Deucravacitinib long-term efficacy with continuous treatment in plaque psoriasis: 2-year results from the phase 3 POETYK PSO-1 and PSO-2 trials

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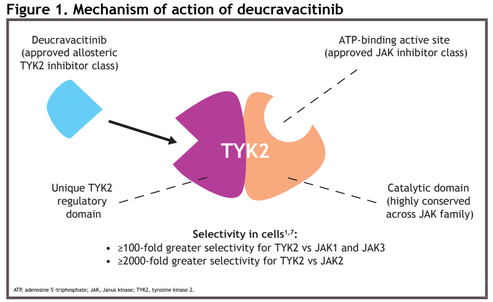
Synopsis

- Tyrosine kinase 2 (TYK2) is an intracellular enzyme that mediates signaling of cytokines (eg, interleukin-23, Type I interferons) that 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**), representing the first in a new class of small molecules
- Two phase 3 trials, POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751), demonstrated that deucravacitinib was significantly more efficacious than placebo (based on the coprimary endpoints of ≥75% reduction from baseline in Psoriasis Area and Severity Index [PASI 75] and static Physician Global Assessment score of 0 [clear] or 1 [almost clear] with a ≥2-point improvement from baseline [sPGA 0/1]) and apremilast at Week 16 and was well tolerated in patients with moderate to severe plaque psoriasis[8,9]
  - Clinical responses were maintained through 52 weeks in patients who received continuous deucravacitinib treatment from baseline[10]
- Patients completing POETYK PSO-1 and PSO-2 could enroll in the POETYK long-term extension (LTE) trial (NCT04036435)

Figure 1. Mechanism of action of deucravacitinib



Objectives

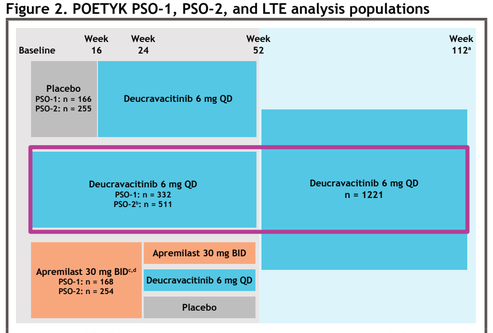
- To evaluate long-term efficacy responses (up to ≈2 years) in patients who were randomized to deucravacitinib in POETYK PSO-1 or PSO-2 and who entered the POETYK LTE trial:
  - Patients who received continuous deucravacitinib treatment from baseline
  - Patients who received continuous deucravacitinib treatment from baseline and who achieved PASI 75 at Week 24

Methods

Study designs

- POETYK PSO-1 and PSO-2 were 52-week, phase 3, double-blind trials that randomized adults with moderate to severe plaque psoriasis 1:2:1 to oral placebo, deucravacitinib 6 mg once daily, or apremilast 30 mg twice daily (**Figure 2**)
  - Patients were diagnosed with moderate to severe plaque psoriasis based on PASI ≥12, sPGA ≥3, and body surface area (BSA) involvement ≥10%
- At Week 52, patients were eligible to enroll in the POETYK LTE trial and receive open-label deucravacitinib 6 mg once daily

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



[a]Data are reported through the POETYK LTE trial cutoff date of October 1, 2021. [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 (achievement of sPASI 50) 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; LTE, long-term extension; PASI, Psoriasis Area and Severity Index; PASI 50/75, ≥50%/≥75% reduction from baseline in PASI; QD, once daily.

Efficacy population

- Pooled POETYK PSO-1 and PSO-2 patient populations
  - Overall analysis: patients who received continuous deucravacitinib treatment from Day 1 until Week 112
  - Responder analysis: Week 24 PASI 75 responders who received continuous deucravacitinib treatment from Day 1 until Week 112
    - Week 24 was chosen as the time point for peak responses observed with deucravacitinib
    - In POETYK PSO-2, only patients who achieved PASI 75 and continued on deucravacitinib at Week 24 (50% of PASI 75 responders based on study design) were analyzed

Efficacy outcomes

- Achievement of PASI 75, ≥90% reduction from baseline in PASI (PASI 90), and sPGA 0/1

Statistical analysis

- Analyses were conducted through the data cutoff date of October 1, 2021 (Week 112)
- Consistent with recommendations for assessing long-term efficacy outcomes in psoriasis clinical trials,[11] two methods for imputation of missing data were used as sensitivity analyses in addition to as observed values:
  - **Modified nonresponder imputation (mNRI)**[12]: patients who either discontinued treatment prior to Week 112 or reached Week 112 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
  - **Treatment failure rules (TFR)**[13]: patients who discontinued treatment due to lack of efficacy or worsening of psoriasis were imputed as nonresponders; all other missing data were not imputed

Results

Baseline patient demographics and disease characteristics

- A total of 513 patients received continuous deucravacitinib treatment from Day 1 in POETYK PSO-1/PSO-2 until Week 112 in POETYK LTE (**Table 1**), including 336 patients who had achieved PASI 75 at Week 24 (PSO-1, n = 203; PSO-2, n = 133)
  - Baseline patient demographics and disease characteristics were similar in both groups

Table 1. Baseline patient demographics and disease characteristics

Parameter	Deucravacitinib (n = 513)	Deucravacitinib Week 24 PASI 75 responders (n = 336)
Age, mean (SD), y	46.9 (13.3)	46.3 (13.8)
Weight, mean (SD), kg	89.9 (22.2)	86.6 (22.1)
Female, n (%)	159 (31.0)	122 (36.3)
Race, n (%)		
White	440 (85.8)	284 (84.5)
Asian	64 (12.5)	47 (14.0)
Black or African American	5 (1.0)	1 (0.3)
Other	4 (0.8)	4 (1.2)
Age at disease onset, mean (SD), y	29.0 (14.7)	28.8 (15.3)
Disease duration, mean (SD), y	18.8 (12.6)	18.3 (13.0)
PASI score, mean (SD)	21.1 (7.9)	21.3 (8.0)
sPGA score, n (%)		
3 (moderate)	401 (78.2)	265 (78.9)
4 (severe)	112 (21.8)	71 (21.1)
BSA involvement, mean (SD), %	26.9 (15.8)	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.

Efficacy of continuous deucravacitinib treatment from Day 1

- High clinical response rates achieved at Week 52 in POETYK PSO-1/PSO-2 were maintained at Week 112 in the POETYK LTE trial among patients receiving continuous deucravacitinib treatment from Day 1 (mNRI) (**Figures 3-5**)
  - PASI 75: Week 52, 73.0%; Week 112, 76.2%
  - PASI 90: Week 52, 46.3%; Week 112, 48.3%
  - sPGA 0/1: Week 52, 58.5%; Week 112, 58.4%
- Results were consistent regardless of data imputation methodology (mNRI, TFR, as-observed values)

Figure 3. PASI 75 response rates in patients who received continuous deucravacitinib from baseline until Week 112

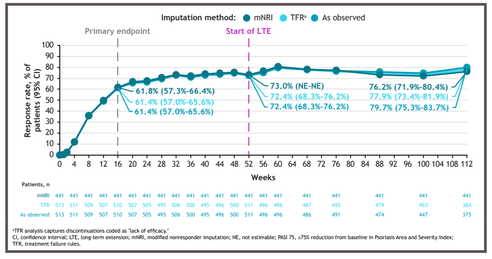


Figure 4. PASI 90 response rates in patients who received continuous deucravacitinib treatment from baseline until Week 112

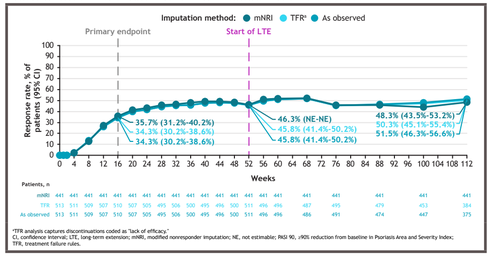
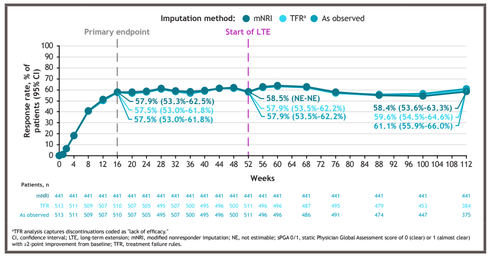


Figure 5. sPGA 0/1 response rates in patients who received continuous deucravacitinib treatment from baseline until Week 112



Efficacy in Week 24 PASI 75 responders

- High response rates at Week 52 in POETYK PSO-1/PSO-2 were maintained at Week 112 in the POETYK LTE trial among patients receiving continuous deucravacitinib treatment from Day 1 who had achieved PASI 75 at Week 24 (mNRI) (**Figures 6-8**)
  - PASI 75: Week 52, 90.3%; Week 112, 89.2%
  - PASI 90: Week 52, 62.1%; Week 112, 61.1%
  - sPGA 0/1: Week 52, 73.8%; Week 112, 70.5%
- Results were consistent regardless of data imputation methodology

Figure 6. PASI 75 response rates in Week 24 PASI 75 responders who received continuous deucravacitinib treatment from baseline until Week 112

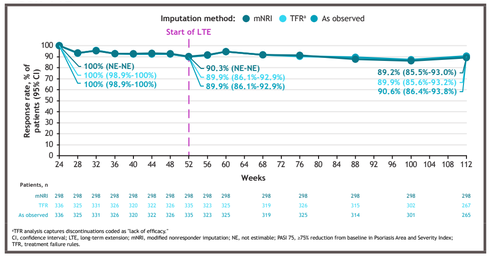


Figure 7. PASI 90 response rates in Week 24 PASI 75 responders who received continuous deucravacitinib treatment from baseline until Week 112

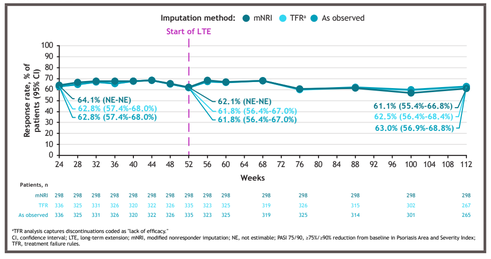
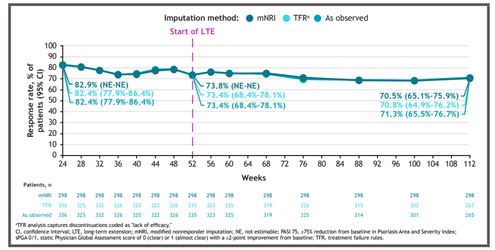


Figure 8. sPGA 0/1 response rates in Week 24 PASI 75 responders who received continuous deucravacitinib treatment from baseline until Week 112



Conclusions

- Clinical efficacy was maintained through 2 years in the pooled POETYK PSO-1/PSO-2 trials in deucravacitinib-treated patients who entered the POETYK LTE trial
  - High clinical efficacy responses (PASI 75, PASI 90, and sPGA 0/1) achieved at Week 52 were maintained overall through Week 112 in patients who received continuous deucravacitinib treatment from Day 1 and in patients who achieved PASI 75 at Week 24
  - Efficacy results were consistent across evaluated data imputation methods, including mNRI, TFR, and as-observed values
- These findings, which are consistent with previous results,[8-10] provide additional support that deucravacitinib is an efficacious long-term treatment for patients with moderate to severe plaque psoriasis

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