Deucravacitinib in plaque psoriasis: 3-year safety and efficacy results from the phase 3 POETYK PSO-1 and PSO-2 trials

April W. Armstrong,1,3 Mark Lebwohl,2 Richard B. Warren,1,2 Howard Sofen,3 Shinichi Imafuku,4 Mamitario Ohtsuki,5 Lynda Spelman,6 Thierry Passeron,7 Kim A. Papp,8 Renata M. Kisa,9 Victoria Berger,10 Elien Vritzali,7 Kim Hoyt,10 Matthew J. Colston,11 Subhasish Banerjee,4 Bruce Strober,12 Diamant Thaqi,13 Andrew Blauvelt14

1 University of California San Diego; 2Weill Cornell Medicine at Mount Sinai; 3Mount Sinai, New York, NY, UK; 4 MHCR Manchester Biomedical Research Centre; Manchester; 5Astellas, Cambridge, England, UK; 6Department of Dermatology, University of Pennsylvania; 7Department of Dermatology, Oregon Health and Science University; 8Mayo Clinic, Jacksonville, Florida, USA; 9Dermatology Centre, Northern Care Alliance NHS Foundation Trust, Salford, UK; 10Dermatology Centre, Northern Care Alliance NHS Foundation Trust, Salford, UK; 11Department of Dermatology, University of California, San Diego; 12Department of Dermatology, University of California San Diego; 13Department of Dermatology, University of California San Diego; 14Department of Dermatology, University of California San Diego

Synopsis

• Tyrosine kinase (TK) inhibitors are a versatile class of agents that mediate signaling of cytokines, growth factor receptors, and integrins.
• Deucravacitinib, a selective, novel, oral, 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.
• Deucravacitinib uniquely binds to the regulatory domain of TYK2 rather than to the catalytic domain where Janus kinase (JAK) 1,2,3 inhibitors bind—thus avoiding the JAK family.

Background

Deucravacitinib 6 mg QD, or apremilast 30 mg twice daily (BID) (the TYK2 inhibitor class), is a selective inhibitor of TYK2, the catalytic domain where JAK 1,2,3 inhibitors bind—thus avoiding the JAK family; driving sustained clinical benefit in patients with moderate-to-severe plaque psoriasis (Ps) in a 2-year trial. Deucravacitinib was well tolerated in patients with Ps, with an adverse event (AE) profile consistent with earlier studies. The purpose of this study was to evaluate the long-term safety and efficacy of deucravacitinib in adults with moderate-to-severe Ps.

Objectives

The primary objective was to evaluate the 3-year safety and efficacy of deucravacitinib 6 mg QD in patients with moderate-to-severe plaque Ps who participated in the randomized 2-year phase 3 POETYK PSO-1 and POETYK PSO-2 trials. Secondary objectives were to evaluate the long-term safety, tolerability, and exposure to deucravacitinib, as well as to compare efficacy over 3 years with that over 2 years.

Methods

Study design

• POETYK PSO-1 and PSO-2 were global, 52-week, phase 3, double-blind trials that randomized patients with moderate-to-severe plaque Ps to deucravacitinib 6 mg QD or placebo starting at Week 0, through Week 52.
• Patients randomized to deucravacitinib continued treatment through Week 52.
• Patients randomized to placebo continued treatment through Week 52 or were enrolled in a 3-year extension, the POETYK Long-term extension (LTE) trial, through Week 152.
• Week 152 was defined as the cut-off date for the POETYK LTE trial; however, exposure data were collected through Week 156.

Results

• Of 1194 patients who participated in the double-blind trials (POETYK PSO-1 and PSO-2), 550 were randomized to deucravacitinib 6 mg QD and 516 to placebo.
• A total of 114 patients received deucravacitinib 6 mg QD at baseline in the POETYK LTE (POETYK PSO-1 or PSO-2) and 150 patients were randomized to deucravacitinib 6 mg QD through Week 156.
• Baseline patient demographics and disease characteristics for the overall population are presented in Table 1.

Efficacy

• The proportion of patients who achieved PASI 75, PASI 90, and sPGA 0/1 was sustained in patients who were continuously treated with deucravacitinib at Day 1 of the parent trials (Figure 1, A and B, respectively).
• The proportion of patients who achieved PASI 75, PASI 90, and sPGA 0/1 was sustained in patients who were continuously treated with deucravacitinib throughout the 3-year period (Figure 1, A and B, respectively).

Overall safety

• Overall cumulative safety outcomes through 2 and 3 years are presented in Table 3.
• Adverse drug reactions (ADRs) were reported by 76.8% (74.4%-79.0%) and 75.3% (73.0%-77.5%) of patients at 2 and 3 years, respectively.

Conclusions

Deucravacitinib demonstrated a consistent safety profile through 3 years with no new or unexpected safety signals. The proportion of patients achieved PASI 75, PASI 90, and sPGA 0/1 was sustained in patients who were continuously treated with deucravacitinib throughout the 3-year period.

Figure 1. Mechanism of action of deucravacitinib.