Deucravacitinib in plaque psoriasis: maintenance of response over 3 years in the phase 3 POETYK PSO-1 and PSO-2 trials

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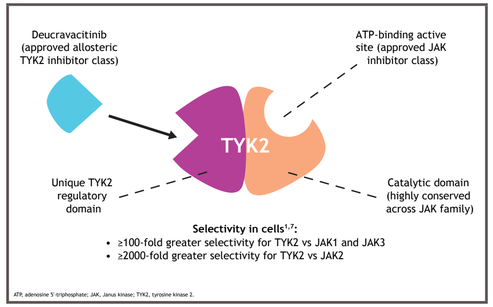
Background

- Tyrosine kinase 2 (TYK2) is an intracellular enzyme that mediates signaling of cytokines (eg, interleukin [IL]-23, IL-12, Type I interferons [IFNs])[1]
  - IL-23 and Type I IFNs are involved in psoriasis pathogenesis[1]
- Deucravacitinib, an oral, selective, allosteric TYK2 inhibitor, is approved in the US, EU, and other countries for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy[2-6]
- Deucravacitinib uniquely binds to the regulatory domain of TYK2 rather than to the catalytic domain where Janus kinase (JAK) 1,2,3 inhibitors bind[1,7] (**Figure 1**), driving its selectivity and representing the first in a new class of oral drugs

Figure 1. Mechanism of action of deucravacitinib



- Deucravacitinib was superior to placebo and apremilast in the global, 52-week, phase 3 POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751) trials in moderate to severe plaque psoriasis[8,9]
- Patients completing POETYK PSO-1 and PSO-2 could enroll in the POETYK long-term extension (LTE) (NCT04036435) trial and receive open-label deucravacitinib 6 mg once daily (QD)
- Deucravacitinib maintained long-term efficacy through 2 years with no new safety signals[10]

Objective

- To evaluate clinical efficacy for up to 3 years (148 weeks) in a subset of patients who received continuous deucravacitinib treatment from Day 1 in the parent trials and entered the POETYK LTE trial

Methods

Study design

- In POETYK PSO-1 and PSO-2, eligible patients were randomized 1:2:1 to oral placebo, deucravacitinib 6 mg QD, or apremilast 30 mg twice daily (BID) (**Figure 2**)[8,9]
- At Week 52, patients could enter the POETYK LTE trial and receive open-label deucravacitinib 6 mg QD

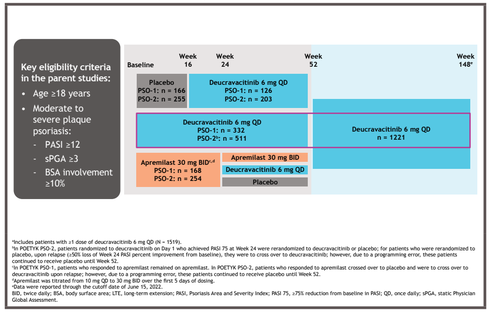
Patient population

- Patients pooled from POETYK PSO-1 and PSO-2 who received continuous deucravacitinib from Day 1, achieved ≥75% reduction from baseline in Psoriasis Area and Severity Index (PASI 75) at Week 16 (primary endpoint) or at Week 24 (peak response), and enrolled in the POETYK LTE trial

Outcomes

- Efficacy of deucravacitinib and maintenance of response through Week 148 (3 years)
- Achievement of PASI 75, ≥90% reduction from baseline in PASI (PASI 90), and static Physician Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline (sPGA 0/1)

Figure 2. POETYK PSO-1, PSO-2, and LTE analysis populations[a]



[a]Includes patients with ≥1 dose of deucravacitinib 6 mg QD (N = 1519).
[b]In POETYK PSO-2, patients randomized to deucravacitinib on Day 1 who achieved PASI 75 at Week 24 were rerandomized to deucravacitinib or placebo; for patients who were rerandomized to placebo, upon relapse (≥50% loss of Week 24 PASI percent improvement from baseline), they were to cross over to deucravacitinib; however, due to a programming error, these patients continued to receive placebo until Week 52.
[c]In POETYK PSO-1, patients who responded to apremilast remained on apremilast. In POETYK PSO-2, patients who responded to apremilast crossed over to placebo and were to cross over to deucravacitinib upon relapse (≥50% loss of Week 52 to 64 PASI 50 percent improvement); however, due to a programming error, these patients continued to receive placebo until Week 52.
[d]Apremilast titrated from 10 mg QD to 30 mg BID over the first 5 days of dosing.
[e]Data were reported through the cutoff date of June 15, 2022.
BID, twice daily; BSA, body surface area; LTE, long-term extension; PASI, Psoriasis Area and Severity Index; PASI 75, ≥75% reduction from baseline in PASI; QD, once daily; sPGA, static Physician Global Assessment.

Statistical analysis

- Efficacy was analyzed through the data cutoff date of June 15, 2022
- The Clopper-Pearson method was used to calculate 95% confidence intervals (CIs)
- In addition to as-observed analysis, two methods of imputation for missing data were used to evaluate long-term efficacy, as recently done with other agents[11,12]
  - **Treatment failure rules (TFR)**[11]: patients who discontinued treatment due to lack of efficacy or worsening of psoriasis were imputed as nonresponders; all other missing data were not imputed
  - **Modified nonresponder imputation (mNRI)**[12]: patients who either discontinued prior to Week 148 or reached Week 148 were included; patients with missing data who discontinued treatment due to worsening of psoriasis were imputed as nonresponders; all other missing data were imputed by multiple imputation
  - Only patients who discontinued or reached Week 148 by the cutoff date were included

Results

- 513 patients completed 52 weeks in the parent trials and received continuous deucravacitinib treatment from Day 1 (**Table 1**)
- 313 (61.4%) patients treated with deucravacitinib achieved PASI 75 at Week 16 and 336 (66.5%) patients achieved PASI 75 at Week 24

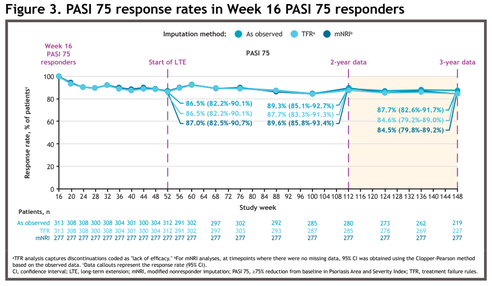
Table 1. Baseline patient demographics and disease characteristics

Parameter	Total (N = 513)	Deucravacitinib Week 16 PASI 75 responders (n = 313)	Deucravacitinib Week 24 PASI 75 responders (n = 336)
Age, mean (SD), y	46.9 (13.3)	46.3 (13.9)	46.3 (13.8)
Weight, mean (SD), kg	89.9 (22.2)	86.7 (21.7)	86.6 (22.1)
Body mass index, mean (SD), kg/m²	30.3 (7.0)	29.5 (6.6)	29.5 (7.0)
Female, n (%)	159 (31.0)	110 (35.1)	122 (36.3)
Race, n (%)			
White	440 (85.8)	262 (83.7)	284 (84.5)
Asian	64 (12.5)	45 (14.4)	47 (14.0)
Black or African American	5 (1.0)	2 (0.6)	1 (0.3)
Other	4 (0.8)	4 (1.3)	4 (1.2)
Age at disease onset, mean (SD), y	29.0 (14.7)	29.1 (15.3)	28.8 (15.3)
Disease duration, mean (SD), y	18.8 (12.6)	18.0 (12.4)	18.3 (13.0)
PASI score, mean (SD)	21.1 (7.9)	21.8 (8.2)	21.3 (8.0)
sPGA score, n (%)			
3 (moderate)	401 (78.2)	241 (77.0)	265 (78.9)
4 (severe)	112 (21.8)	72 (23.0)	71 (21.1)
BSA involvement, mean (SD), %	26.9 (15.8)	28.1 (16.1)	27.0 (15.8)

BSA, body surface area; PASI, Psoriasis Area and Severity Index; PASI 75, ≥75% reduction from baseline in PASI; SD, standard deviation; sPGA, static Physician Global Assessment.

- PASI 75 response rates were maintained from the start of the POETYK LTE trial to Week 148 in Week 16 and Week 24 PASI 75 responders (**Figure 3**; **Figure 4**)
- PASI 90 response rates were maintained from the start of the POETYK LTE trial in more than half of the Week 16 and Week 24 PASI 75 responders (**Figure 5**; **Figure 6**)
- sPGA 0/1 response rates were also maintained from Week 52 to Week 148 in Week 16 and Week 24 PASI 75 responders (**Figure 7**; **Figure 8**)
- Results were consistent regardless of imputation method
- Deucravacitinib demonstrated a consistent safety profile through 3 years with no increases in adverse events (AEs) or serious AE rates over time and no emergence of any new safety signals[13]

Figure 3. PASI 75 response rates in Week 16 PASI 75 responders



[a]TFR analysis captures discontinuations coded as 'lack of efficacy.' [b]For mNRI analyses, at timepoints where there were no missing data, 95% CI was obtained using the Clopper-Pearson method based on the observed data. [c]Data calculis represent the response rate (95% CI).
CI, confidence interval; LTE, long-term extension; mNRI, modified nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index; TFR, treatment failure rules.

Figure 4. PASI 75 response rates in Week 24 PASI 75 responders

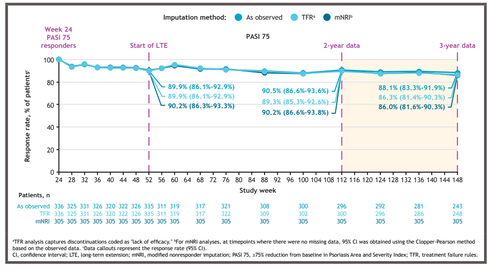


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Figure 5. PASI 90 response rates in Week 16 PASI 75 responders

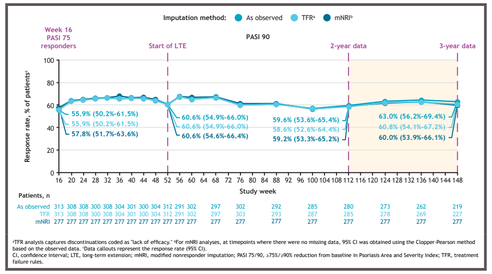

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Figure 6. PASI 90 response rates in Week 24 PASI 75 responders

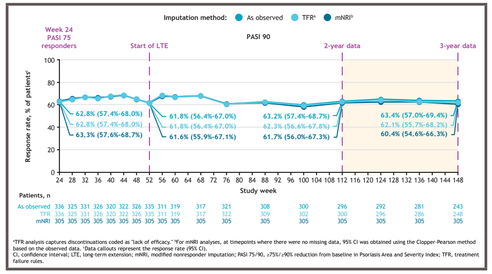

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Figure 7. sPGA 0/1 response rates in Week 16 PASI 75 responders

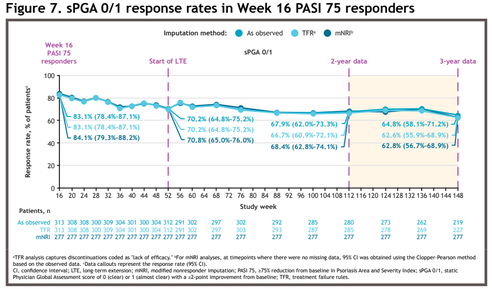

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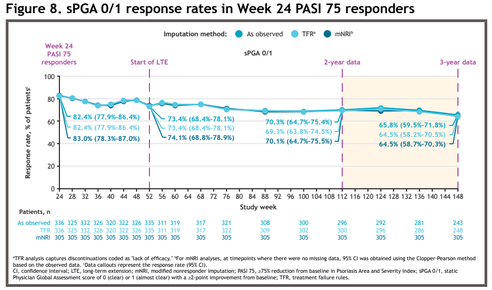
Figure 8. sPGA 0/1 response rates in Week 24 PASI 75 responders



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Conclusions

- Clinical efficacy was maintained for up to 148 weeks with continuous deucravacitinib treatment in the majority of patients who achieved PASI 75 at Week 16 or Week 24 in the parent trials and had enrolled in the POETYK LTE trial
- These findings further support the long-term use of once-daily oral deucravacitinib as an effective treatment for patients with moderate to severe plaque psoriasis

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Acknowledgments

- This study was sponsored by Bristol Myers Squibb
- Writing and editorial assistance was provided by Regina Kelly, MA, of Peloton Advantage, LLC, an OPEN Health company, funded by Bristol Myers Squibb

Disclosures

- **BS:** Consultant (honoraria): AbbVie, Almirall, Amgen, Arcutis, Arena, Aristea, Asana, Boehringer Ingelheim, Bristol Myers Squibb, Connect Biopharma, Dermavant, Eli Lilly, Equillium, GSK, 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, and Sanofi Genzyme; Co-scientific director (consulting fee): CorEvitas Psoriasis Registry; Investigator: AbbVie, Cara Therapeutics, CorEvitas Psoriasis Registry, Dermavant, Dermira, and Novartis
- **HS:** Clinical investigator: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Janssen, Leo Pharma, Novartis, and Sun Pharma
- **SI:** Grants and personal fees: AbbVie, Eisai, Janssen, Kyowa Kirin, Leo Pharma, Maruho, Sun Pharma, Taiho Yakuhin, Tanabe Mitsubishi, and Torii Yakuhin; Personal fees: Amgen/Celgene, Boehringer Ingelheim, Bristol Myers Squibb, Daiichi Sankyo, Eli Lilly, GSK, Novartis, and UCB
- **CP:** Grants and consultant: AbbVie, Almirall, Amgen/Celgene, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Janssen, Leo Pharma, Merck, Mylan, Novartis, Pfizer, Sandoz, and UCB
- **MG:** Advisory board, principal investigator, and consulting/lecture fees: AbbVie, Amgen/Celgene, Arcutis, Bausch Health, Boehringer Ingelheim International GmbH, Eli Lilly, Janssen, Novartis, Sanofi Genzyme, Sun Pharma, and UCB; Advisory board, primary investigator, and lecture fees: Galderma SA, Leo Pharma, Pfizer, and Regeneron; Advisory board, primary investigator and consultant fees: Aslan; Primary investigator and consultant fees: Akros Pharma and Kyowa Kirin; Primary investigator: Aristea, AnaptysBio, Bristol Myers Squibb, Coherus Biosciences, GSK, Incyte, Dermira, Medimmune, Meiji Seika, Merck, MoonLake, and Nimbus Therapeutics; Advisory board: Asana Biosciences
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- **SJS:** Nothing to disclose
- **TP:** Advisory board and consulting fees: AbbVie, Almirall, Amgen/Celgene, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galderma, Incyte, Janssen, Leo Pharma, Novartis, Pfizer, Sanofi Genzyme, Sun Pharma, and UCB
- **RMK, VB, EV, MJC, and SB:** Employees and shareholders: Bristol Myers Squibb
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- **LSG:** Consultant, advisory board member, and/or speaker: AbbVie, Amgen, Arcutis, Aslan, Bausch Health, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Dermira, Eli Lilly, Galderma, Incyte, Janssen, Leo Pharma, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB
- **AFA:** Grants (funds to institution): AbbVie, Almirall, Amgen, Arcutis, Bristol Myers Squibb, Cara Therapeutics, Castle Biosciences, Dermavant, Galderma, Leo Pharma, Novartis, Valeant (Bausch Health), and Vyne; Advisory board/consulting: AbbVie, Allergan, Almirall, Amgen, Arcutis, Bausch Health, Beiersdorf, Bristol Myers Squibb, Cara Therapeutics, Castle Biosciences, Cutera, Dermavant, Eli Lilly, EPI Health, Galderma, Incyte, Janssen, Leo Pharma, L'Oreal, Ortho, Pfizer, Sanofi-Regeneron, Swiss American, UCB, VisualDx, and Vyne; Speaker: Bristol Myers Squibb, Pfizer, Regeneron, and Sanofi Genzyme; Royalties: Springer, Wiley-Blackwell, Wolters Kluwer Health
- **DT:** Research support and principal investigator (clinical trial funds to institution): AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galderma, Janssen-Cilag, Leo Pharma, Novartis, Pfizer, Regeneron, Roche, Sandoz-Hexal, Sanofi, and UCB; Consultant: AbbVie, Almirall, Boehringer Ingelheim, Bristol Myers Squibb, Galapagos, Leo Pharma, Novartis, Pfizer, and UCB; Lecturer: AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Janssen, Eli Lilly, Leo Pharma, Novartis, Pfizer, Roche-Posay, Sanofi, Target RWE, and UCB; Scientific advisory board: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Janssen-Cilag, Leo Pharma, Novartis, Pfizer, Sanofi, and UCB
- **AB:** Speaker (with honoraria): AbbVie, Bristol Myers Squibb, Eli Lilly, Pfizer, Regeneron, and Sanofi; Scientific adviser (with honoraria): AbbVie, Abcentra, Aclaris, Affibody, Allgos, Almirall, Alumis, Amgen, AnaptysBio, Apogee, Arcutis, Arena, Aslan, Athenex, Bluefin Biomedicine, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, CTI BioPharma, Dermavant, EcoR1, Eli Lilly, Escient, Evelo Biosciences, Evommune, Forte Biosciences, Galderma, Highlightll Pharma, Incyte, InnoventBio, Janssen, Landos, Leo Pharma, Lipidio, Merck, Nektar, Novartis, Pfizer, Raln, Rapt, Regeneron, Sanofi Genzyme, Sphenix Global Insights, Sun Pharma, Takeda, TLL Pharmaceutical, TrialSpark, UCB, Union, Ventyx Biosciences, Viblome, and Xencor; Clinical study investigator (institution has received clinical study funds): AbbVie, Acelyrin, Allakos, Almirall, Alumis, Amgen, Arcutis, Athenex, Boehringer Ingelheim, Bristol Myers Squibb, Concert, Dermavant, Eli Lilly, Evelo Biosciences, Evommune, Galderma, Incyte, Janssen, Leo Pharma, Merck, Novartis, Pfizer, Regeneron, Sanofi, Sun Pharma, UCB, and Ventyx Biosciences
- **ML:** Research funds on behalf of Mount Sinai: AbbVie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Cara Therapeutics, Dermavant, Eli Lilly, Incyte, Janssen, Ortho Dermatologics, Regeneron, and UCB; Consultant: Aditum Bio, Almirall, AltruBio, AnaptysBio, Arcutis, Aristea, Avotres, Boehringer Ingelheim, Brickell Biotech, Bristol Myers Squibb, Cara Therapeutics, Castle Biosciences, Cellrion, CorEvitas Psoriasis Registry, Dermavant, Dr. Reddy's Laboratories, EPI Health, Evommune, Forte Biosciences, Galderma, Genentech, Incyte, Leo Pharma, Meiji Seika Pharma, Mindera Health, Pfizer, Seanergy, Strata, Trevi, and Verrica

Presented at the San Diego Dermatology Symposium; February 2-4, 2024; San Diego, CA
This is an encore of the 2023 32nd European Academy of Dermatology & Venereology Congress poster

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