Deucravacitinib Improves Psoriasis Symptoms and Signs Diary Domain Scores in Patients With Moderate to Severe Plaque Psoriasis: Results From the Phase 3 POETYK PSO-1 and POETYK PSO-2 Studies

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Introduction

- Tyrosine kinase 2 (TYK2) is an intracellular kinase that mediates signaling of key cytokines (interleukin [IL]-23, IL-12, and Type I interferons [IFNs]) involved in psoriasis pathogenesis[1]
- Deucravacitinib is a novel, oral, and selective inhibitor that binds to the regulatory domain of TYK2, and thereby via an allosteric mechanism inhibits signaling of IL-23, IL-12, and Type I IFN[1]
- In the Phase 3 POETYK PSO-1 and PSO-2 trials, deucravacitinib demonstrated superiority compared with placebo and apremilast for multiple endpoints, including clinical and patient-reported outcomes[2]
  - Results from the Psoriasis Symptoms and Signs Diary (PSSD) focusing on patient-reported symptoms were previously described at the 2021 American Academy of Dermatology annual meeting[2]

Objective

- To compare the effect of deucravacitinib vs placebo and vs apremilast on item-level changes over time for patient-reported psoriasis symptoms and signs measured by the PSSD, and to further evaluate the contribution of individual subdomains on symptom and sign scores in POETYK PSO-1 and PSO-2

Methods

Study designs

- POETYK PSO-1 (NCT03624127) and PSO-2 (NCT03611751) were 52-week, Phase 3, double-blind trials that randomized patients with moderate to severe plaque psoriasis (body surface area [BSA] involvement ≥10%, Psoriasis Area and Severity Index [PASI] score ≥12, static Physician's Global Assessment [sPGA] score ≥3) 2:1:1 to deucravacitinib 6 mg once daily, placebo, or apremilast 30 mg twice daily[2]
- Patients recorded psoriasis symptoms and signs daily (24-h recall) using the PSSD
  - The PSSD is a patient-reported instrument that assesses the severity of 5 symptoms (burning, itch, pain, skin tightness, stinging) and 6 signs (bleeding, cracking, dryness, redness, scaling, shedding or flaking) on a numerical scale ranging from 0 (absent) to 10 (worst imaginable)[3,4]
  - Psoriasis symptom and sign summary scores (0-100) were derived based on average scores for the individual symptom and sign domains

Results

Baseline disease characteristics

- A total of 666 and 1020 patients were randomized in PSO-1 and PSO-2, respectively[2]
- In both trials, PSSD total and symptom and sign summary scores were similar across groups at baseline (**Table 1**)

Table 1. Baseline PSSD total and summary scores

Mean PSSD score (min, max)	POETYK PSO-1			POETYK PSO-2		
	Placebo (n=166)	Deucravacitinib (n=332)	Apremilast (n=168)	Placebo (n=255)	Deucravacitinib (n=511)	Apremilast (n=254)
Total	53.4 (6.1, 100.0)	53.5 (0.0, 100.0)	57.4 (1.0, 100.0)	52.9 (0.0, 100.0)	55.0 (5.9, 100.0)	54.5 (8.2, 100.0)
Symptom	51.4 (0.3, 100.0)	51.7 (0.0, 100.0)	56.2 (2.0, 100.0)	50.1 (0.0, 100.0)	52.3 (1.0, 100.0)	51.9 (0.0, 100.0)
Sign	55.5 (9.4, 100.0)	55.3 (0.0, 100.0)	58.6 (0.0, 100.0)	55.7 (0.0, 100.0)	57.7 (5.7, 100.0)	57.2 (11.7, 100.0)

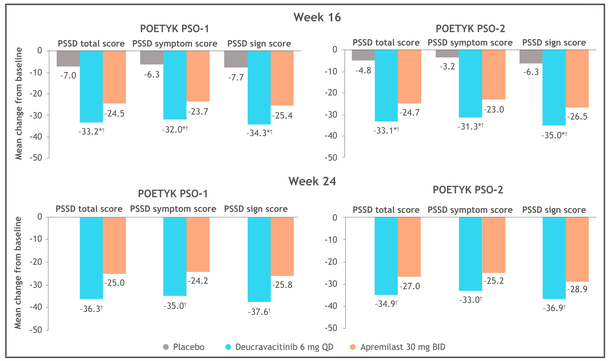
max, maximum; min, minimum; PSSD, Psoriasis Symptoms and Signs Diary.

- PSSD symptom and sign domain scores were also similar across groups at baseline (data not shown)

PSSD scores

- Deucravacitinib-treated patients experienced significantly greater improvements in mean change from baseline in PSSD total scores, symptom summary scores, and sign summary scores compared with those receiving placebo or apremilast at Week 16 and Week 24 (**Figure 1**)

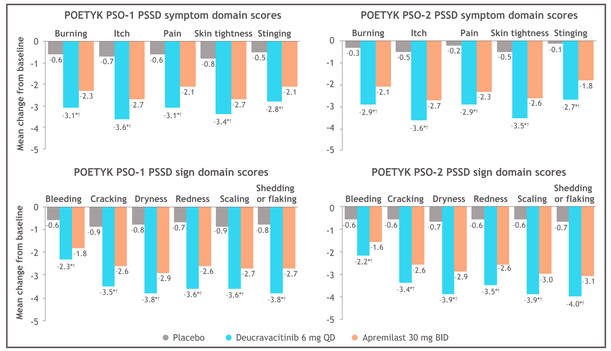
Figure 1. Mean change from baseline in PSSD total scores, symptom summary scores, and sign summary scores at Week 16 and Week 24



*P<0.0001 vs placebo. †P<0.0001 vs apremilast.
Modified baseline observation carried forward was used to impute missing data.
BID, twice daily; PSSD, Psoriasis Symptoms and Signs Diary; QD, once daily.

- Significantly greater improvements from baseline were observed in all individual symptom and sign domain scores at Week 16 for patients treated with deucravacitinib compared with placebo or apremilast and were consistent between PSO-1 and PSO-2 (**Figure 2**)
  - The greatest improvements in psoriasis symptoms were observed for itch, skin tightness, and pain in both studies
  - The greatest improvements in psoriasis signs were observed for dryness, scaling, and shedding or flaking

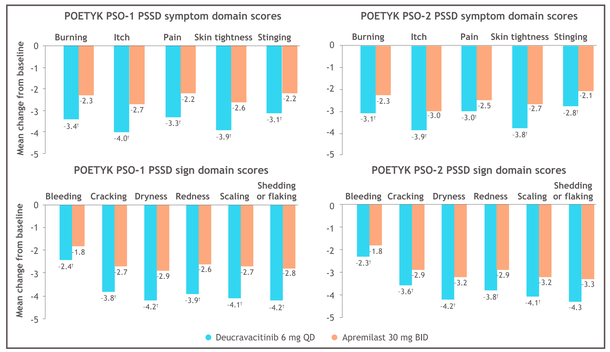
Figure 2. Mean change from baseline in PSSD symptom domain scores and PSSD sign domain scores at Week 16



*P<0.0001 vs placebo. †P<0.01 vs apremilast.
Modified baseline observation carried forward was used to impute missing data.
BID, twice daily; PSSD, Psoriasis Symptoms and Signs Diary; QD, once daily.

- Benefits favoring deucravacitinib increased or were maintained through Week 24 and were consistent between PSO-1 and PSO-2 (**Figure 3**)

Figure 3. Mean change from baseline in PSSD symptom domain scores and PSSD sign domain scores at Week 24



†P<0.01 vs apremilast.
Modified baseline observation carried forward was used to impute missing data.
BID, twice daily; PSSD, Psoriasis Symptoms and Signs Diary; QD, once daily.

Conclusions

- In this post hoc analysis, deucravacitinib treatment was significantly superior to placebo and apremilast in improving individual patient-reported psoriasis symptoms and signs at Week 16 in patients with moderate to severe plaque psoriasis
  - Benefits favoring deucravacitinib were maintained at Week 24
- The greatest symptom improvement was consistently observed for the itch domain
  - This may prove particularly meaningful to patients given the prevalence and burden of itch, a symptom that affects the vast majority of patients with psoriasis[5]
- Improvements in the patient-reported psoriasis symptoms and signs burden are consistent with the higher clinical response rates previously reported in deucravacitinib-treated patients in PSO-1 and PSO-2[2]

References

1. Burke JR et al. *Sci Transl Med* 2019;11:1-16. **2.** Armstrong A et al. Presented at the Annual Meeting of the American Academy of Dermatology; April 23-25, 2021. **3.** Feldman SR et al. *J Dermatol Trans Surg* 2016;20:19-26. **4.** Mathias SD et al. *J Dermatol Treat* 2016;27:322-327. **5.** Komiya E et al. *Int J Mol Sci* 2020;21:8406.

Acknowledgments

- We would like to thank the patients and investigators who participated in these clinical trials.
- These clinical trials were sponsored by Bristol Myers Squibb. Professional medical writing from Lisa Feder, PhD, and editorial assistance were provided by Peloton Advantage, LLC, an OPEN Health company, Parsippany, NJ, USA, and were funded by Bristol Myers Squibb.

Relationships and Activities

- **AWA:** Grants and personal fees: AbbVie, Bristol Myers Squibb, Eli Lilly, Janssen, Leo Pharma, and Novartis; Personal fees: Boehringer Ingelheim/Parexel, Celgene, Dermavant, Genentech, GlaxoSmithKline, Menlo Therapeutics, Merck, Modernizing Medicine, Ortho Dermatologics, Pfizer, Regeneron, Sanofi Genzyme, Science 37, Sun Pharma, and Valeant; Grants: Dermira, Kyowa Hakko Kirin, and UCB, outside the submitted work
- **BS:** Honoraria or consultation fees: AbbVie, Almirall, Amgen, Arcutis, Arena, Aristea, Asana, Boehringer Ingelheim, Bristol Myers Squibb, Connect Biopharma, Dermavant, Eli Lilly, Equillium, GlaxoSmithKline, Immunic Therapeutics, Janssen, Leo Pharma, Maruho, Meiji Seika Pharma, Mindera, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, UCB, and Ventyxbio; Speaker: AbbVie, Eli Lilly, Janssen, and Sanofi Genzyme; Scientific co-director (consulting fee): CorEvitas' Psoriasis Registry; Investigator: AbbVie, Cara, CorEvitas' Psoriasis Registry, Dermavant, Eli Lilly/Dermira, and Novartis
- **KBG:** Grant support and consulting fees: AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, and UCB; Consulting fees: Amgen, Almirall, Dermira, Leo Pharma, Pfizer, and Sun Pharma
- **JZ, BB, RMK, JT, and JK:** Employees and shareholders: Bristol Myers Squibb
- **KP:** Speakers bureau: AbbVie, Amgen, Astellas, Celgene, Eli Lilly, Galderma, Janssen, Kyowa Hakko Kirin, Leo Pharma, Merck Sharp & Dohme, Novartis, Pfizer, and Valeant; Grant/research support: AbbVie, Akros, Allergan, Amgen, Anacor, Arcutis, AstraZeneca, Baxalta, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Coherus, Dermira, Dow Pharma, Eli Lilly, Galderma, Genentech, GlaxoSmithKline, Janssen, Kyowa Hakko Kirin, Leo Pharma, MedImmune, Meiji Seika Pharma, Merck Serono, Novartis, Pfizer, Regeneron, Roche, Sanofi Genzyme, Takeda, UCB, and Valeant; Consultant: AbbVie, Akros, Amgen, Arcutis, Astellas, AstraZeneca, Baxalta, Baxter, Boehringer Ingelheim, Bristol Myers Squibb, CanFite, Celgene, Coherus, Dermira, Dow Pharma, Eli Lilly, Forward Pharma, Galderma, Genentech, Janssen, Kyowa Hakko Kirin, Leo Pharma, Meiji Seika Pharma, Merck Serono, Merck Sharp & Dohme, Mitsubishi Pharma, Novartis, Pfizer, Regeneron, Roche, Sanofi Genzyme, Takeda, UCB, and Valeant; Honoraria: AbbVie, Akros, Amgen, Baxter, Boehringer Ingelheim, Celgene, Coherus, Eli Lilly, Forward Pharma, Galderma, GlaxoSmithKline, Janssen, Kyowa Hakko Kirin, Merck Serono, Merck Sharp & Dohme, Novartis, Pfizer, Takeda, UCB, and Valeant; Scientific officer/steering committee/advisory board: AbbVie, Akros, Amgen, Anacor, Astellas, Baxter, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Dow Pharma, Eli Lilly, Galderma, Janssen, Kyowa Hakko Kirin, Merck Serono, Merck Sharp & Dohme, Novartis, Pfizer, Regeneron, Sanofi Genzyme, and Valeant

Presented at the Fall Clinical Dermatology Conference®; October 21—24, 2021; Las Vegas, NV, and Virtual
This is an encore of the 2021 EADV 30th Congress poster

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