Deucravacitinib, an Oral, Selective Tyrosine Kinase 2 (TYK2) Inhibitor, Versus Placebo and Apremilast in Moderate to Severe Plaque Psoriasis: Efficacy Analysis by Baseline Disease Characteristics From the Phase 3 POETYK PSO-1 and PSO-2 Trials

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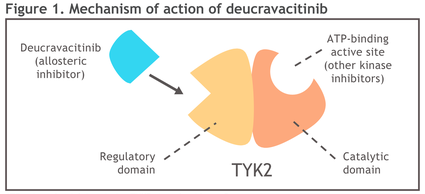
Introduction

- Deucravacitinib
  - Novel, oral, selective tyrosine kinase 2 (TYK2) inhibitor with a unique mechanism of action distinct from Janus kinase (JAK) 1/2/3 inhibitors (**Figure 1**)[1]
    - Binds to the TYK2 regulatory domain with high selectivity and inhibits TYK2 via an allosteric mechanism[1]
      - ≥100-fold greater selectivity for TYK2 vs JAK 1/3 and ≥2000-fold greater selectivity for TYK2 vs JAK 2 in cells[1,2]
    - Inhibits TYK2-mediated signaling of cytokines involved in psoriasis pathogenesis (eg, interleukin [IL]-23, IL-12, and Type I interferons)[1]

Figure 1. Mechanism of action of deucravacitinib



ATP, adenosine triphosphate; TYK2, tyrosine kinase 2.

- Deucravacitinib has demonstrated good efficacy and tolerability in Phase 2 trials in patients with moderate to severe plaque psoriasis[3] and with active psoriatic arthritis[4]
- In 2 pivotal Phase 3 trials in patients with moderate to severe plaque psoriasis, POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751), a significantly greater proportion of patients achieved ≥75% reduction from baseline in Psoriasis Area and Severity Index (PASI 75) score and a static Physician's Global Assessment (sPGA) score of 0 or 1 (0/1) at Week 16 with deucravacitinib compared with placebo or apremilast[5]

Objective

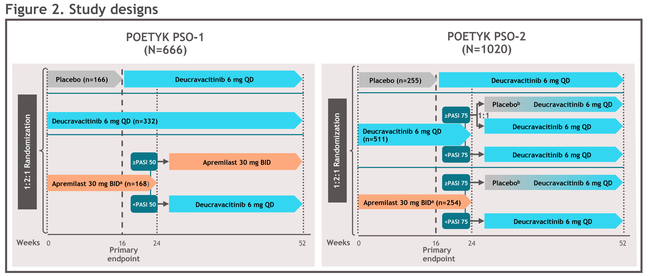
- The present analyses were performed to evaluate the efficacy of deucravacitinib at Week 16 by prespecified baseline disease characteristics in the Phase 3 POETYK PSO-1 and PSO-2 trials

Methods

Key design elements

- The POETYK PSO-1 and PSO-2 study designs are shown in **Figure 2**
- Key eligibility criteria
  - Adults with moderate to severe plaque psoriasis
  - PASI ≥12, sPGA ≥3, body surface area (BSA) ≥10%
  - Stratified by geographic region, body weight, and prior biologic use
- Coprimary endpoints were the proportion of patients who achieved PASI 75 and sPGA 0/1 responses vs placebo at Week 16
- Data from subgroups with the following predefined baseline disease characteristics in PSO-1 and PSO-2 were pooled and analyzed for the coprimary endpoints vs placebo and vs apremilast at Week 16:
  - Moderate vs severe disease
    - PASI score: 12–20 vs ≥20
    - sPGA score: 3 vs 4
    - BSA involvement: 10%–20% vs >20%
  - Disease duration: <10 y vs ≥10 y
  - Age at disease onset subgroups: <18 y, 18–39 y, ≥40 y
- Additional subgroups for age at disease onset (<18 y, 18–39 y, 40–55 y, >55 y) and disease duration (1–5 y, 5–15 y, 15–20 y, >20 y) were analyzed post hoc
- Differences between treatment groups were calculated using a stratified Cochran-Mantel-Haenszel test
- Missing data were imputed with nonresponder imputation

Figure 2. Study designs



[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.

Results

Baseline patient demographics and disease characteristics

- Baseline patient demographics and disease characteristics were largely similar across treatment groups in pooled data from the 2 trials (**Table 1**)

Table 1. Baseline patient demographics and disease characteristics

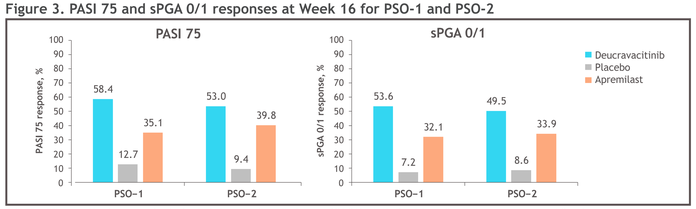
	Pooled POETYK PSO-1 and PSO-2			
	Placebo (n=421)	Deucravacitinib (n=843)	Apremilast (n=422)	Total (n=1686)
Age, y, mean (SD)	47.5 (13.7)	46.5 (13.5)	45.7 (12.8)	46.6 (13.4)
Weight, kg, mean (SD)	90.6 (21.1)	90.6 (21.9)	91.1 (22.0)	90.7 (21.7)
Female, n (%)	127 (30.2)	277 (32.9)	155 (36.7)	559 (33.2)
Race, n (%)				
White	360 (85.5)	741 (87.9)	368 (87.2)	1469 (87.1)
Asian	42 (10.0)	83 (9.8)	40 (9.5)	165 (9.8)
Other	19 (4.5)	19 (2.3)	14 (3.3)	52 (3.1)
Age at disease onset, y, mean (SD)	29.6 (15.2)[a]	28.8 (14.9)	28.1 (14.7)	28.8 (14.9)
<18 y, n (%)	102 (24.2)	208 (24.7)	112 (26.5)	422 (25.0)
18–39 y, n (%)	205 (48.7)	438 (52.0)	215 (50.9)	858 (50.9)
≥40 y, n (%)	113 (26.8)	197 (23.4)	95 (22.5)	405 (24.0)
Disease duration, y, mean (SD)	18.9 (12.9)[a]	18.6 (12.7)	18.5 (12.1)	18.6 (12.6)
<10 y, n (%)	119 (28.3)	261 (31.0)	112 (26.5)	492 (29.2)
≥10 y, n (%)	301 (71.5)	582 (69.0)	310 (73.5)	1193 (70.8)
Prior systemic treatment use, n (%)				
Biologic	146 (34.7)	295 (35.0)	145 (34.4)	586 (34.8)
No prior systemic therapy	173 (41.1)	369 (43.8)	173 (41.0)	715 (42.4)
sPGA, n (%)				
3 = moderate	345 (81.9)	665 (78.9)	335 (79.4)	1345 (79.8)
4 = severe	75 (17.8)	178 (21.1)	87 (20.6)	340 (20.2)
PASI, mean (SD) (overall)	20.9 (8.6)	21.1 (8.0)	21.6 (8.6)	21.2 (8.3)
PASI 12–20, n (%)	254 (60.3)	475 (56.3)	241 (57.1)	970 (57.5)
PASI >20, n (%)	167 (39.7)	368 (43.7)	181 (42.9)	716 (42.5)
BSA, mean (SD) (overall)	25.3 (16.1)	26.4 (15.8)	27.6 (16.4)	26.4 (16.0)
BSA 10%–20%, n (%)	226 (53.7)	421 (49.9)	200 (47.4)	847 (50.2)
BSA >20%, n (%)	195 (46.3)	422 (50.1)	222 (52.6)	839 (49.8)

[a]Age at disease onset and disease duration were not reported for 1 patient in the placebo arm of PSO-2.
BSA, body surface area; PASI, Psoriasis Area and Severity Index; sPGA, static Physician's Global Assessment.

Efficacy

- In the overall populations, significantly greater proportions of patients receiving deucravacitinib vs placebo and vs apremilast achieved PASI 75 and sPGA 0/1 responses at Week 16 in each study (**Figure 3**)[5]

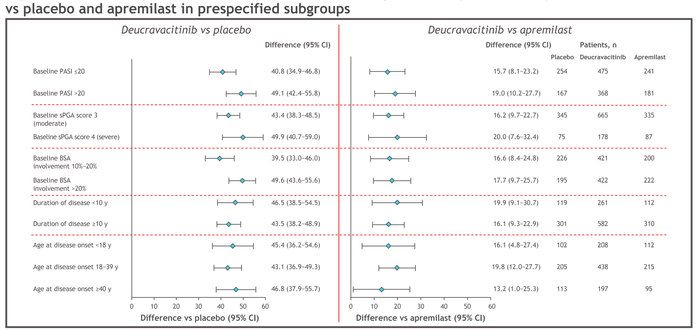
Figure 3. PASI 75 and sPGA 0/1 responses at Week 16 for PSO-1 and PSO-2



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

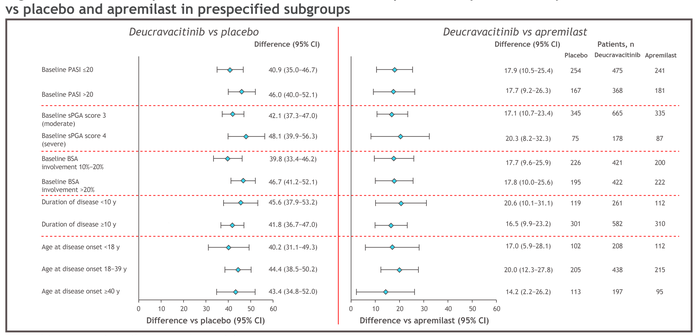
- Pooled data from PSO-1 and PSO-2 demonstrated a consistent and favorable treatment benefit by PASI 75 and sPGA 0/1 responses for deucravacitinib compared with placebo and apremilast in all prespecified baseline disease subgroups at Week 16:
  - Disease severity by PASI, sPGA, and BSA
  - Disease duration
  - Age of disease onset (**Figure 4** and **Figure 5**)

Figure 4. PASI 75 response at Week 16: PSO-1 and PSO-2 pooled analysis – efficacy of deucravacitinib vs placebo and apremilast in prespecified subgroups



Missing data were imputed with nonresponder imputation.
BSA, body surface area; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index; sPGA, static Physician's Global Assessment.

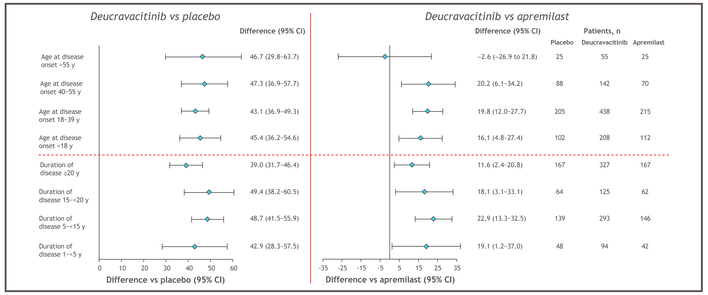
Figure 5. sPGA 0/1 response at Week 16: PSO-1 and PSO-2 pooled analysis – efficacy of deucravacitinib vs placebo and apremilast in prespecified subgroups



Missing data were imputed with nonresponder imputation.
BSA, body surface area; PASI, Psoriasis Area and Severity Index; sPGA 0/1, static Physician's Global Assessment score of 0 or 1.

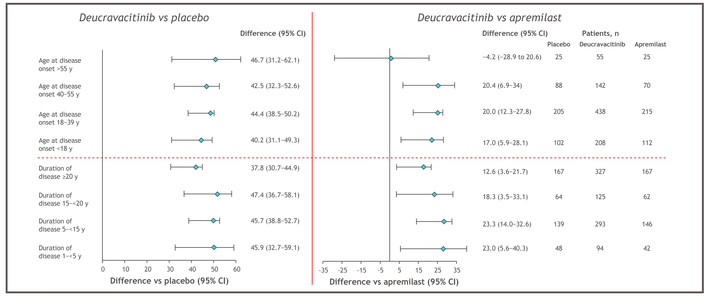
- Analysis of pooled data from PSO-1 and PSO-2 demonstrated favorable efficacy for deucravacitinib against placebo and apremilast across most post hoc subgroups with additional strata (**Figure 6** and **Figure 7**)

Figure 6. PASI 75 response at Week 16: PSO-1 and PSO-2 pooled analysis – efficacy of deucravacitinib vs placebo and apremilast in post hoc subgroups



Missing data were imputed with nonresponder imputation.
PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index.

Figure 7. sPGA 0/1 response at Week 16: PSO-1 and PSO-2 pooled analysis – efficacy of deucravacitinib vs placebo and apremilast in post hoc subgroups



Missing data were imputed with nonresponder imputation.
sPGA 0/1, static Physician's Global Assessment score of 0 or 1.

Conclusions

- Patients treated with deucravacitinib had PASI 75 and sPGA 0/1 responses that were superior to placebo and apremilast across nearly all prespecified and post hoc baseline disease parameters, including measures of baseline disease severity, duration of psoriasis, and age at disease onset
- Taken together with the primary results from the Phase 3 POETYK trials,[5] these findings suggest that deucravacitinib has the potential to become a treatment of choice and new standard of care for patients with moderate to severe plaque psoriasis

References

1. Burke JR et al. *Sci Transl Med* 2019;11:1-16. **2.** Wrobleski ST et al. *J Med Chem* 2019;62:8973-8995. **3.** Papp K et al. *N Engl J Med* 2018;349:1313-1321. **4.** Mease PJ et al. Presented at the Annual Scientific Meeting of the American College of Rheumatology; November 5-9, 2020. **5.** Armstrong A et al. Presented at the Annual Meeting of the American Academy of Dermatology; April 23-25, 2021.

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