Deucravacitinib improves Dermatology Life Quality Index in moderate to severe psoriasis: Results from the phase 3 POETYK PSO-1 and POETYK PSO-2 trials

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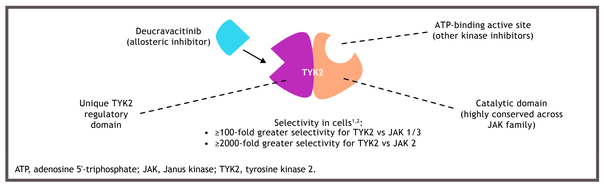
Introduction

- Deucravacitinib
  - An oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor, approved in the United States and other countries for the treatment of adults with moderate-to-severe PsO who are candidates for systemic therapy or phototherapy
  - It has a unique mechanism of action distinct from Janus kinase (JAK) 1/2/3 inhibitors[1] (**Figure 1**)
    - Binds to the TYK2 regulatory domain and inhibits TYK2 via an allosteric mechanism[1]
    - 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 5′-triphosphate; JAK, Janus kinase; TYK2, tyrosine kinase 2.

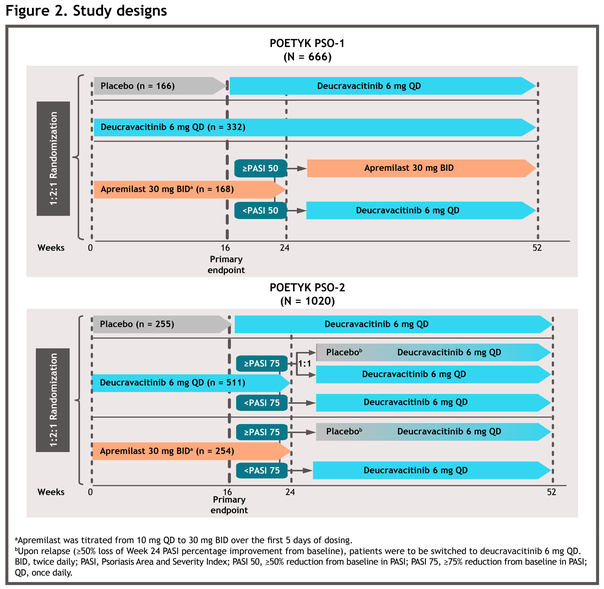
- Deucravacitinib has demonstrated robust efficacy and tolerability in phase 2 trials in patients with moderate to severe plaque psoriasis[3] and with active psoriatic arthritis[4] compared with placebo, and in 2 pivotal phase 3 trials in patients with moderate to severe plaque psoriasis, POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751), compared with placebo or apremilast[5]
- The Dermatology Life Quality Index (DLQI) is a validated patient-reported outcome (PRO) measure consisting of 10 questions each scored on a 0 (not at all) to 3 (very much) scale regarding the impact of a dermatologic condition on symptoms, feelings, daily activities, leisure, work, school, personal relationships, and treatment during the previous week
  - Scores range from 0—30, with higher scores indicating a higher level of impairment
  - Scores 0—1: no impact on patient's life; 2—5: small effect on patient's life; 6—10: moderate effect on patient's life; 11—20: very large effect on patient's life; 21—30: extremely large effect on patient's life
- This analysis assessed improvements in DLQI compared with placebo and apremilast from the phase 3, double-blind, POETYK PSO-1 and PSO-2 trials to determine the impact of deucravacitinib on quality of life

Methods

Study designs

- The study designs for POETYK PSO-1 and PSO-2 are summarized in **Figure 2**
- Key eligibility criteria
  - Age ≥18 years
  - Diagnosis of moderate to severe plaque psoriasis
    - Psoriasis Area and Severity Index (PASI) ≥12, static Physician's Global Assessment (sPGA) ≥3, and body surface area involvement ≥10%
- Randomization stratified by geographic region, body weight, and prior biologic use
- All patients were eligible for a long-term extension study after 52 weeks of treatment
- Coprimary endpoints for deucravacitinib vs placebo (Week 16)
  - PASI 75 (≥75% reduction from baseline in PASI)
  - sPGA score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline (sPGA 0/1)

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, Psoriasis Area and Severity Index; PASI 50, ≥50% reduction from baseline in PASI; PASI 75, ≥75% reduction from baseline in PASI; QD, once daily.

Outcomes

- Improvements in DLQI score were evaluated in POETYK PSO-1 and PSO-2 using:
  - Change from baseline
  - Percentage achieving DLQI 0/1 response
  - Meaningful within-patient change threshold (MCT)-based responder analysis
- Improvements in DLQI question 1 (itchy, sore, painful stinging skin) were evaluated in POETYK PSO-1 and PSO-2 using:
  - Change from baseline
  - MCT responder analysis

Analysis population

- Analyses were conducted using the PRO analysis set population
  - Any patient who had completed ≥1 DLQI item at baseline and ≥1 DLQI item postbaseline
- Anchors for determining MCT: Patient Global Impression of Severity (PGI-S) and Patient Global Impression of Change (PGI-C)
  - Both are global rating anchor scales used to interpret scores from PRO measurements
  - Used as anchors to derive the MCT for DLQI in POETYK PSO-1
- PGI-S: Patients were asked to respond to the question "How severe are your psoriasis symptoms currently?" at baseline and at Weeks 16, 24, and 52 (or early discontinuation)
  - Answers were based on a 4-point scale ranging from 0 (none) to 3 (severe)
- PGI-C: Patients were asked to respond to the question "Since you started taking the study medication, how would you rate the overall impact of psoriasis on your life currently?" at Weeks 16, 24, and 52 (or early discontinuation)
  - Answers were based on a 7-point scale ranging from 1 (very much worse) to 7 (very much better)
- MCT derivation and analysis
  - DLQI MCTs were derived applying anchor-based methods in POETYK PSO-1, using PGI-S and PGI-C as the anchors, with supported distribution-based methods calculated (1/2 SD and standard error of measurement)
  - Anchor- and distribution-based methods were triangulated to derive the MCT using blinded data from POETYK PSO-1
  - Correlations were derived with a criterion of ≥0.40 between categorical change on the PGI-S and PGI-C anchors and change from baseline in DLQI scores
  - Distributional parameters (mean, SD, CI) of within-group change from baseline in DLQI were calculated for each level of categorical change on the anchors to determine the MCT for each domain
- Derived MCTs were then used to determine the proportion of patients achieving meaningful improvements in DLQI from baseline to Week 52

Results

Baseline POETYK PSO-1 and PSO-2 DLQI scores

- This analysis included 1148 patients from POETYK PSO-1 (deucravacitinib, n = 303; placebo, n = 150) and POETYK PSO-2 (deucravacitinib, n = 462; placebo, n = 233)
- Baseline scores on PSSD items were similar across treatment groups and studies (**Table 1**)

Table 1. Baseline DLQI

Mean DLQI (min, max)	POETYK PSO-1			POETYK PSO-2		
	Placebo (n = 163)	Deucravacitinib (n = 328)	Apremilast (n = 160)	Placebo (n = 246)	Deucravacitinib (n = 496)	Apremilast (n = 250)
Total DLQI	11.4 (1.0, 30.0)	12.1 (0, 30.0)	12.4 (1.0, 30.0)	11.8 (1.0, 30.0)	11.8 (1.0, 30.0)	12.5 (0, 30.0)
DLQI question 1	2.0 (0, 3.0)	2.1 (0, 3.0)	2.2 (1.0, 3.0)	2.1 (0, 3.0)	2.1 (0, 3.0)	2.1 (0, 3.0)

DLQI, Dermatology Life Quality Index.

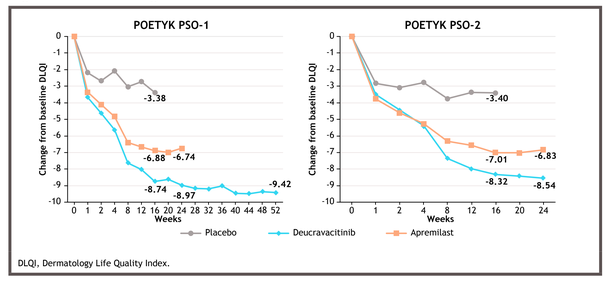
Correlation coefficients of DLQI changes and MCTs

- Correlation coefficients for change from baseline to Week 16 for DLQI and PGI-S and PGI-C were 0.511 and 0.537, respectively, demonstrating suitability of the anchors for estimating the within-patient MCT for DLQI
  - MCTs were set at total DLQI improvement ≥4 and total DLQI improvement ≥5
  - MCT ≥1 and MCT ≥2 were set for individual DLQI questions

Change from baseline in DLQI and DLQI 0/1 response

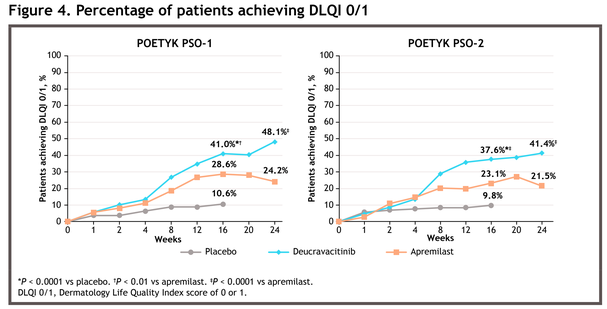
- Mean changes from baseline in DLQI were greater for patients treated with deucravacitinib as early as:
  - Week 1 vs placebo in POETYK PSO-1 (-3.67 vs -2.18) and PSO-2 (-3.49 vs -2.82; **Figure 3**)
  - Week 4 vs apremilast in POETYK PSO-1 (-5.63 vs -4.83) and Week 8 in PSO-2 (-7.35 vs -6.31; **Figure 3**)
- In POETYK PSO-1, mean change from baseline DLQI results were maintained through Week 52 with continuous deucravacitinib treatment (**Figure 3**)
- Significantly greater proportions of patients in POETYK PSO-1 and PSO-2 achieved DLQI 0/1 with deucravacitinib vs placebo at Week 16 and vs apremilast at Week 16 and Week 24 (**Figure 4**)

Figure 3. Mean change from baseline DLQI



DLQI, Dermatology Life Quality Index.

Figure 4. Percentage of patients achieving DLQI 0/1

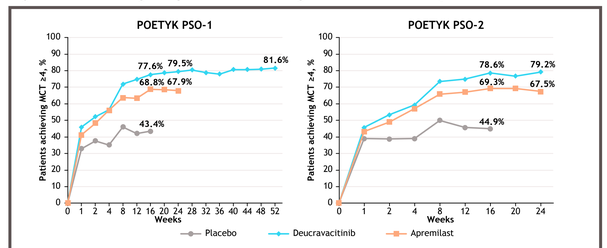


*P < 0.0001 vs placebo. †P < 0.01 vs apremilast. ‡P < 0.0001 vs apremilast.
DLQI 0/1, Dermatology Life Quality Index score of 0 or 1.

MCT analysis

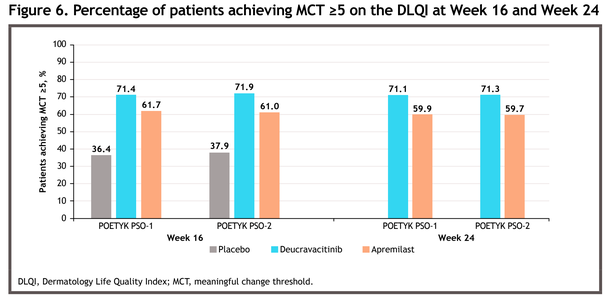
- MCT ≥4 (≥4-point improvement from baseline on DLQI; **Figure 5**)
  - Greater proportions of deucravacitinib-treated patients achieved MCT ≥4 at Week 16 vs placebo and apremilast
    - POETYK PSO-1: 77.6% vs 43.4% and 68.8%, respectively
    - POETYK PSO-2: 78.6% vs 44.9% and 69.3%, respectively
  - Responses were also higher with deucravacitinib vs apremilast at Week 24
    - POETYK PSO-1: 79.5% vs 67.9%, respectively
    - POETYK PSO-2: 79.2% vs 67.5%, respectively
  - In POETYK PSO-1, 81.6% achieved MCT ≥4 at Week 52 with continuous deucravacitinib treatment
- MCT ≥5 (**Figure 6**)
  - Results were similar when applying an MCT ≥5

Figure 5. Percentage of patients achieving MCT ≥4 on the DLQI



DLQI, Dermatology Life Quality Index; MCT, meaningful change threshold.

Figure 6. Percentage of patients achieving MCT ≥5 on the DLQI at Week 16 and Week 24



DLQI, Dermatology Life Quality Index; MCT, meaningful change threshold.

Change from baseline in DLQI question 1 (itchy, sore, painful stinging skin)

- Greater proportions of patients achieved MCT ≥1 and MCT ≥2 for DLQI question 1 with deucravacitinib in POETYK PSO-1 and PSO-2 at Weeks 16 and 24 (**Table 2**)

Table 2. Patients achieving MCT ≥1 and MCT ≥2 for DLQI question 1 (itchy, sore, painful stinging skin)

Baseline	POETYK PSO-1			POETYK PSO-2		
	Placebo (n = 163)	Deucravacitinib (n = 328)	Apremilast (n = 160)	Placebo (n = 246)	Deucravacitinib (n = 496)	Apremilast (n = 250)
Median (min, max)	2 (0, 3)	2 (0, 3)	2 (1, 3)	2 (0, 3)	2 (0, 3)	2 (0, 3)
Week 16						
MCT ≥1	39.2% (56/143)	76.6% (236/308)	66.0% (93/141)	40.2% (86/214)	76.8% (345/449)	62.4% (136/218)
MCT ≥2	10.5% (15/143)	38.3% (118/308)	21.3% (30/141)	8.9% (19/214)	32.5% (146/449)	25.2% (55/218)
Week 24						
MCT ≥1	NA	79.9% (238/298)	65.7% (90/137)	NA	80.6% (345/428)	64.1% (132/206)
MCT ≥2	NA	39.9% (119/298)	22.6% (31/137)	NA	35.3% (151/428)	22.3% (46/206)

DLQI, Dermatology Life Quality Index; MCT, meaningful change threshold; NA, not applicable.

Conclusions

- Deucravacitinib improved overall DLQI as early as Week 1 vs placebo and Week 4 vs apremilast
- Significantly greater proportions of patients treated with deucravacitinib achieved DLQI 0/1 response vs placebo at Week 16 and vs apremilast at Week 16 and Week 24
- Patients reported greater relief of itch and pain symptoms with deucravacitinib vs placebo at Week 16 and vs apremilast at Week 16 and Week 24
- Higher proportions of patients reached MCT ≥4 and MCT ≥5 with deucravacitinib vs placebo at Week 16 and vs apremilast at Week 16 and Week 24, with sustained responses to deucravacitinib observed through Week 52

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Acknowledgments

- These clinical trials were sponsored by Bristol Myers Squibb
- Medical writing and editorial assistance was provided by Lisa Feder, PhD, of Peloton Advantage, LLC, an OPEN Health company, and funded by Bristol Myers Squibb

Disclosures

- **MA:** Consultant, lecturer, researcher, and/or recipient of research grants: AbbVie, Amgen, Bayer, Beiersdorf, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Centocor, Dermira, Eli Lilly, Galderma, Genzyme, GlaxoSmithKline, Hexal, Incyte, Janssen, Leo Pharma, Medac, Menlo, Merck Sharp & Dohme, Mylan B.V., Novartis, Pfizer, Regeneron, Sandoz, Sanofi, Stallergenes, Trevi, and UCB
- **BS:** Consultant (honoraria): AbbVie, Almirall, Amgen, Arcutis, Arena, Aristea, Asana, Boehringer Ingelheim, Bristol Myers Squibb, Connect Biopharma, Dermavant, Eli Lilly, Equillium, Evelo Biosciences, GlaxoSmithKline, Immunic Therapeutics, Janssen, Leo Pharma, Maruho, Meiji Seika Pharma, Mindera Health, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, UCB, Ventyx Biosciences, and vTv Therapeutics; Speaker: AbbVie, Eli Lilly, Janssen, Regeneron, and Sanofi Genzyme; Scientific co-director (consulting fee): CorEvitas' (Corrona) Psoriasis Registry; Investigator: AbbVie, Cara Therapeutics, CorEvitas' (Corrona) Psoriasis Registry, Dermavant, Dermira, and Novartis
- **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
- **JB, TPP, and SH:** Funding for analytic planning and execution activities associated with this research: Bristol Myers Squibb
- **JZ, BB, SB, and RMK:** Employees and stockholders: Bristol Myers Squibb
- **KAP:** Consultant: AbbVie, Acelyrin, Akros, Amgen, Aralez Pharmaceuticals, Arcutis, Avillion, Bausch Health/Valeant, Boehringer Ingelheim, Bristol Myers Squibb, Can-Fite Biopharma, Celgene, Celltrion, Coherus, Dermavant, Dermira, Dice Therapeutics, Dow Pharma, Eli Lilly, Evelo, Forbion, Galderma, Incyte, Janssen, Kyowa Hakko Kirin, Leo Pharma, Meiji Seika Pharma, Merck (MSD), Mitsubishi Pharma, Novartis, Pfizer, Regeneron, Reistone, Roche, Sanofi Aventis/Genzyme, Sandoz, Sun Pharma, Takeda, UCB, vTv Therapeutics, and Xencor; Speakers bureau: AbbVie, Amgen, Bausch Health/Valeant, Celgene, Eli Lilly, Galderma, Incyte, Janssen, Kyowa Hakko Kirin, Leo, Merck (MSD), Novartis, Pfizer, and Sanofi Aventis/Genzyme; Clinical research grants: AbbVie, Akros, Amgen, Anacor, Arcutis, Avillion, Bausch Health/Valeant, Boehringer Ingelheim, Bristol Myers Squibb, Can-Fite Biopharma, Celgene, Coherus, Dermavant, Dermira, Dice Therapeutics, Dow Pharma, Eli Lilly, Evelo, Galderma, Gilead, GSK, Incyte, Janssen, Kyowa Hakko Kirin, Leo Pharma, Merck (MSD), Novartis, Pfizer, Regeneron, Roche, Sanofi Aventis/Genzyme, Sun Pharma, Takeda, and UCB; Honoraria: AbbVie, Acelyrin, Akros, Amgen, Aralez Pharmaceuticals, Bausch Health/Valeant, Boehringer Ingelheim, Celgene, Celltrion, Coherus, Dermavant, Dice Therapeutics, Eli Lilly, Forbion, Galderma, Janssen, Kyowa Hakko Kirin, Leo Pharma, Meiji Seika Pharma, Merck (MSD), Mitsubishi Pharma, Novartis, Pfizer, Reistone, Sanofi Aventis/Genzyme, Sandoz, Sun Pharma, Takeda, UCB, vTv Therapeutics, and Xencor; Scientific officer: Akros, Anacor, Arcutis, Dice Therapeutics, and Kyowa Hakko Kirin; Steering committees: AbbVie, Amgen, Bausch Health/Valeant, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, Kyowa Hakko Kirin, Merck (MSD), Novartis, Pfizer, Regeneron, Reistone, and Sanofi Aventis/Genzyme; Advisory boards: AbbVie, Amgen, Bausch Health/Valeant, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Dice Therapeutics, Dow Pharma, Eli Lilly, Galderma, Janssen, Merck (MSD), Novartis, Pfizer, Regeneron, Sanofi Aventis/Genzyme, Sun Pharma, and UCB

Presented at the 2023 Dermatology Refresher Symposium for NPs and PAs; April 21-23, 2023; Miami, FL
This is an encore of the AAD 2022 poster

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