Deucravacitinib long-term efficacy through 4 years in Week 16 placebo crossover patients in the phase 3 POETYK PSO-1, PSO-2, and LTE program

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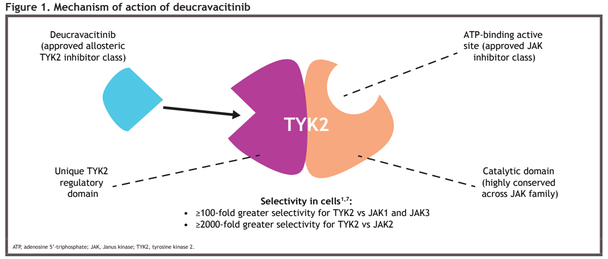
Synopsis

- Tyrosine kinase 2 (TYK2) is an intracellular enzyme that mediates signaling of select inflammatory 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 TYK2 regulatory domain rather than to the catalytic domain where Janus kinase (JAK) 1,2,3 inhibitors bind[1,7] (**Figure 1**), driving its selectivity for TYK2 and representing the first in a new class of oral drugs

Figure 1. Mechanism of action of deucravacitinib



ATP, adenosine 5′-triphosphate; JAK, Janus kinase; TYK2, tyrosine kinase 2.

- Two global, 52-week, phase 3 trials, POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751), in patients with moderate to severe plaque psoriasis showed that deucravacitinib 6 mg once daily (QD) was well tolerated and was significantly more efficacious than placebo and apremilast at Week 16 based on the key endpoints[8,9]:
  - PASI 75 (≥75% reduction from baseline in Psoriasis Area and Severity Index)
  - sPGA 0/1 (static Physician Global Assessment score of 0 [clear] or 1 [almost clear])
- Patients who completed the POETYK PSO-1 and PSO-2 parent trials could enroll in the ongoing POETYK long-term extension (LTE) (NCT04036435) trial and receive open-label deucravacitinib
- Clinical efficacy was previously reported to be maintained well after peak response through 1 year in the parent trials and 2 additional years in the POETYK LTE trial in deucravacitinib-treated patients[10,11]

Objective

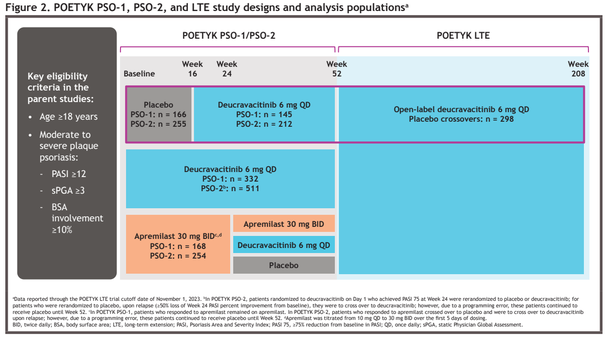
- To evaluate the long-term clinical efficacy of deucravacitinib in patients who crossed over from placebo to deucravacitinib at Week 16 in POETYK PSO-1 and PSO-2 and subsequently enrolled in the POETYK LTE trial

Methods

Study designs

- In the POETYK PSO-1 and PSO-2 trials, adults with moderate to severe plaque psoriasis (PASI ≥12, sPGA ≥3, and body surface area involvement ≥10% at baseline) were randomized 1:2:1 to oral placebo, deucravacitinib 6 mg QD, or apremilast 30 mg twice daily (BID) (**Figure 2**)
- Patients randomized to placebo crossed over to deucravacitinib at Week 16
- At Week 52, eligible patients were allowed to enroll in the POETYK LTE trial and receive open-label deucravacitinib 6 mg QD

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



[a]Data reported through the POETYK LTE trial cutoff date of November 1, 2023. [b]In POETYK PSO-2, patients randomized to deucravacitinib on Day 1 who achieved PASI 75 at Week 24 were rerandomized to placebo or deucravacitinib; 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; however, due to a programming error, these patients continued to receive placebo until Week 52. [d]Apremilast was titrated from 10 mg QD to 30 mg BID over the first 5 days of dosing.
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.

Study population

- Patients from POETYK PSO-1 and PSO-2 who were randomized to oral placebo at baseline and crossed over to deucravacitinib 6 mg QD at Week 16, continued treatment through Week 52, and entered the POETYK LTE trial

Outcomes

- Efficacy was assessed in patients with up to 192 weeks of deucravacitinib exposure (following 16 weeks of placebo) at Week 208 of the study (4 years)
- Achievement of PASI 75, ≥90% reduction from baseline in PASI (PASI 90), 100% reduction from baseline in PASI (PASI 100), sPGA 0/1, and sPGA 0 (clear)

Statistical analysis

- Efficacy was analyzed through the data cutoff date of November 1, 2023 (Week 208)
- 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
  - **Treatment failure rules (TFR)[12]:** 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)[13]:** patients who either discontinued prior to Week 208 or reached Week 208 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

Results

Patients

- Baseline demographics and disease characteristics for patients who received deucravacitinib from Day 1 (n = 513) and those who crossed over from placebo to deucravacitinib in POETYK PSO-1 or PSO-2 and enrolled in the POETYK LTE trial (n = 298) are presented in **Table 1**

Table 1. Baseline patient demographics and disease characteristics

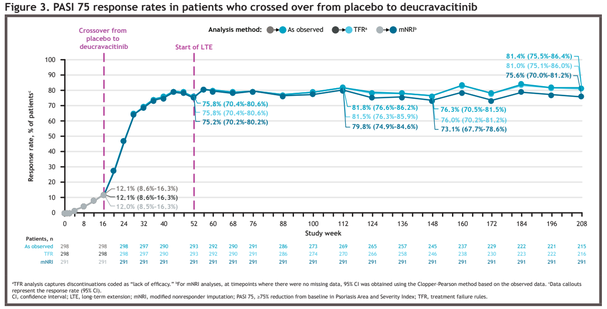
Parameter	POETYK PSO-1 + PSO-2 + LTE Deucravacitinib from Day 1 (n = 513)	POETYK PSO-1 + PSO-2 + LTE Placebo to deucravacitinib (n = 298)
Age, mean (SD), y	46.9 (13.3)	47.6 (13.8)
Weight, mean (SD), kg	89.9 (22.2)	89.4 (20.9)
Female, n (%)	159 (31.0)	91 (30.5)
Race, n (%)		
White	440 (85.8)	250 (83.9)
Asian	64 (12.5)	34 (11.4)
Black or African American	5 (1.0)	8 (2.7)
Other	4 (0.8)	6 (2.0)
Age at disease onset, mean (SD), y	29.0 (14.7)	29.1 (15.1)
Disease duration, mean (SD), y	18.8 (12.6)	19.4 (12.9)
PASI score, mean (SD)	21.1 (7.9)	21.0 (8.4)
sPGA score, n (%)		
3 (moderate)	401 (78.2)	247 (82.9)
4 (severe)	112 (21.8)	51 (17.1)
BSA involvement, mean (SD), %	26.9 (15.8)	25.8 (16.0)
Prior systemic therapy, n (%)	300 (58.5)	185 (62.1)
Nonbiologic	206 (40.2)	139 (46.6)
Biologic	191 (37.2)	105 (35.2)

BSA, body surface area; LTE, long-term extension; PASI, Psoriasis Area and Severity Index; SD, standard deviation; sPGA, static Physician Global Assessment.

PASI response rates

- After placebo-treated patients crossed over to deucravacitinib at Week 16, PASI 75 rates improved through Week 52 and were maintained well through Week 208 (**Figure 3**)
  - Response rates were comparable regardless of imputation method used

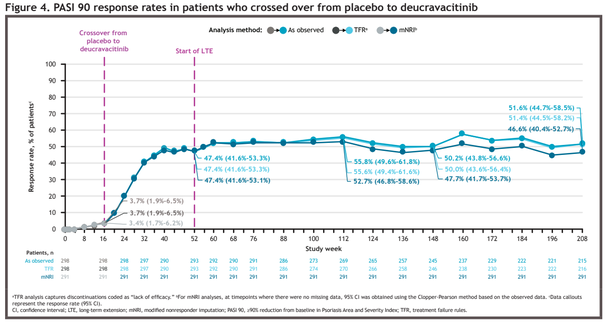
Figure 3. PASI 75 response rates in patients who crossed over from placebo to deucravacitinib



[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 callouts 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.

- PASI 90 and PASI 100 response rates also improved following crossover to deucravacitinib through Week 52 and were maintained well through Week 208, regardless of imputation method (**Figure 4** and **Figure 5**)

Figure 4. PASI 90 response rates in patients who crossed over from placebo to deucravacitinib



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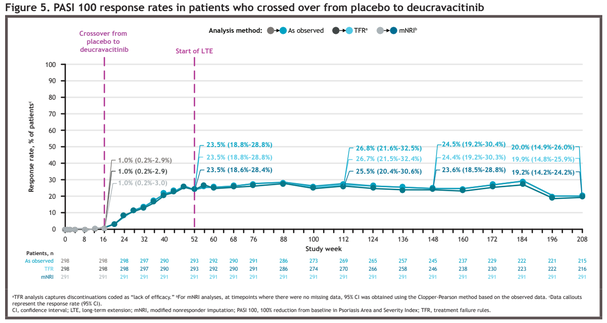
CI, confidence interval; LTE, long-term extension; mNRI, modified nonresponder imputation; PASI 90, ≥90% reduction from baseline in Psoriasis Area and Severity Index; TFR, treatment failure rules.

Figure 5. PASI 100 response rates in patients who crossed over from placebo to deucravacitinib



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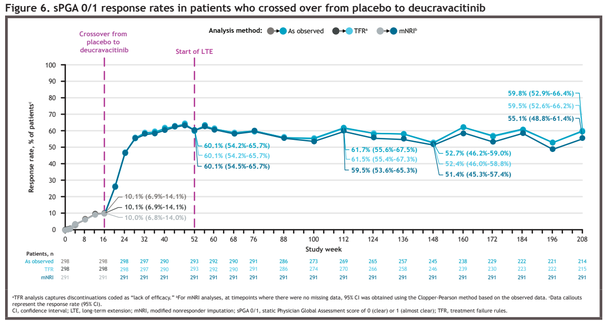
CI, confidence interval; LTE, long-term extension; mNRI, modified nonresponder imputation; PASI 100, 100% reduction from baseline in Psoriasis Area and Severity Index; TFR, treatment failure rules.

sPGA response rates

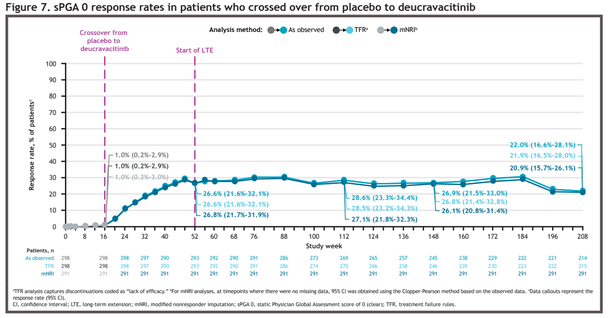
- sPGA 0/1 and sPGA 0 response rates following crossover from placebo to deucravacitinib improved rapidly and were then maintained well through Week 208 (**Figure 6** and **Figure 7**)
  - Response rates were similar regardless of imputation method

Figure 6. sPGA 0/1 response rates in patients who crossed over from placebo to deucravacitinib



[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 callouts represent the response rate (95% CI).
CI, confidence interval; LTE, long-term extension; mNRI, modified nonresponder imputation; sPGA 0/1, static Physician Global Assessment score of 0 (clear) or 1 (almost clear); TFR, treatment failure rules.

Figure 7. sPGA 0 response rates in patients who crossed over from placebo to deucravacitinib



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CI, confidence interval; LTE, long-term extension; mNRI, modified nonresponder imputation; sPGA 0/1, static Physician Global Assessment score of 0 (clear) or 1 (almost clear); TFR, treatment failure rules.

Conclusions

- Long-term maintenance of efficacy in patients who originally received placebo and crossed over to deucravacitinib at Week 16 in POETYK PSO-1 and PSO-2 was observed
  - Long-term efficacy response rates were similar to those observed in patients who received deucravacitinib treatment from Day 1 of the parent studies[14]
- These findings thus replicate previous observations in patients treated with deucravacitinib from Day 1 in the two phase 3 trials[8,9]
- The results further support the effectiveness of long-term treatment with once-daily oral deucravacitinib in patients with moderate to severe plaque psoriasis

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Acknowledgments

- This study was sponsored by Bristol Myers Squibb and was supported by the NIHR Manchester Biomedical Research Centre (NIHR203308)
- Writing and editorial assistance was provided by Kimberly MacKenzie, PhD, of Peloton Advantage, LLC, an OPEN Health company, funded by Bristol Myers Squibb

Disclosures

- **ML:** Research funds on behalf of Mount Sinai: AbbVie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Cara Therapeutics, Dermavant, Incyte, Janssen, Lilly, Ortho Dermatologics, Regeneron, and UCB; Consultant: Almirall, AltruBio, AnaptysBio, Arcutis, Avotres, Boehringer Ingelheim, Brickell Biotech, Bristol Myers Squibb, Castle Biosciences, Cellarion, CorEvitas Psoriasis Registry, Dermavant, EPI Health, Evommune, Forte Biosciences, Galderma, Genentech, Incyte, Leo Pharma, Meiji Seika Pharma, Mindera Health, Pfizer, Seanergy, Strata, Trevi, and Verrica
- **RBW:** Research grants: AbbVie, Almirall, Amgen, Janssen, Leo Pharma, Lilly, Novartis, Pfizer, and UCB; Consulting fees: AbbVie, Almirall, Amgen, Astellas, Boehringer Ingelheim, Dice Therapeutics, GSK, Janssen, Leo Pharma, Lilly, Novartis, Pfizer, Sanofi, UCB, and Union Therapeutics
- **SI:** Grants and/or personal fees: AbbVie, Alexion Pharma, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Daiichi Sankyo, Eisai, Janssen, GSK, Kaken, Kyowa Kirin, Leo Pharma, Lilly, Maruho, Novartis, Sun Pharma, Taiho Yakuhin, Torii Yakuhin, and UCB
- **JB:** Research funds payable to the Psoriasis Treatment Center of New Jersey: AbbVie, Amgen, Arcutis, Boehringer Ingelheim, Bristol Myers Squibb/Celgene, CorEvitas Psoriasis Registry, Dermavant, Dermira/UCB, Glenmark, Janssen Biotech, Kadmon, Leo Pharma, Lilly, Lycera, Menlo Therapeutics, Novartis, Pfizer, Regeneron, Sun Pharma, Taro, and Valeant; Consultant: AbbVie, Amgen, Janssen Biotech, Lilly, Novartis, Sun Pharma, and Valeant; Speaker: AbbVie, Celgene, Janssen Biotech, Lilly, and Novartis
- **AWA:** Research investigator, scientific advisor, and/or speaker: AbbVie, Almirall, Arcutis, Aslan, Beiersdorf, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Dermira, EPI Health, Incyte, Janssen, Leo Pharma, Lilly, Mindera Health, Nimbus, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi, Sun Pharma, and UCB
- **TP:** Advisory board and consulting fees: AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Galderma, Incyte, Janssen, Leo Pharma, Lilly, Novartis, Pfizer, Sanofi Genzyme, Sun Pharma, and UCB
- **SB and TS:** Employees at the time of study conduct and shareholders: Bristol Myers Squibb
- **MJC:** Employee and shareholder: Bristol Myers Squibb
- **KH:** Consultant: Bristol Myers Squibb via Syneos Health
- **DT:** Research support and principal investigator (clinical trial funds to institution): AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Galderma, Janssen-Cilag, Leo Pharma, Lilly, Novartis, Pfizer, Regeneron, Sanofi, and UCB; Consultant: AbbVie, Almirall, Boehringer Ingelheim, Bristol Myers Squibb, Leo Pharma, Novartis, Pfizer, and UCB; Lecturer: AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Janssen, Leo Pharma, Lilly, Novartis, Pfizer, Roche-Posay, Sanofi, Target RWE, and UCB; Scientific advisory board: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Janssen-Cilag, Leo Pharma, Lilly, Novartis, Pfizer, Sanofi, and UCB
- **AB:** Speaker (with honoraria): Lilly and UCB; Scientific adviser (received honoraria): AbbVie, Abcentra, Aclaris, Affibody, Aligos, Almirall, Alumis, Amgen, Anaptysbio, Apogee, Arcutis, Arena, Aslan, Athenex, Bluefin Biomedicine, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Celldex, CTI BioPharma, Dermavant, EcoR1, Escient, Evelo, Evommune, Forte, Galderma, Highlightll Pharma, Incyte, InnoventBio, Janssen, Landos, Leo Pharma, Lilly, Lipidio, Microbion, Merck, Monte Rosa Therapeutics, Nektar, Novartis, Overtone Therapeutics, Paragon, Pfizer, Q32 Bio, Rani, Rapt, Regeneron, Sanofi Genzyme, Spherix Global Insights, Sun Pharma, Takeda, TLL Pharmaceutical, TrialSpark, UCB, Union, Ventyx, Viblome, and Xencor; Clinical study investigator (institution has received clinical study funds): AbbVie, Aclaris, Allakos, Almirall, Alumis, Amgen, Arcutis, Athenex, Boehringer Ingelheim, Bristol Myers Squibb, Concert, Dermavant, DermBiont, Evelo, Evommune, Galderma, Incyte, Janssen, Leo Pharma, Lilly, Merck, Novartis, Pfizer, Regeneron, Sanofi, Sun Pharma, Takeda, UCB, and Ventyx; Stock owner: Lipidio and Oruka

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