Deucravacitinib long-term efficacy in Week 16 placebo crossovers: 3-year results from the POETYK PSO program

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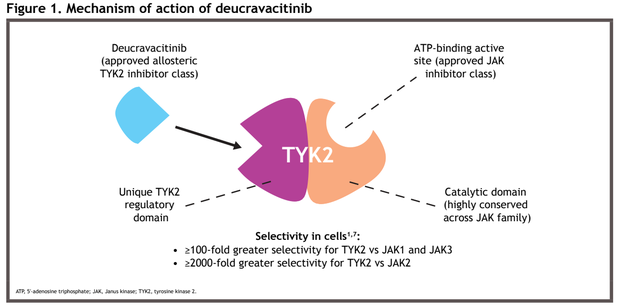
Synopsis

- 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



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

- Deucravacitinib was significantly more efficacious than placebo or apremilast and was well tolerated in patients with moderate to severe plaque psoriasis in the global, 52-week, phase 3 POETYK PSO-1 and PSO-2 trials[8,9]
- All patients who completed POETYK PSO-1 and PSO-2 were eligible to enroll in the ongoing POETYK long-term extension (LTE) trial
- Patients treated with continuous deucravacitinib from Day 1 in POETYK PSO-1 and PSO-2 maintained long-term efficacy responses through 3 years (Week 148) of the POETYK LTE trial[10]

Objective

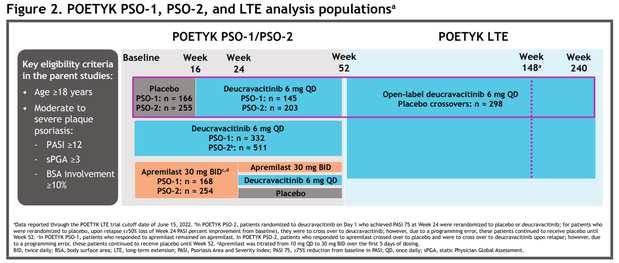
- To examine the long-term clinical efficacy of deucravacitinib among patients who crossed over from placebo at Week 16 in POETYK PSO-1 and PSO-2 and subsequently enrolled in the POETYK LTE trial

Methods

Study designs

- In POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751), eligible patients were randomized 1:2:1 to oral placebo, deucravacitinib 6 mg once daily (QD), or apremilast 30 mg twice daily (BID) (**Figure 2**)
- Patients randomized to placebo at baseline crossed over to deucravacitinib 6 mg QD at Week 16 in both trials
- At Week 52, patients could enter the POETYK LTE (NCT04036435) trial and receive open-label deucravacitinib 6 mg QD

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



[a]Data reported through the POETYK LTE trial cutoff date of June 15, 2022. [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 response 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.

Outcomes

- Efficacy was assessed in patients with up to 132 weeks of deucravacitinib exposure (following 16 weeks of placebo) at Week 148 of the study (data cutoff, June 15, 2022), using:
  - PASI 75: ≥75% reduction from baseline in Psoriasis Area and Severity Index (PASI)
  - PASI 90: ≥90% reduction from baseline in PASI
  - sPGA 0/1: static Physician Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline

Statistical analysis

- Efficacy was analyzed through the cutoff date of June 15, 2022
- 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)**[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
- The Clopper-Pearson method was used to calculate 95% confidence intervals (CIs)
  - For mNRI, the Clopper-Pearson method was used only if there were no missing data; otherwise, the Rubin's method was used

Results

Patients

- Baseline demographics and disease characteristics of patients who crossed over from placebo to deucravacitinib at Week 16 in both POETYK PSO-1 and PSO-2 and went on to enroll in the POETYK LTE trial (n = 298) are shown in **Table 1**

Table 1. Baseline patient demographics and disease characteristics

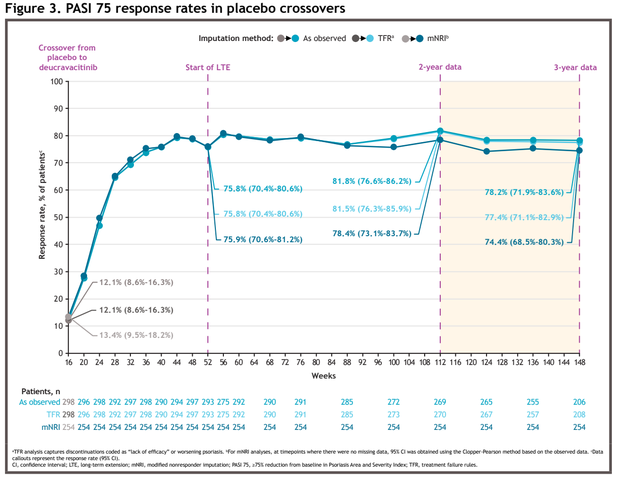
Parameter	POETYK PSO-1 + PSO-2 + LTE Placebo to deucravacitinib (n = 298)
Age, mean (SD), y	47.6 (13.8)
Weight, mean (SD), kg	89.4 (20.9)
Female, n (%)	91 (30.5)
Race, n (%)	
White	250 (83.9)
Asian	34 (11.4)
Black or African American	8 (2.7)
Other	6 (2.0)
Age at disease onset, mean (SD), y	29.1 (15.1)
Disease duration, mean (SD), y	19.4 (12.9)
PASI score, mean (SD)	21.0 (8.4)
sPGA score, n (%)	
3 (moderate)	247 (82.9)
4 (severe)	51 (17.1)
BSA involvement, mean (SD), %	25.8 (16.0)
Prior systemic therapy, n (%)	185 (62.1)
Nonbiologic	139 (46.6)
Biologic	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.

Efficacy

- After crossing over to deucravacitinib at Week 16, PASI 75 response rates improved and were maintained through Week 148 (**Figure 3**)
  - Response rates were similar regardless of imputation methodology

Figure 3. PASI 75 response rates in placebo crossovers

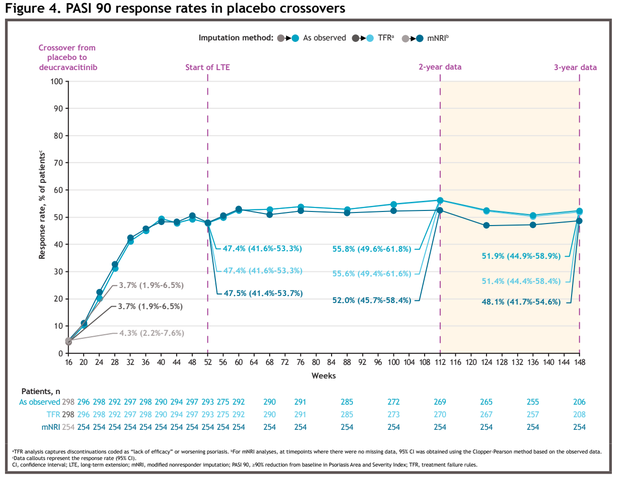


[a]TFR analysis captures discontinuations coded as "lack of efficacy" or worsening psoriasis. [b]For mNRI analyses, at timepoints where there were no missing data, 95% CI was obtained using the Clopper-Pearson method based on the observed data. [c]Data callouts represent the response rate (95% CI).
CI, 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.

Efficacy

- PASI 90 response rates also improved and were durable through Week 148 following crossover to deucravacitinib regardless of imputation method (**Figure 4**)

Figure 4. PASI 90 response rates in placebo crossovers



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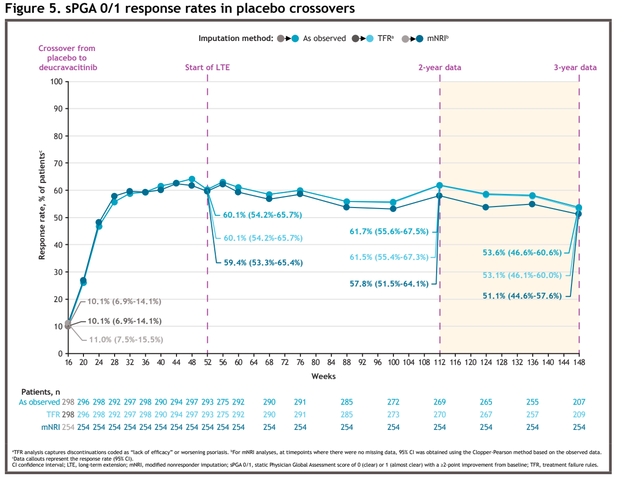
CI, confidence interval; LTE, long-term extension; mNRI, modified nonresponder imputation; PASI 90, ≥90% reduction from baseline in Psoriasis Area and Severity Index; TFR, treatment failure rules.

Efficacy

- sPGA 0/1 response rates following crossover from placebo to deucravacitinib rapidly improved and were then maintained through Week 148 (**Figure 5**)
  - Responses were similar regardless of imputation methodology

Figure 5. sPGA 0/1 response rates in placebo crossovers



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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) with a ≥2-point improvement from baseline; TFR, treatment failure rules.

Conclusions

- Deucravacitinib treatment was associated with long-term maintenance of efficacy in patients who had originally received placebo and had crossed over to deucravacitinib at Week 16 in POETYK PSO-1 and PSO-2
  - Long-term efficacy response rates were similar to those observed in patients who were treated with deucravacitinib from Day 1 of the parent studies[10]
- These findings further support once-daily oral deucravacitinib as being an effective long-term treatment for patients with moderate to severe plaque psoriasis

References

1. Burke JR, et al. *Sci Transl Med*. 2019;11:eaaw1736. **2.** Sotyktu [package insert]. Princeton, NJ, USA: Bristol Myers Squibb; September 2022. **3.** Sotyktu [summary of product characteristics]. Dublin, Ireland: Bristol Myers Squibb Pharmaceutical Operations; March 2023. **4.** Sotyktu [package insert]. Tokyo, Japan: Bristol Myers Squibb K.K.; September 2022. **5.** Sotyktu [product information]. Mulgrave, VIC, Australia: Bristol Myers Squibb Australia Pty. Ltd.; December 2022. **6.** Sotyktu [product monograph]. Montreal, QC, Canada: Bristol Myers Squibb Canada Co.; November 2022. **7.** Wrobleski ST, et al. *J Med Chem*. 2019;62:8973-8995. **8.** Armstrong AW, et al. *J Am Acad Dermatol*. 2023;88:29-39. **9.** Strober B, et al. *J Am Acad Dermatol*. 2023;88:40-51. **10.** Armstrong AW, et al. Presented at the 32nd EADV Congress; 11-14 October 2023; Berlin, Germany. **11.** Reich K, et al. *Br J Dermatol*. 2021;185:1146-1159. **12.** Papp K, et al. *Br J Dermatol*. 2021;185:1135-1145.

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