Deucravacitinib in plaque psoriasis: 2-year laboratory results from the phase 3 POETYK PSO program

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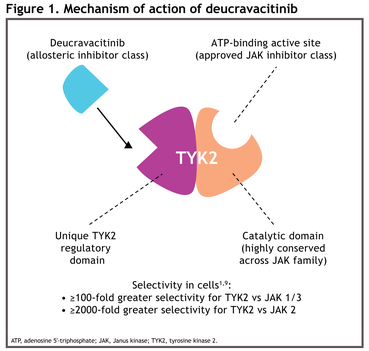
Synopsis

- Tyrosine kinase 2 (TYK2) is an intracellular enzyme that mediates signaling of cytokines (interleukin-23 and Type I interferons) involved in psoriasis pathogenesis[1]
- Deucravacitinib 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[2]
  - Deucravacitinib, an oral, selective, allosteric TYK2 inhibitor, has a unique mechanism of action, the first in a new class of small molecules[1] (**Figure 1**)
- The selectivity of deucravacitinib facilitates a more targeted therapeutic approach that avoids signature laboratory changes seen with the Janus kinase (JAK) 1/2/3 inhibitors
  - In the phase 2 trial and the phase 3 trials (POETYK PSO-1 and PSO-2) in plaque psoriasis, deucravacitinib treatment did not result in neutropenia, elevated liver enzyme and serum creatinine levels, and dyslipidemia — adverse events that have been associated with JAK 1/2/3 inhibitors[3-7]
- Deucravacitinib demonstrated a robust efficacy profile, including superiority to placebo and apremilast and durability and maintenance of response, in 2 multinational phase 3 trials in patients with moderate to severe plaque psoriasis[5,6,8]
- Patients who completed the POETYK PSO-1 and PSO-2 trials could enroll in the ongoing POETYK long-term extension (LTE) trial

Figure 1. Mechanism of action of deucravacitinib



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

Objective/Purpose

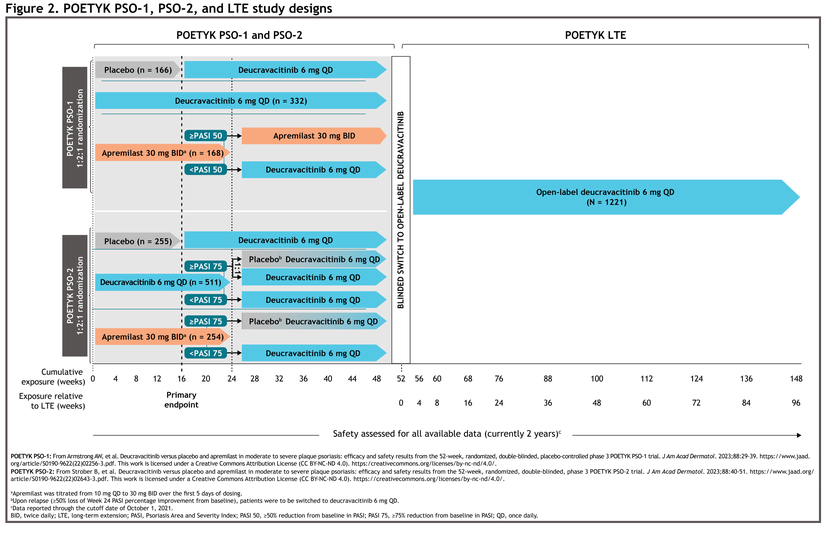
- To determine whether there were any clinically relevant changes in blood laboratory parameters with up to 2 years of deucravacitinib treatment in the POETYK PSO-1, PSO-2, and LTE trials
- To evaluate whether deucravacitinib treatment elicits changes in the blood that are known to occur with JAK 1/2/3 inhibitors

Methods

Study designs

- POETYK PSO-1 (NCT03624127) and PSO-2 (NCT03611751) were 52-week, multinational, phase 3, double-blind trials that randomized patients with moderate to severe plaque psoriasis 2:1:1 to deucravacitinib 6 mg once daily, placebo, or apremilast 30 mg twice daily (**Figure 2**)
- At Week 52, eligible patients were able to enroll in the POETYK LTE trial (NCT04036435) and receive open-label deucravacitinib 6 mg once daily for up to 2 years

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



POETYK PSO-1: 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/.

POETYK PSO-2: 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)00843-3.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.
[c]Data reported through the cutoff date of October 1, 2021.
BID, twice daily; LTE, long-term extension; 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.

Laboratory assessments

- Pooled POETYK PSO-1 + PSO-2 data over Weeks 0-52 and pooled POETYK PSO-1 + PSO-2 + LTE data over Weeks 0-100 are presented
- Changes in laboratory parameters that are known to be affected by JAK 1/2/3 inhibitors[3] were evaluated in blood over time
  - Hematologic parameters: lymphocytes, neutrophils, platelets, and hemoglobin
  - Lipid parameter: total cholesterol
  - Chemistry parameters: creatinine, creatine phosphokinase (CPK), and alanine aminotransferase (ALT)
- Incidences of grade ≥3 laboratory abnormalities (Common Terminology Criteria for Adverse Events [CTCAE] version 5.0) and treatment discontinuations due to laboratory abnormalities were also evaluated through Week 100

Results

Patient population

- This analysis included 1519 patients who received ≥1 dose of deucravacitinib in POETYK PSO-1, PSO-2, and/or the LTE through the data cutoff date of October 1, 2021
- Total deucravacitinib exposure was 2482.0 person-years (PY)
- In total, 1179 (77.6%) and 584 (38.4%) patients had ≥52 weeks and ≥104 weeks, respectively, of continuous deucravacitinib exposure at the data cutoff date
  - Median duration of exposure was 682.0 days (97 weeks)
- Baseline patient demographics and disease characteristics are presented in **Table 1**

Table 1. Baseline patient demographics and disease characteristics

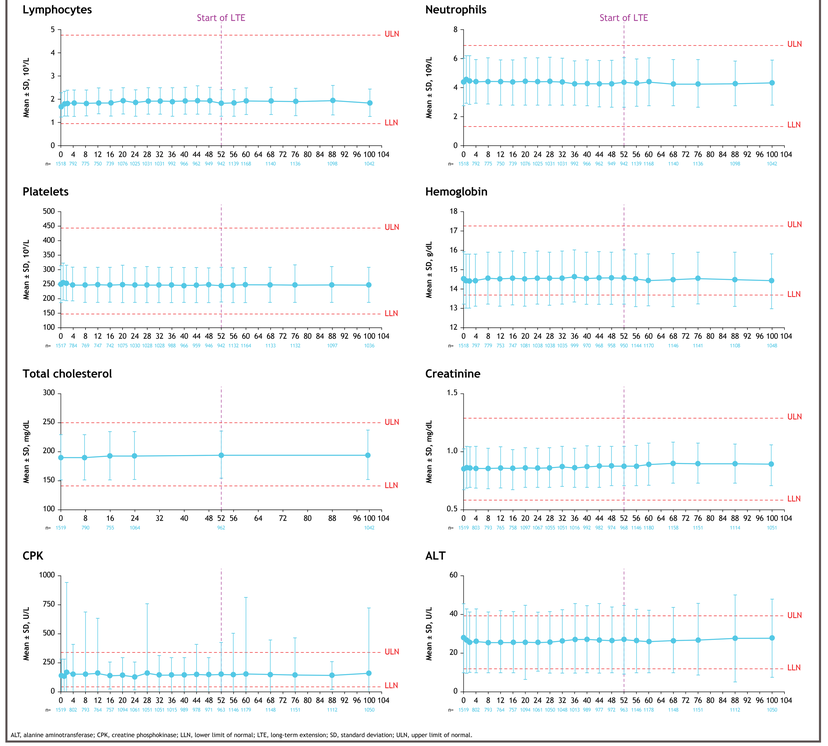
Parameter	POETYK PSO-1 + PSO-2 + LTE Deucravacitinib (N = 1519)
Age, mean (SD), y	46.6 (13.4)
Weight, mean (SD), kg	90.6 (21.6)
Body mass index, mean (SD), kg/m²	30.5 (6.8)
Female, n (%)	493 (32.5)
Race, n (%)	
White	1325 (87.2)
Asian	153 (10.1)
Black or African American	23 (1.5)
Other	18 (1.2)
Age at disease onset, mean (SD), y	28.8 (14.9)
Disease duration, mean (SD), y	18.7 (12.7)
PASI, mean (SD)	21.1 (8.1)
sPGA, n (%)	
3 (moderate)	1211 (79.7)
4 (severe)	308 (20.3)
BSA involvement, mean (SD), %	26.2 (15.8)

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

Laboratory assessments

- No clinically meaningful changes were observed over Weeks 0-100 in any of the evaluated laboratory parameters in the pooled POETYK PSO-1/PSO-2/LTE population (**Figure 3**)
  - Laboratory parameters remained within normal ranges for most patients throughout this period
- Grade ≥3 laboratory abnormalities were rare (**Table 2**)
  - Frequencies of individual events were comparable across groups over the first 52 weeks (POETYK PSO-1 and PSO-2), and no increases were seen with deucravacitinib treatment through Week 100 in the POETYK LTE
  - Grade ≥3 CPK elevations occurred rarely, were mostly transient, and were observed at a similar incidence in each treatment group over the first 52 weeks; almost all were related to recent physical exertion, and none was serious
- Discontinuations due to laboratory abnormalities were low and balanced across treatment groups over the first 52 weeks and were also low through Week 100 in the POETYK LTE (**Table 3**)
  - ALT elevations in deucravacitinib-treated patients (**Table 2**) were predominantly transient, and none was serious or resulted in treatment discontinuation

Figure 3. Changes in hematologic, lipid, and chemistry parameters over 2 years in patients receiving deucravacitinib in POETYK PSO-1 + PSO-2 + LTE



ALT, alanine aminotransferase; CPK, creatine phosphokinase; LLN, lower limit of normal; LTE, long-term extension; SD, standard deviation; ULN, upper limit of normal.

Table 2. CTCAE grades 3 and 4 abnormalities in laboratory parameters over 1 and 2 years

		At 1 year (POETYK PSO-1 + PSO-2, Weeks 0-52)						At 2 years (POETYK PSO-1 + PSO-2 + LTE, Weeks 0-100)	
		Placebo (n = 666)		Deucravacitinib (n = 1364)		Apremilast (n = 422)		Deucravacitinib (n = 1519)	
Parameter	Grade	Baseline n (%)	Week 52 n (%)	Baseline n (%)	Week 52 n (%)	Baseline n (%)	Week 52 n (%)	Baseline n (%)	Week 100 n (%)
Lymphocyte count decreased	3	0	1 (0.2)[a]	0	2 (0.1)[b]	0	1 (0.2)[c]	0	2 (0.1)[d]
	4	0	0	0	0	0	0	0	0
Neutrophil count decreased	3	0	1 (0.2)[a]	1 (0.1)[b]	4 (0.3)[b]	0	0	1 (0.1)[d]	5 (0.3)[d]
	4	0	1 (0.2)[a]	0	0	0	1 (0.2)[c]	0	1 (0.1)[d]
Platelet count decreased	3	0	1 (0.2)[e]	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
Anemia	3	0	0	0	0	0	1 (0.2)[c]	0	1 (0.1)[d]
	4	0	0	0	0	0	0	0	0
High cholesterol	3	0	0	0	1 (0.1)[f]	0	0	0	1 (0.1)[g]
	4	0	0	0	0	0	0	0	0
Creatinine increased	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
CPK increased	3	1 (0.2)[a]	4 (0.6)[a]	3 (0.2)[b]	19 (1.4)[b]	1 (0.2)[h]	7 (1.7)[h]	3 (0.2)[i]	25 (1.7)[i]
	4	0	3 (0.5)[a]	0	13 (1.0)[b]	0	1 (0.2)[h]	0	26 (1.7)[i]
ALT increased	3	2 (0.3)[a]	0	1 (0.1)[b]	4 (0.3)[b]	0	0	1 (0.1)[i]	10 (0.7)[i]
	4	0	0	0	0	0	0	0	0

[a]n = 658. [b]n = 1351. [c]n = 418. [d]n = 1503. [e]n = 657. [f]n = 1317. [g]n = 1454. [h]n = 419. [i]n = 1504.
ALT, alanine aminotransferase; CPK, creatine phosphokinase; CTCAE, Common Terminology Criteria for Adverse Events; LTE, long-term extension.

Table 3. Laboratory abnormality adverse events leading to treatment discontinuation over 1 and 2 years

	At 1 year (POETYK PSO-1 + PSO-2, Weeks 0-52)						At 2 years (POETYK PSO-1 + PSO-2 + LTE, Weeks 0-100)	
	Placebo (n = 666) Total exposure = 240.9 PY		Deucravacitinib (n = 1364) Total exposure = 969.0 PY		Apremilast (n = 422) Total exposure = 221.1 PY		Deucravacitinib (n = 1519) Total exposure = 2482.0 PY	
Parameter	n (%)	EAIR/100 PY	n (%)	EAIR/100 PY[a]	n (%)	EAIR/100 PY[a]	n (%)	EAIR/100 PY[a]
Lymphopenia	0	0	1 (0.1)	0.1	0	0	1 (0.1)	0.0
Blood CPK increased	0	0	2 (0.1)	0.2	1 (0.2)	0.4	3 (0.2)	0.1
Hepatic function abnormal	1 (0.2)[b]	0.4	1 (0.1)[c]	0.1	0	0	1 (0.1)	0.0
AST increased	0	0	0	0	1 (0.2)	0.4	0	0

[a]Incidences are expressed as EAIRs per 100 PY to account for variable exposure due to treatment switches at Weeks 16 and 24.
[b]Patient who received placebo during Weeks 0-16 had ALT >3x ULN on Days 1 and 8; total bilirubin levels remained in the normal range. The patient discontinued placebo and ALT levels improved.
[c]Patient who received deucravacitinib during Weeks 0-16 had ALT and AST elevations ≥3x ULN and bilirubin elevation >2x ULN on Day 58. Deucravacitinib treatment was discontinued and ALT, AST, and bilirubin levels improved.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatine phosphokinase; EAIR, exposure-adjusted incidence rate; LTE, long-term extension; PY, person-years; ULN, upper limit of normal.

Conclusions

- In the large, phase 3 POETYK PSO-1, PSO-2, and LTE trials in patients with plaque psoriasis, no trends or clinically meaningful changes in multiple hematologic, lipid, and chemistry parameters were observed in 1519 patients with 2482.0 PY of deucravacitinib exposure
  - Signature laboratory changes associated with JAK 1/2/3 inhibitors were not observed over 2 years of deucravacitinib exposure
- CTCAE grade ≥3 laboratory abnormalities and treatment discontinuations due to laboratory abnormalities in deucravacitinib-treated patients were rare, and were comparable to incidence rates observed with placebo and apremilast over the first 52 weeks
- Deucravacitinib, a once-daily oral drug, has the potential to become a treatment of choice and new standard of care for patients who require systemic therapy for their moderate to severe plaque psoriasis

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