Deucravacitinib long-term efficacy with continuous treatment in plaque psoriasis: 2-year results from the phase 3 POETYK PSO program

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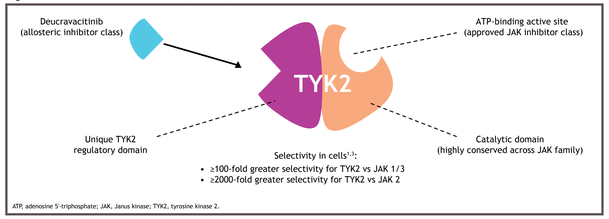
Synopsis

- Tyrosine kinase 2 (TYK2) is an intracellular enzyme that mediates signaling of cytokines (eg, interleukin-23, Type I interferons) involved in psoriasis pathogenesis[1]
- Deucravacitinib, an oral, selective, allosteric TYK2 inhibitor, is approved by the US Food and Drug Administration for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy[2]
- Deucravacitinib binds to the TYK2 regulatory domain rather than to the more conserved catalytic domain where Janus kinase (JAK) 1/2/3 inhibitors bind[1] (**Figure 1**)

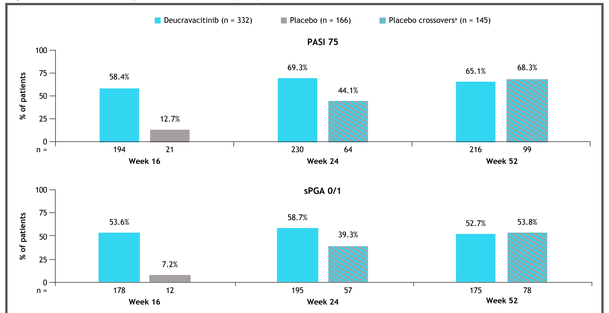
Figure 1. Mechanism of action of deucravacitinib



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

- Deucravacitinib was studied at 6 mg once daily in two global phase 3 pivotal trials, POETYK PSO-1 (NCT03624127) and PSO-2 (NCT03611751)[4,5]
  - Only POETYK PSO-1 included a continuous deucravacitinib treatment arm from Day 1 to Week 52
  - Placebo patients crossed over to deucravacitinib at Week 16 in both trials
- POETYK PSO-1 demonstrated (**Figure 2**[a]):
  - Significantly greater response rates for ≥75% reduction from baseline in Psoriasis Area and Severity Index (PASI 75) and static Physician's Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline (sPGA 0/1) at Week 16 with deucravacitinib vs placebo and apremilast[4]
  - Clinical efficacy that was maintained through Week 52 with continuous deucravacitinib treatment[7]
- Patients completing the POETYK PSO-1 trial could enroll in the POETYK long-term extension (LTE) trial and receive open-label deucravacitinib 6 mg once daily
- The 2-year safety profile of deucravacitinib in the POETYK LTE trial was consistent with that observed from Weeks 0–52 of the POETYK PSO-1 and PSO-2 trials, and there were no emerging safety signals[8]

Figure 2. Clinical efficacy in POETYK PSO-1 (NRI)[6]



[a]Patients initially randomized to placebo crossed over to deucravacitinib at Week 16.
NRI, nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index; sPGA 0/1, static Physician's Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline.

Objectives

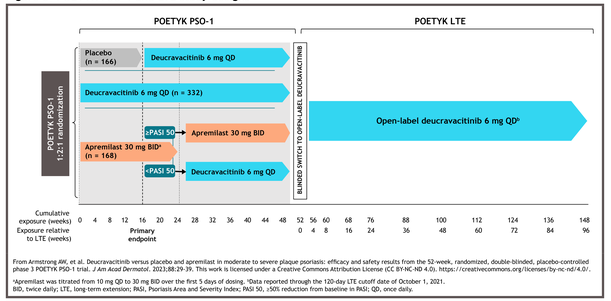
- To examine long-term efficacy responses in POETYK PSO-1 patients who:
  - Received continuous deucravacitinib treatment from Day 1 and entered the POETYK LTE
  - Achieved PASI 75 response on deucravacitinib at Week 16, continued on deucravacitinib, and entered the POETYK LTE

Methods

Study designs and analysis populations

- The study designs for the POETYK PSO-1 and LTE trials are illustrated in **Figure 3**
- Patients meeting the following criteria were eligible to enroll in the study:
  - Age ≥18 years
  - Diagnosis of moderate to severe plaque psoriasis
    - Baseline PASI ≥12, sPGA ≥3, and body surface area involvement ≥10%
- Patient randomization in POETYK PSO-1 was stratified by geographic region, body weight, and prior biologic use
- Analysis populations were defined as:
  - **Continuous deucravacitinib treatment from baseline:** patients who received continuous deucravacitinib from Day 1 (Week 0) and entered the POETYK LTE
    - Since results with nonresponder imputation (NRI) were shown earlier from Weeks 0-52,[4,5] only Weeks 52-112 results are shown here
  - **Continuous deucravacitinib Week 16 PASI 75 responders:** patients who received continuous deucravacitinib from Day 1, achieved PASI 75 at Week 16, and entered the POETYK LTE

Figure 3. POETYK PSO-1 and LTE study designs



From Armstrong AW, et al. Deucravacitinib versus placebo and apremilast in moderate to severe plaque psoriasis: efficacy and safety results from the 52-week, randomized, double-blinded, placebo-controlled phase 3 POETYK PSO-1 trial. J Am Acad Dermatol. 2023;88:29-39. This work is licensed under a Creative Commons Attribution License (CC BY-NC-ND 4.0). https://creativecommons.org/licenses/by-nc-nd/4.0/.

[a]Apremilast was titrated from 10 mg QD to 30 mg BID over the first 5 days of dosing. [b]Data reported through the 120-day LTE cutoff date of October 1, 2021.
BID, twice daily; LTE, long-term extension; PASI, Psoriasis Area and Severity Index; PASI 50, ≥50% reduction from baseline in PASI; QD, once daily.

Outcome measures

- Efficacy was assessed in patients with up to 112 weeks (=2 years) of continuous deucravacitinib exposure as of the cutoff date of October 1, 2021
  - PASI 75
  - ≥90% reduction from baseline in PASI (PASI 90)
  - sPGA 0/1
- In addition to the as-observed analysis, 2 methods of imputation for missing data were used to evaluate long-term efficacy:
  - **Treatment failure rules (TFR)**[9]: patients who discontinued treatment or the study due to worsening of psoriasis or lack of efficacy were imputed as nonresponders
  - **Modified NRI (mNRI)**[10]: multiple imputation analysis was used for imputation of missing values, and patients who discontinued due to worsening of psoriasis were imputed as nonresponders
    - Only patients who discontinued or had reached Week 112 by the cutoff date of October 1, 2021, were included

Results

Baseline patient demographics and disease characteristics

- Baseline demographics and disease characteristics for POETYK PSO-1 patients randomized to deucravacitinib who rolled over to the POETYK LTE are presented in **Table 1**
- A total of 332 patients were randomized to deucravacitinib
  - 265 patients completed the study and entered the POETYK LTE
  - 173 PASI 75 responders at Week 16 entered the POETYK LTE

Table 1. Baseline patient demographics and disease characteristics

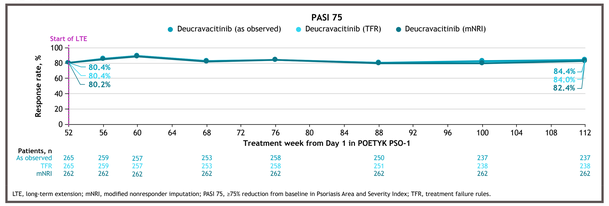
	Patients randomized to deucravacitinib entering POETYK LTE	
Parameter	Total (N = 265)	Week 16 PASI 75 responders (n = 173)
Age, mean (SD), y	46.0 (13.7)	45.2 (14.0)
Weight, mean (SD), kg	87.0 (22.2)	84.7 (22.4)
Female, n (%)	87 (32.8)	58 (33.5)
Race, n (%)		
White	211 (79.6)	133 (76.9)
Asian	51 (19.2)	37 (21.4)
Black or African American	1 (0.4)	1 (0.6)
Other	2 (0.8)	2 (1.2)
Age at disease onset, mean (SD), y	29.8 (15.1)	29.8 (15.1)
Disease duration, mean (SD), y	17.0 (12.2)	16.2 (11.8)
PASI, mean (SD)	21.8 (8.3)	22.6 (8.9)
sPGA, n (%)		
3 (moderate)	208 (78.5)	129 (74.6)
4 (severe)	57 (21.5)	44 (25.4)
BSA involvement, mean (SD), %	27.2 (15.6)	28.3 (15.6)

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

PASI 75 and PASI 90 outcomes

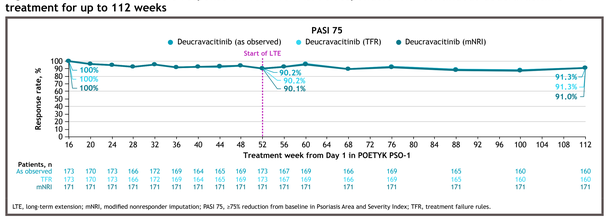
- Overall, PASI 75 responses were consistent from Weeks 52-112 in all patients with continuous deucravacitinib treatment (**Figure 4**)
- PASI 75 response rates were maintained from Weeks 16-112 in Week 16 PASI 75 responders (**Figure 5**)
- Overall, PASI 90 responses were consistent from Weeks 52-112 (**Figure 6**)
- PASI 90 response rates were maintained from Weeks 16-112 in Week 16 PASI 75 responders (**Figure 7**)

Figure 4. PASI 75 response from Week 52 in all patients with continuous deucravacitinib treatment for up to 112 weeks



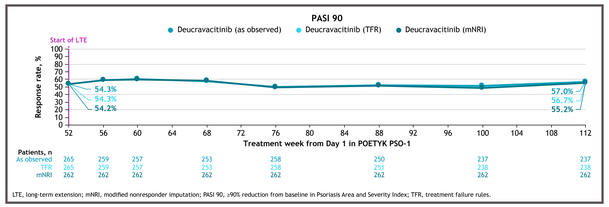
LTE, long-term extension; mNRI, modified nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index; TFR, treatment failure rules.

Figure 5. Maximum of PASI 75 response in Week 16 PASI 75 responders with continuous deucravacitinib treatment for up to 112 weeks



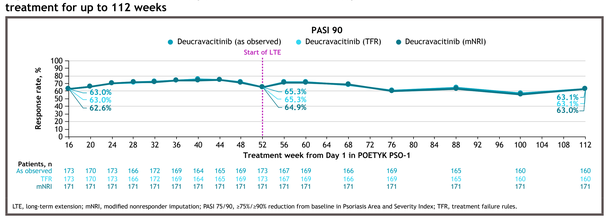
LTE, long-term extension; mNRI, modified nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index; TFR, treatment failure rules.

Figure 6. PASI 90 response from Week 52 in all patients with continuous deucravacitinib treatment for up to 112 weeks



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 7. Maximum of PASI 90 response in Week 16 PASI 75 responders with continuous deucravacitinib treatment for up to 112 weeks

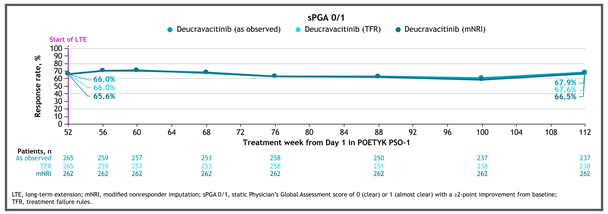


LTE, long-term extension; mNRI, modified nonresponder imputation; PASI 75/90, ≥75%/≥90% reduction from baseline in Psoriasis Area and Severity Index; TFR, treatment failure rules.

sPGA 0/1 outcomes

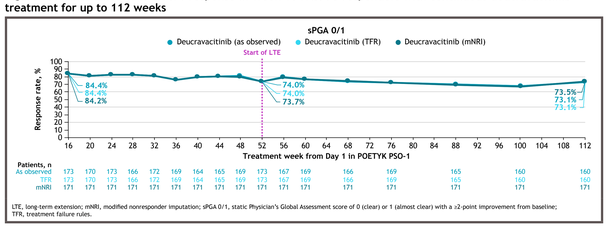
- Overall, sPGA 0/1 responses were consistent from Weeks 52-112 (**Figure 8**)
- sPGA 0/1 responses were maintained from Weeks 16-112 in Week 16 PASI 75 responders (**Figure 9**)

Figure 8. sPGA 0/1 response from Week 52 in all patients with continuous deucravacitinib treatment for up to 112 weeks



LTE, long-term extension; mNRI, modified nonresponder imputation; sPGA 0/1, static Physician's Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline; TFR, treatment failure rules.

Figure 9. Maximum of sPGA 0/1 response in Week 16 PASI 75 responders with continuous deucravacitinib treatment for up to 112 weeks



LTE, long-term extension; mNRI, modified nonresponder imputation; sPGA 0/1, static Physician's Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline; TFR, treatment failure rules.

Conclusions

- Continuous treatment with deucravacitinib for up to 112 weeks resulted in durable efficacy
  - High efficacy responses in patients from the POETYK PSO-1 study who received continuous deucravacitinib from Day 1 to Week 52 have been previously reported[4]
  - Clinical outcomes were consistent from Weeks 52-112 in these patients who entered the POETYK LTE
  - Clinical efficacy responses were maintained well through Week 112 among those who achieved PASI 75 at Week 16 with deucravacitinib treatment
- Deucravacitinib, a once-daily oral drug, has the potential to become a treatment of choice and new standard of care for patients who require systemic therapy for their moderate to severe plaque psoriasis

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1. Burke JR, et al. *Sci Transl Med.* 2019;11:eaaw1736. **2.** SOTYKTU™ (deucravacitinib) [package insert]. Princeton, NJ, USA: Bristol-Myers Squibb Company; September 2022. **3.** Wrobleski ST, et al. *J Med Chem.* 2019;62:8973-8995. **4.** Armstrong AW, et al. *J Am Acad Dermatol.* 2023;88:40-51. **5.** Armstrong A, et al. Presented at the Annual Meeting of the AAD; April 23-25, 2021.**7.** Warren RB, et al. Presented at the 30th EADV Congress; September 29-October 2, 2021. **8.** Warren RB, et al. Presented at the EADV Spring Symposium; May 12-14, 2022. **9.** Reich K, et al. *Br J Dermatol.* 2021;185:1146-1159. **10.** Papp K, et al. *Br J Dermatol.* 2021;185:1135-1145.

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