placebo (n = 421), deucravacitinib (n = 843), and apremilast (n = 422). [b]A total of 666 patients were randomized 1:2:1 to placebo (n = 166), deucravacitinib (n = 332), and apremilast (n = 168). [c]n = 119. BSA, body surface area; PASI, Psoriasis Area and Severity Index; SD, standard deviation.

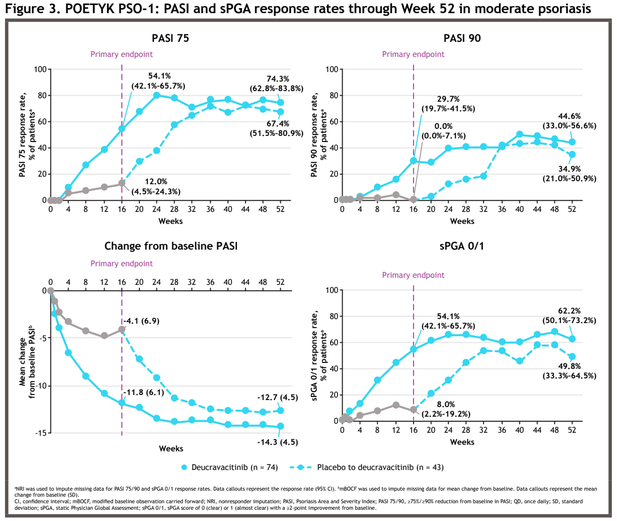
- PASI 75 and PASI 90 response rates, change from baseline PASI, and sPGA 0/1 response rate were higher with deucravacitinib 6 mg QD vs placebo through Week 16 in the subgroup of patients with psoriasis of moderate severity from the pooled POETYK PSO-1 and PSO-2 population; these responses increased through Week 24 (**Figure 2**)
- PASI 75, PASI 90, change from baseline PASI, and sPGA 0/1 response rates at Week 16 were maintained or increased through Week 52 with continuous deucravacitinib treatment in this subgroup of patients from the POETYK PSO-1 population who were initially randomized to deucravacitinib (**Figure 3**)
  - Response rates with continuous deucravacitinib increased through Week 24 and were maintained through Week 52
  - PASI 75, PASI 90, change from baseline PASI, and sPGA 0/1 response rates at Week 52 in patients who crossed over from placebo to deucravacitinib were comparable to those who received continuous deucravacitinib treatment from Day 1
  - Peak response rates and the changes from baseline observed at Week 24 were sustained until Week 52 in patients who were initially randomized to deucravacitinib
- PASI 75, PASI 90, change from baseline PASI, and sPGA 0/1 response rates at Week 16 increased through Week 52 in the placebo crossovers in the POETYK PSO-1 population (**Figure 3**)

Figure 2. Pooled POETYK PSO-1 and PSO-2: PASI and sPGA response rates through Week 24 in moderate psoriasis



[a]NRI was used to impute missing data for PASI 75/90 and sPGA 0/1 response rates. Data callouts represent the response rate (95% CI). [b]mBOCF was used to impute missing data for mean change from baseline. Data callouts represent the mean change from baseline (SD).
CI, confidence interval; mBOCF, modified baseline observation carried forward; NRI, nonresponder imputation; PASI, Psoriasis Area and Severity Index; PASI 75/90, ≥75%/≥90% reduction from baseline in PASI; QD, once daily; SD, standard deviation; 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. POETYK PSO-1: PASI and sPGA response rates through Week 52 in moderate psoriasis



[a]NRI was used to impute missing data for PASI 75/90 and sPGA 0/1 response rates. Data callouts represent the response rate (95% CI). [b]mBOCF was used to impute missing data for mean change from baseline. Data callouts represent the mean change from baseline (SD).
CI, confidence interval; mBOCF, modified baseline observation carried forward; NRI, nonresponder imputation; PASI, Psoriasis Area and Severity Index; PASI 75/90, ≥75%/≥90% reduction from baseline in PASI; QD, once daily; SD, standard deviation; sPGA, static Physician Global Assessment; sPGA 0/1, sPGA score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline.

- PASI 75, PASI 90, and sPGA 0/1 response rates in the subgroup of patients with moderate psoriasis were comparable to response rates in the overall study population of patients with moderate to severe psoriasis (**Table 2** and **Table 3**)

Table 2. Efficacy in patients with moderate to severe vs moderate psoriasis in the pooled POETYK PSO-1 and PSO-2 population (NRI)

Response rate, % of patients	Moderate to severe[10]		Moderate	
	Placebo (n = 421)	Deucravacitinib (n = 843)	Placebo (n = 120)	Deucravacitinib (n = 222)
PASI 75				
Week 16	10.7[a]	55.2[a]	11.7[a]	49.1[a]
Week 24	–	62.9[b]	–	63.8[b]
PASI 90				
Week 16	3.3[a]	30.4[a]	2.5[a]	27.5[a]
Week 24	–	36.4[b]	–	33.0[b]
sPGA 0/1				
Week 16	8.1[a]	51.1[a]	9.2[a]	47.3[a]
Week 24	–	53.3[b]	–	51.1[b]

[a]Patients were initially randomized to placebo from Weeks 0 to 16, followed by blinded crossover to deucravacitinib from Weeks 16 to 52. [b]In POETYK PSO-2, PASI 75 responders at Week 24 on deucravacitinib were rerandomized 1:1 to continue deucravacitinib or switch to placebo. Hence, data at Week 52 with continuous treatment without changes are not available in the pooled results.[9]
NRI, nonresponder imputation; PASI 75/90, ≥75%/≥90% reduction from baseline in Psoriasis Area and Severity Index; sPGA 0/1, static Physician Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline.

Table 3. Efficacy in patients with moderate to severe vs moderate psoriasis in POETYK PSO-1 (NRI)

Response rate, % of patients	Moderate to severe[a]		Moderate	
	Placebo to deucravacitinib (n = 166)	Deucravacitinib (n = 332)	Placebo to deucravacitinib (n = 43)	Deucravacitinib (n = 74)
PASI 75				
Week 16	12.7[a]	58.4[a]	12.0[a]	54.1[a]
Week 24	44.1	69.3	37.2	79.7
Week 52	68.3	65.1	67.4	74.3
PASI 90				
Week 16	4.2[a]	35.5[a]	0.0[a]	29.7[a]
Week 24	21.0	42.2	11.6	39.2
Week 52	48.9	53.5	34.9	44.6
sPGA 0/1				
Week 16	7.2[a]	53.6[a]	8.0[a]	54.1[a]
Week 24	39.3	58.7	30.2	64.9
Week 52	53.8	52.7	48.8	62.2

[a]Patients were initially randomized to placebo from Weeks 0 to 16, followed by blinded crossover to deucravacitinib from Weeks 16 to 52.
NRI, nonresponder imputation; PASI 75/90, ≥75%/≥90% reduction from baseline in Psoriasis Area and Severity Index; sPGA 0/1, static Physician Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline.

Conclusions

- Efficacy of deucravacitinib was confirmed in moderate plaque psoriasis and was largely consistent with that in the published primary analyses in the POETYK PSO-1 and PSO-2 study populations with moderate to severe plaque psoriasis[8,9]
- Deucravacitinib was efficacious through 52 weeks in patients with moderate plaque psoriasis[8,9]
  - Clinical responses improved through Week 24 and were maintained in patients who received continuous deucravacitinib treatment through Week 52[8,9]
  - Week 52 response rates in patients who crossed over from placebo to deucravacitinib treatment at Week 16 were comparable to those observed with continuous deucravacitinib treatment from Day 1[8]

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Acknowledgments

- This study was sponsored by Bristol Myers Squibb
- Writing and editorial assistance was provided by Barbara Zeman, PhD, of Peloton Advantage, LLC, an OPEN Health company, funded by Bristol Myers Squibb

Disclosures

- **AB:** Speaker (with honoraria): AbbVie, Lilly, Pfizer, and UCB, Scientific advisor (with honoraria): AbbVie, Abcentra, Aclaris, Affibody, Aligos, Almirall, Alumis, Amgen, Anaptysbio, Apogee, Arcutis, Arena, Aslan, Athenex, Bluefin Biomedicine, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, CTI BioPharma, Dermavant, EcoR1, Eclipse, Evelo Biosciences, Evommune, Forte, Galderma, Highlight Pharma, Incyte, InnoventBio, Janssen, Landos, Leo Pharma, Lilly, Lipidio, Microbion, Merck, Monte Rosa Therapeutics, NeKtar, Novartis, Overtone Therapeutics, Paragon, Pfizer, Q32 Bio, Rani, Rapt, Regeneron, Sanofi Genzyme, Sphera Global Insights, Sun Pharma, Takeda, TLL Pharmaceutical, TrialSpark, UCB, Union, Ventyx Biosciences, Viblome, and Xencor; Clinical study investigator (institution has received clinical study funds): AbbVie, Acelyrin, Aldeyra, Almirall, Alumis, Amgen, Arcutis, Athenex, Boehringer Ingelheim, Bristol Myers Squibb, Concert, Dermavant, Evelo Biosciences, Evommune, Galderma, Incyte, Janssen, Leo Pharma, Lilly, Merck, Novartis, Pfizer, Regeneron, Sanofi, Sun Pharma, UCB, and Ventyx Biosciences
- **MJK:** Advisory board and consulting fees: AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Janssen, Leo Pharma, Lilly, Novartis, Principia, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB; Advisory board, primary investigator, and lecture fees: Galderma SA, Leo Pharma, Pfizer, and Regeneron; Advisory board, primary investigator and consultant fees: Asian Pharmaceuticals; Primary investigator and consultant fees: Akros Pharma and Kyowa Kirin; Primary investigator: Arbutus, Anaptysbio, Bristol Myers Squibb, Coherus Biosciences, Dermira, GSK, Incyte, Medimmune, Meiji Seika, Merck, MoonLake Immunotherapeutics, and Nimbus Therapeutics; Advisory board: Asana Biosciences
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