Systemic exposure and safety profile of delgocitinib cream in adults with moderate to severe chronic hand eczema in the phase 3 DELTA-2 trial

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Introduction/Background: In the DELTA-2 (NCT04872101) Phase 3 trial, delgocitinib cream 20 mg/g, a topical pan-Janus kinase inhibitor, was well-tolerated and demonstrated significant improvement in all efficacy endpoints versus cream vehicle in adults with moderate to severe chronic hand eczema (CHE).

Objectives: The objectives of this analysis were (1) to examine systemic exposure of delgocitinib cream 20 mg/g in adults with moderate to severe CHE in the randomized, double-blind, vehicle-controlled DELTA-2 trial (2) to compare the DELTA-2 systemic exposure with corresponding data following oral administration of delgocitinib in a Phase 1 trial, (3) to present a summary of safety related to delgocitinib cream from the randomized, double-blind, vehicle-controlled DELTA-2 trial.

Methods: Pharmacokinetic blood sampling in DELTA-2 was performed 2-6 hours after delgocitinib application at Weeks 1, 4, and 16 using a liquid chromatography/mass
spectrometry-based method (lower limit of quantitation: 5 pg/ml). In the Phase 1 trial (NCT05050279), single oral doses of delgocitinib were tested in healthy volunteers with sampling performed for up to 24-hours post-administration.

**Results:** In DELTA-2, minimal systemic exposure was recorded in 313 delgocitinib-treated patients, with the highest geometric mean plasma concentration being 0.21 ng/ml at Week 1 (n=286). In the Phase 1 trial, the lowest oral delgocitinib dose tested (1.5 mg; n=8) is regarded as subtherapeutic and showed a peak systemic exposure (geometric mean Cmax) of 7.2 ng/ml. In DELTA-2, adverse events (AEs) were reported by 45.7% (n=143/313; delgocitinib cream) and 44.7% (n=71/159; cream vehicle) of patients, with COVID-19 being most common (11.5% vs 12.6%, respectively). The rate of possibly or probably related AEs was low and similar between delgocitinib cream and cream vehicle. No deaths were reported. Few serious AEs were reported with none assessed as related to the study drug.

**Conclusions:** The DELTA-2 trial demonstrated minimal systemic exposure in association with a favorable safety profile, supporting a lack of meaningful systemic effect from twice-daily applications of delgocitinib cream in patients with moderate to severe CHE.

**Keywords:** chronic hand eczema, delgocitinib, JAK

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