

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

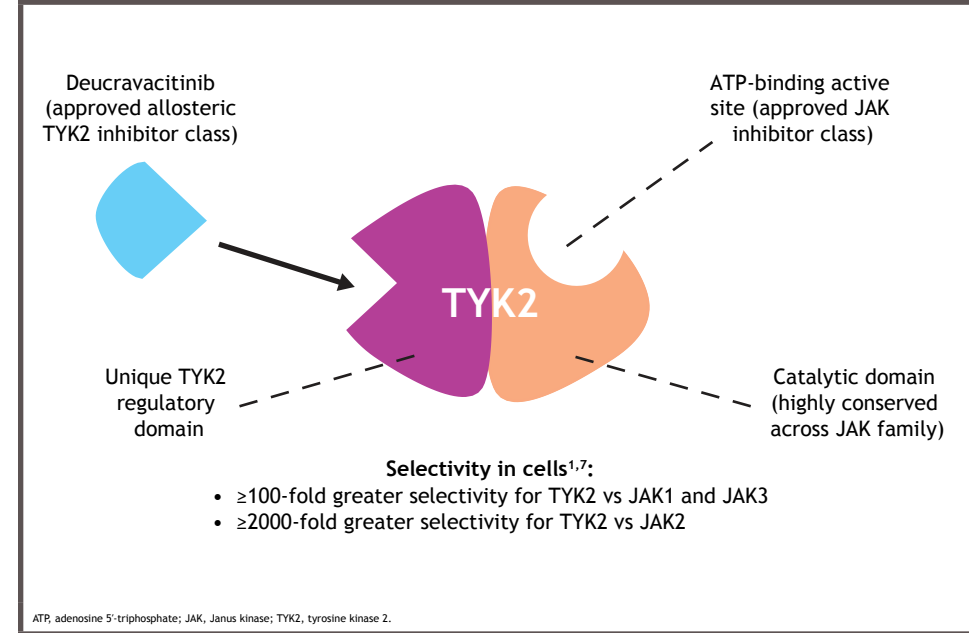
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Introduction

- Tyrosine kinase 2 (TYK2) is an intracellular enzyme that mediates signaling of cytokines (eg, interleukin-23, Type I interferons) that are involved in psoriasis pathogenesis¹
- 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 therapy²⁻⁶
- 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

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 signals¹⁰

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

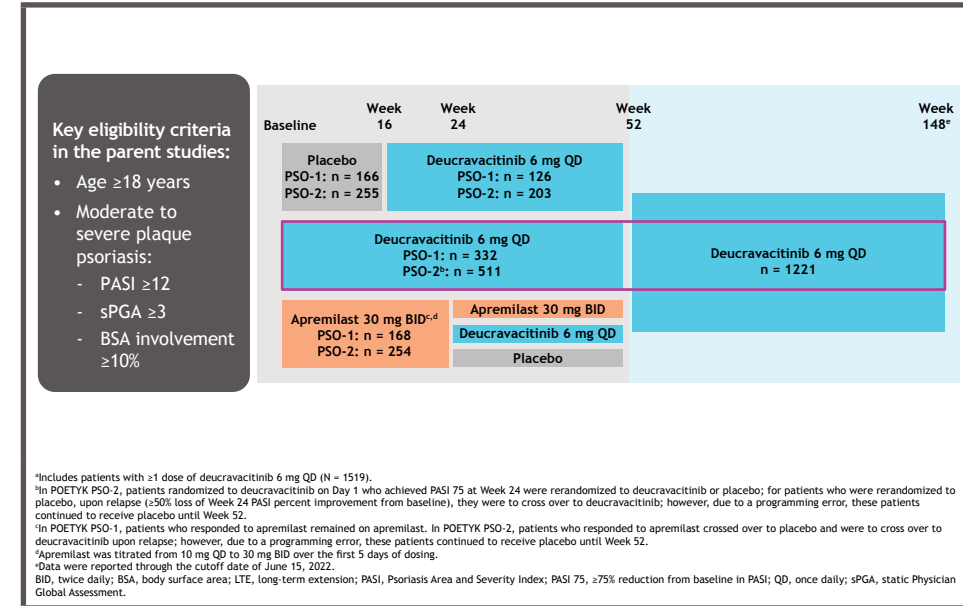
Methods

- 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
- 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



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/m ²	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 signals¹³

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

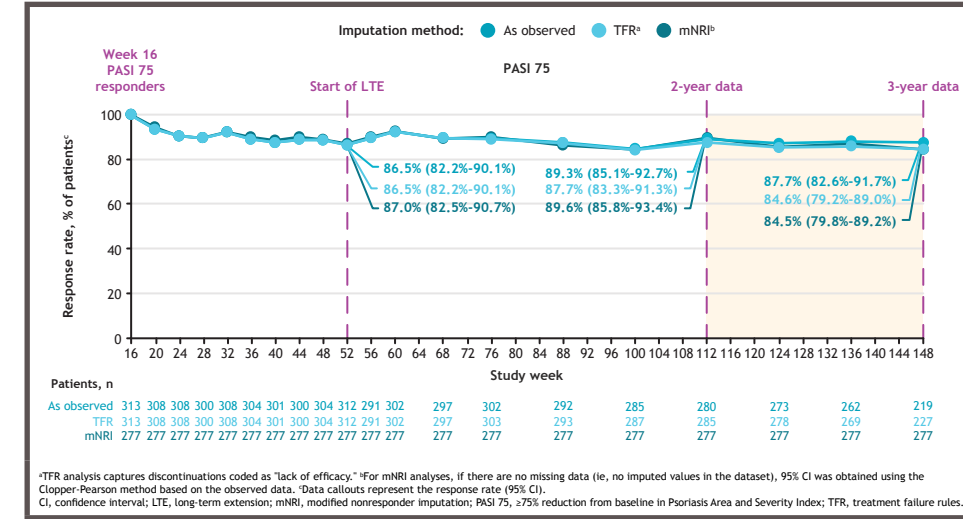


Figure 4. PASI 75 response rates in Week 24 PASI 75 responders

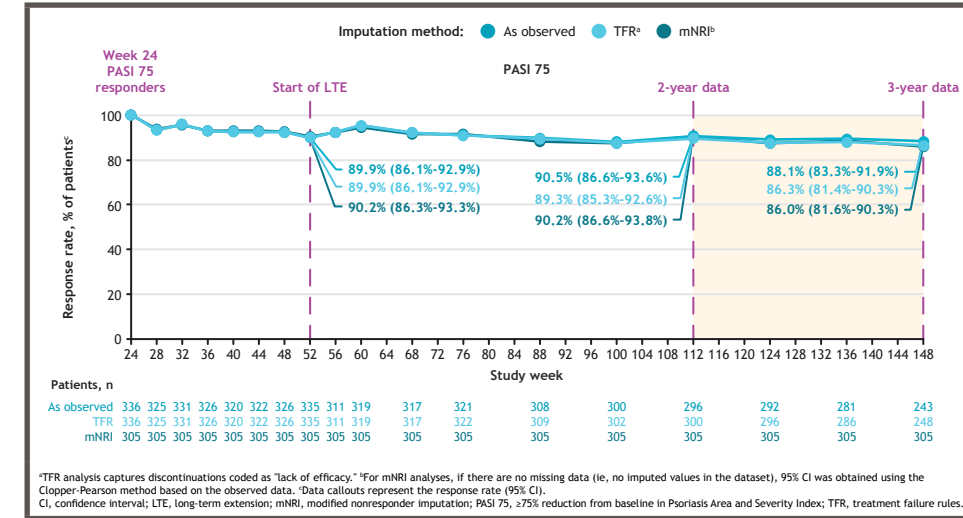


Figure 5. PASI 90 response rates in Week 16 PASI 75 responders

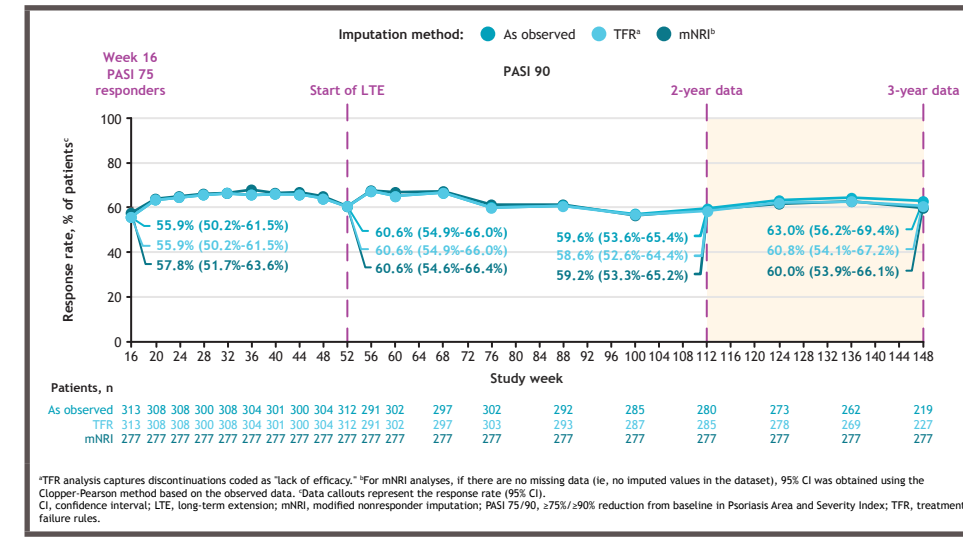


Figure 6. PASI 90 response rates in Week 24 PASI 75 responders

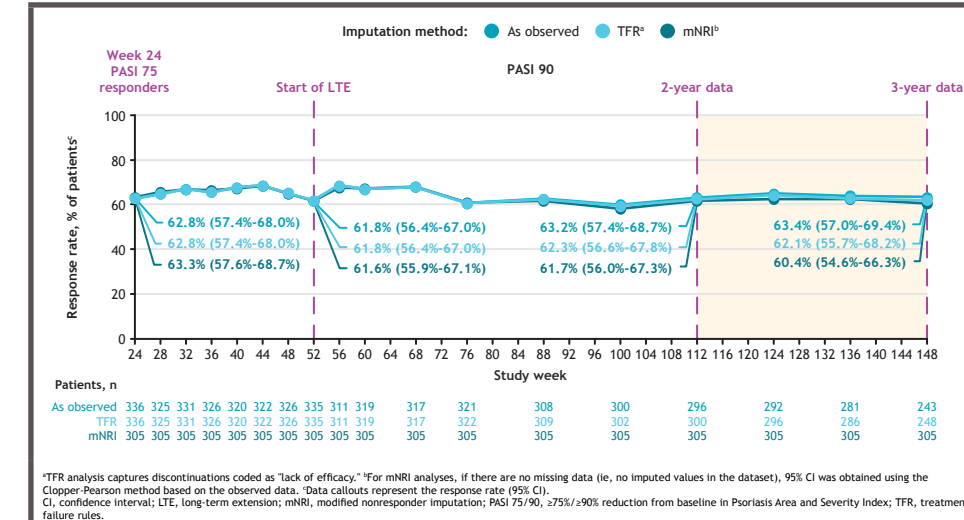


Figure 7. sPGA 0/1 response rates in Week 16 PASI 75 responders

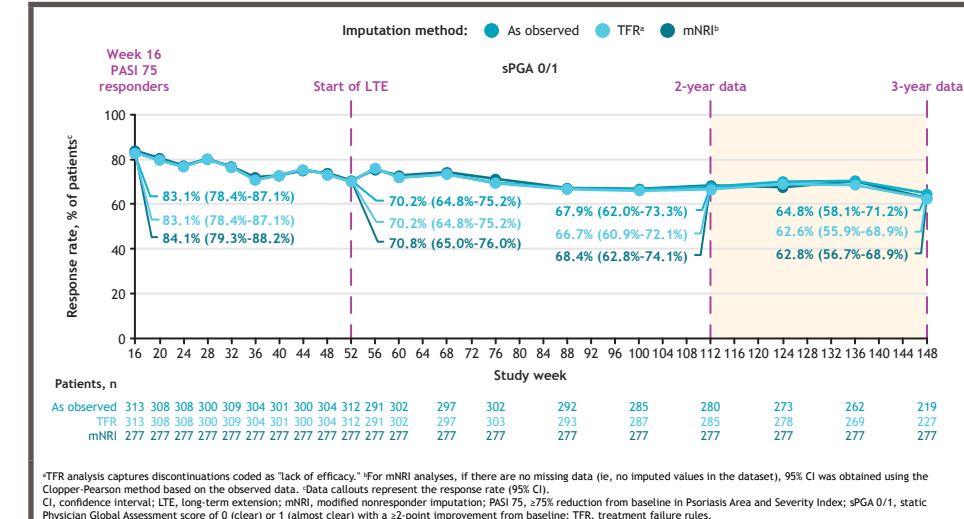
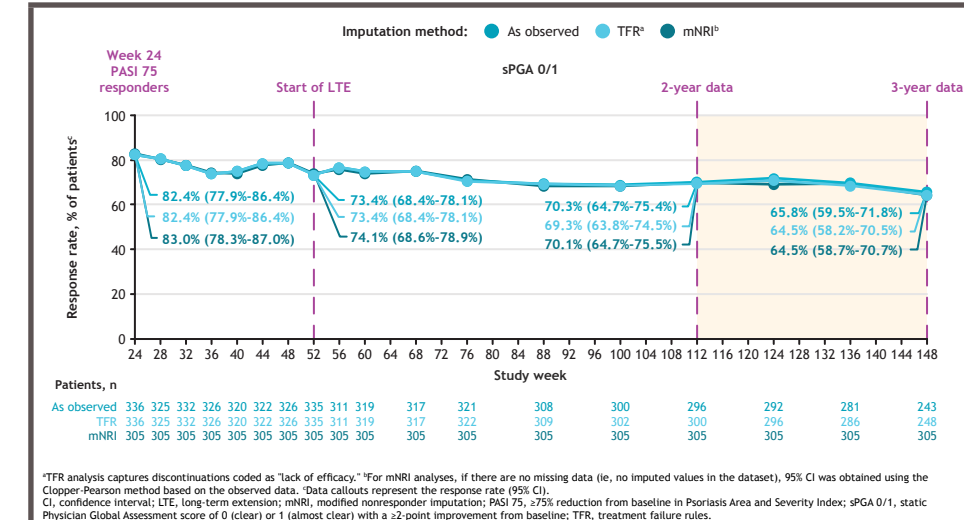


Figure 8. sPGA 0/1 response rates in Week 24 PASI 75 responders



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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