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

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Introduction

• Tyrosine kinase 2 (TK2) is an intracellular enzyme that mediates signaling of cytokines (eg, interleukin-21, Type I interferons) involved in psoriasis pathogenesis.
• Deucravacitinib, an oral, selective, allosteric TK2 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. 1
• Deucravacitinib binds to the TK2 regulatory domain rather than to the more conserved catalytic domain where Janus kinase 1 (JAK1) and JAK3 bind. 1

Figure 1. Mechanism of action of deucravacitinib

• Deucravacitinib was studied at 5 mg once daily in two global phase 3 pivotal trials, POETYK PSO-1 (NCT02416173) and POETYK PSO-2 (NCT02416177). 2
• Only POETYK PSO-1 included a continuous deucravacitinib treatment arm from Day 1 to Week 52.
• Patients crossed over to deucravacitinib at Week 16 in both trials.
• POETYK PSO-1 demonstrated efficacy:
  - Significantly greater response rate for ATX reduction from baseline in Psoriasis Area and Severity Index (PASI) 75 at 12 weeks in the Physician’s Global Assessment (PGA) score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline (PGA 0-1) at Week 12 in all patients with deucravacitinib in plaques and involved skin. 3
  - Clinical efficacy that was maintained through Week 52 with continuous deucravacitinib treatment. 4
  - Retrospective analysis of an 112-week extension in the POETYK PSO-1 long-term extension (LTE) trial and receive open-label deucravacitinib 6 mg once daily.
  - The 1-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 unexpected safety signals. 5

Figure 2. Clinical efficacy in POETYK PSO-1 (N=332)

Objectives

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

Methods

Study design and analytic 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 75 and body surface area involvement ≥10%
  - Randomization in POETYK PSO-1 was stratified by geographic region, body weight, and prior b.i.d. therapy.

• 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 trial.
  - Since results with sPGA 0/1 outcomes were shown earlier from Weeks 0-52, only Week 52-112 results are shown here.

• Continuous deucravacitinib treatment: patients who received continuous deucravacitinib from Week 1, achieved PASI 75 at Week 16, and entered the POETYK LTE trial.

Figure 3. POETYK PSO-1 and LTE study designs

Results

• Baseline patient demographics and disease characteristics
  - Baseline demographic and disease characteristics for POETYK PSO-1 patients randomized to deucravacitinib who roiled over to the LTE are presented in Table 1.
  - With the exception of PASI 75 at Week 16, the deucravacitinib treatment group was comparable to the LTE group.

Table 1. Baseline patient demographics and disease characteristics

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. 6
  - Clinical outcomes were consistent from Weeks 52-112 in these patients who entered the POETYK LTE trial.
  - Clinical efficacy responses were maintained well through Week 112 among those who achieved PASI 75 at Week 16 with continuous deucravacitinib treatment. 7

• Deucravacitinib, a once-daily drug, has the potential to become a treatment of choice and new treatment of care for patients who require systemic therapy for their moderate to severe plaque psoriasis.

References

• Warren RB, et al. Presented at the EADV Spring Symposium; May 12–14, 2022. 8

Acknowledgments

Disclosures

• This study was sponsored by Bristol Myers Squibb.

Figure 4. Baseline demographics and disease characteristics in Week 52 responders in all patients with continuous deucravacitinib treatment for up to 112 weeks

Outcomes measures:

- Efficacy as assessed in patients with up to 112 weeks (2 years) of continuous deucravacitinib exposure as of the cutoff date of October 1, 2021

- Week 52 PASI 75
- Baseline PASI 75 reduction from baseline at Week 52
- PASI 90
- Baseline PASI 90 reduction from baseline at Week 52

- In addition to the abovementioned, 3 methods of imputation for missing data were used to evaluate long-term efficacy:
  - Treatment failure rule (TP):
    - Patients who discontinued treatment or the study due to worsening of psoriasis or lack of efficacy were imputed as nonresponders.
  - Last observation carried forward (LOCF):
    - Multiple imputation analysis was used for imputation of missing values, and patients who discontinued due to worsening of psoriasis were imputed as nonresponders.
  - Last observation carried forward with data imputed from Week 52 (LOCFwD52):
    - Only patients who discontinued or had reached Week 112 by the cutoff date of October 1, 2021, were included.

• This study was designed as a 2 × 2 factorial study to evaluate the effects of deucravacitinib on:
  - PASI 75 and PASI 90 responses
  - Adverse events

• All patients who discontinued deucravacitinib treatment prior to Week 52 were considered nonresponders with respect to the primary and secondary endpoints.

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

Figure 7. Maintenance of PASI 90 response in Week 16 in patients with continuous deucravacitinib treatment for up to 112 weeks

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

Figure 9. Maintenance of PASG 0/1 response in Week 16 in patients with continuous deucravacitinib treatment for up to 112 weeks

Figure 10. Baseline PASG 0/1 response for Week 52 in all patients with continuous deucravacitinib treatment for up to 112 weeks

Figure 11. Baseline PASG 0/1 response for Week 16 in patients with continuous deucravacitinib treatment for up to 112 weeks