Deucravacitinib, an Oral, Selective Tyrosine Kinase 2 (TYK2) Inhibitor, Compared With Placebo and Apremilast in Moderate to Severe Psoriasis: Integrated Laboratory Parameter Results From the Phase 3 POETYK PSO-1 and PSO-2 Trials

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Background

- Tyrosine kinase 2 (TYK2) is an intracellular enzyme that mediates signaling of key cytokines (interleukin [IL]-23, IL-12, and Type I interferons) involved in psoriasis pathogenesis[1,2]
- Deucravacitinib is a novel oral agent that selectively inhibits TYK2 via an allosteric mechanism by uniquely binding to the regulatory domain[2]
- In the Phase 3 POETYK PSO-1 and POETYK PSO-2 trials, deucravacitinib was significantly more efficacious than placebo and apremilast and was well tolerated in patients with moderate to severe plaque psoriasis[3]

Objective

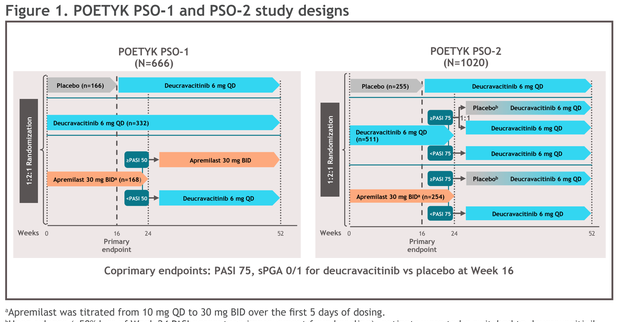
- The present analyses assessed the effects of deucravacitinib on hematologic, lipid, and chemistry parameters in blood in the POETYK trials

Methods

Study designs

- POETYK PSO-1 (NCT03624127) and PSO-2 (NCT03611751) were Phase 3, 52-week, double-blind, randomized, placebo- and active comparator (apremilast)-controlled trials conducted globally (**Figure 1**)[2]
  - Enrolled patients with moderate to severe plaque psoriasis (BSA, ≥10%; PASI, ≥12; sPGA, ≥3) were randomized 1:2:1 to receive oral placebo, deucravacitinib 6 mg once daily, or apremilast 30 mg twice daily during Weeks 0–16
  - Blinded treatment switches occurred at Week 16 and Week 24
    - Patients receiving placebo were switched to deucravacitinib at Week 16
    - Patients receiving apremilast who failed to meet trial-specific efficacy thresholds (PASI 50 in PSO-1; PASI 75 in PSO-2) were switched to deucravacitinib at Week 24

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



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

[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 50, ≥50% reduction from baseline in Psoriasis Area and Severity Index; PASI 75, ≥75% reduction from baseline in PASI; QD, once daily; sPGA 0/1, static Physician's Global Assessment score of 0/1.

Laboratory assessments over Weeks 0–16

- Pooled data from POETYK PSO-1 and PSO-2 are presented
- Standard laboratory parameters in blood were evaluated
  - Hematologic parameters: lymphocytes, neutrophils, platelets, and hemoglobin
  - Lipid parameters: total cholesterol and triglycerides
  - Chemistry parameters: creatine phosphokinase (CPK), creatinine, ALT, and AST
- Toxicity Grades 3–4 (Common Terminology Criteria for Adverse Events [CTCAE] version 5.0), shifts in toxicity grade, and discontinuations due to laboratory abnormalities were also assessed

Laboratory assessments over Weeks 0–52

- Standard laboratory parameters in blood were evaluated in patients enrolled in PSO-1 who received continuous deucravacitinib treatment from baseline to Week 52

Results

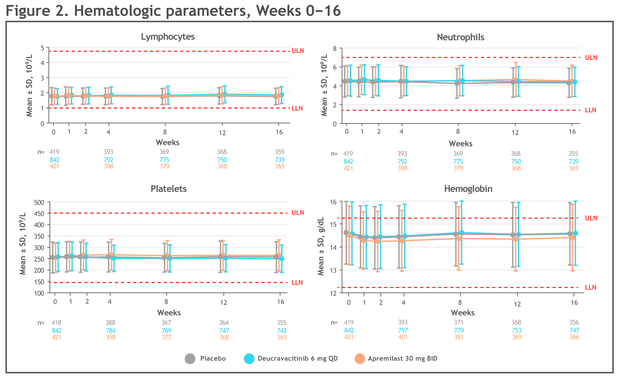
Patient population

- 666 and 1020 patients were randomized in PSO-1 and PSO-2, respectively, and were included in this analysis

Laboratory assessments over Weeks 0–16

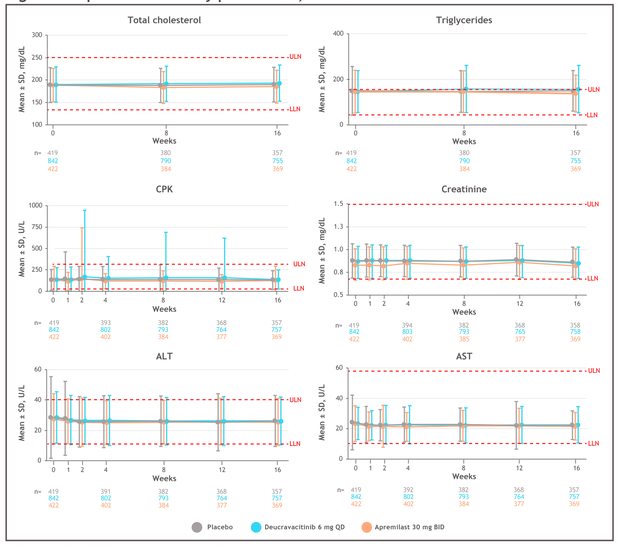
- Overall, no clinically relevant trends were observed over Weeks 0–16 in the levels of any of the assessed laboratory parameters (**Figure 2** and **Figure 3**)
- Laboratory parameters remained within normal ranges for most patients throughout both trials

Figure 2. Hematologic parameters, Weeks 0–16



POETYK PSO-1 and PSO-2 pooled data; Weeks 0–16.
BID, twice daily; LLN, lower limit of normal; QD, once daily; ULN, upper limit of normal.

Figure 3. Lipid and chemistry parameters, Weeks 0–16



POETYK PSO-1 and PSO-2 pooled data; Weeks 0–16.
No Grade 4 CPK elevations were observed during consecutive study visits.
BID, twice daily; CPK, creatine phosphokinase; LLN, lower limit of normal; QD, once daily; ULN, upper limit of normal.

Laboratory parameter grades and shifts (CTCAE version 5.0)

- Grade ≥3 laboratory abnormalities occurred at low frequencies and were comparable across treatment groups (**Table 1**)
  - Triglyceride and CPK elevations were the most common Grade ≥3 laboratory abnormalities and occurred at a similar incidence in each group
- Shifts of ≥2 CTCAE grades (increases) from baseline were balanced overall and infrequent for all treatment groups
  - Triglyceride shifts from Grade ≤2 to Grade ≥3 occurred at a low frequency and were comparable across groups: placebo, 1.3%; deucravacitinib, 1.7%; apremilast, 1.7%
    - There were patients with Grade 3/4 elevations in triglyceride levels at baseline (placebo, 0.7%; deucravacitinib, 0.6%; apremilast, 0.7%), reflecting the comorbidity of metabolic syndrome associated with psoriasis
  - CPK shifts from Grade ≤2 to Grade ≥3 occurred at a low frequency and were comparable across groups: placebo, 0.7%; deucravacitinib, 1.3%; apremilast, 0.5%
    - CPK elevations from baseline to Grade ≥1 postbaseline: placebo, 14.8%; deucravacitinib, 16.6%; apremilast, 11.0%
    - All CPK elevations were asymptomatic, nonserious, and resolved without treatment
    - Most Grade 3/4 CPK elevations were associated with increased recent physical activity during treatment

Table 1. Grade ≥3 laboratory abnormalities, Weeks 0–16

Parameter	Grade	Placebo (n=419) n (%)		Deucravacitinib (n=842) n (%)		Apremilast (n=422) n (%)	
		Baseline	Week 16	Baseline	Week 16	Baseline	Week 16
Lymphocyte count decreased	3 4	0 0	1 (0.2) 0	0 0	1 (0.1) 0	0 0	0 0
Neutrophil count decreased	3 4	0 0	1 (0.2) 0	1 (0.1) 0	1 (0.1) 0	0 0	0 0
Platelet count decreased	3 4	0 0	0 0	0 0	0 0	0 0	0 0
Anemia	3 4	0 N/A	0 N/A	0 N/A	0 N/A	0 N/A	1 (0.2) N/A
Total cholesterol increased	3 4	0 0	0 0	0 0	0 0	0 0	0 0
Triglycerides increased	3 4	2 (0.5) 1 (0.2)	6 (1.5) 0	4 (0.5) 1 (0.1)	13 (1.6) 2 (0.2)	3 (0.7) 0	8 (2.0) 0
CPK increased	3 4	1 (0.2) 0	3 (0.7) 1 (0.2)	1 (0.1) 0	5 (0.6) 6 (0.7)	1 (0.2) 0	2 (0.5) 1 (0.2)
Creatinine increased	3 4	0 0	0 0	0 0	0 0	0 0	0 0
ALT increased	3 4	0 0	0 0	0 0	0 0	0 0	0 0
AST increased	3 4	0 0	0 0	0 0	1 (0.1) 0	0 0	1 (0.2) 0

POETYK PSO-1 and PSO-2 pooled data; Weeks 0–16.
CPK, creatine phosphokinase; N/A, not applicable because there is no hemoglobin value for CTCAE Grade 4 (life-threatening consequences; urgent intervention indicated).

Laboratory abnormality adverse events leading to discontinuation, Weeks 0–16

- Discontinuations due to laboratory abnormalities were low and balanced across treatment groups (**Table 2**)

Table 2. Laboratory abnormality adverse events leading to discontinuation, Weeks 0–16

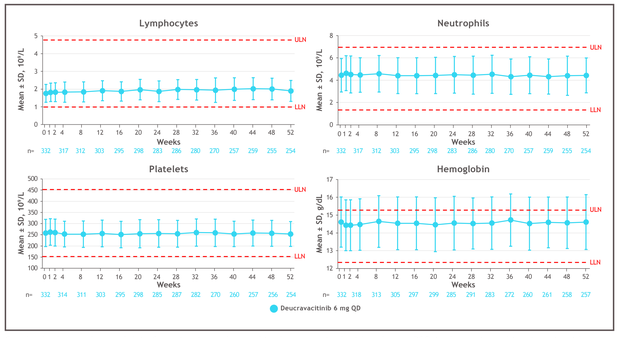
Adverse event (preferred term)	Placebo (n=419) n (%)	Deucravacitinib (n=842) n (%)	Apremilast (n=422) n (%)
Lymphopenia	0	1 (0.1)[a]	0
Blood CPK increased	0	1 (0.1)[b]	1 (0.2)
Hepatic function abnormal	0	1 (0.1)[c]	0
Liver function test abnormal	1 (0.2)	0	0
AST increased	0	0	1 (0.2)

POETYK PSO-1 and PSO-2 pooled data; Weeks 0–16.
[a]Patient had Grade 1 lymphocyte count decreased at baseline and Grade 3 at Week 4; treatment was discontinued and lymphocyte count returned to Grade 2; there were no associated infection adverse events.
[b]Patient had elevated CPK at screening (1796 U/L) and baseline (932 U/L).
[c]Patient had a medical history of fatty liver disease and recent alcohol use (increased alcohol consumption due to ankle injury [2x usual]).
CPK, creatine phosphokinase.

Laboratory assessments over Weeks 0–52

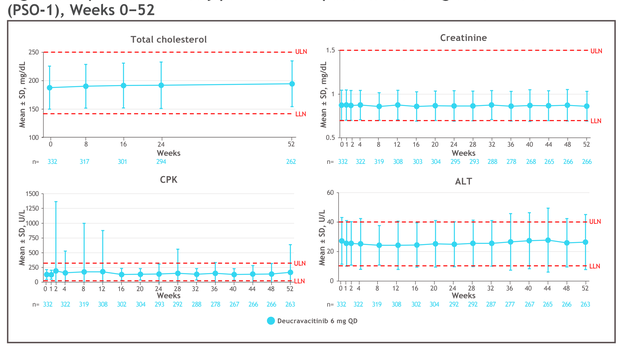
- No clinically relevant cumulative trends were observed in any assessed laboratory parameters in PSO-1 patients who were randomized to deucravacitinib at baseline and who continued to receive treatment until Week 52 (**Figure 4** and **Figure 5**)
- Discontinuation rates due to laboratory abnormalities were not increased between Weeks 16–52 vs Weeks 0–16

Figure 4. Hematologic parameters in patients receiving deucravacitinib (PSO-1), Weeks 0–52



Graphs display as observed data for patients randomized to deucravacitinib at baseline in PSO-1 who continued treatment until Week 52.
LLN, lower limit of normal; QD, once daily; ULN, upper limit of normal.

Figure 5. Lipid and chemistry parameters in patients receiving deucravacitinib (PSO-1), Weeks 0–52



Graphs display as observed data for patients randomized to deucravacitinib at baseline in PSO-1 who continued treatment until Week 52.
CPK, creatine phosphokinase; LLN, lower limit of normal; QD, once daily; ULN, upper limit of normal.

Conclusions

- Patients receiving deucravacitinib treatment showed no meaningful changes in multiple hematologic, chemistry, and lipid parameters in the blood over Weeks 0–16 in 2 large Phase 3 trials in psoriasis (POETYK PSO-1 and PSO-2)
  - Discontinuations due to laboratory abnormalities were rare and balanced across treatment groups
- No trends were evident for any laboratory parameter with continued deucravacitinib treatment over 52 weeks
- These results suggest that routine laboratory monitoring is not warranted during deucravacitinib treatment

References

1. Nogueira M et al. *Drugs* 2020;80:341-351.
2. Burke JR et al. *Sci Transl Med* 2019;11:1-16.
3. Armstrong A et al. Presented at the Annual Meeting of the American Academy of Dermatology; 2021.

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