Abstract N°: 2785

Delgocitinib cream formulation development for Chronic Hand Eczema (CHE): insights from patient preference and skin penetration studies

Christopher Bunick*[1], Christoph Schlapbach[2], Umut Erhan[3], Douglas Maslin[3, 4], Vibeke Hougaard Sunesen[3], Gitte Pommergaard Pedersen[3], Linda Stein Gold[5]

[1]Yale Department of Dermatology, New Haven, United States
[2]Department of Dermatology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland
[3]LEO Pharma A/S, Ballerup, Denmark
[4]Addenbrooke's Hospital, Cambridge, United Kingdom
[5]Henry Ford Health, Detroit, United States

Introduction & Objectives: Chronic Hand Eczema (CHE) is an inflammatory skin disease associated with significant physical and psychosocial burdens and limited approved treatment options. Delgocitinib cream 20 mg/g (2%) is a non-steroidal topical pan-Janus kinase (JAK) inhibitor formulated for application on hands and does not contain parabens, perfumes, or penetration enhancers. It was well tolerated with minimal systemic exposure and has demonstrated efficacy versus cream vehicle in adults with moderate to severe CHE in DELTA 1 (NCT04871711) and DELTA 2 (NCT04872101). To support the initial development of the delgocitinib cream formulation, two studies assessed (1) patients' preference for formulation and (2) delgocitinib skin penetration.

Materials & Methods: The Patient Preference Market Research Study (PPMRS) was conducted as 'Hall test-style' group sessions with patients with CHE, in which five early formulation options (no active substance) were tested simultaneously (3 light creams, 1 lipid cream, and 1 ointment). Formulation characteristics of consistency/feel, application, and appearance were tested. Skin penetration was assessed in an *in vivo* dermal Open Flow Microperfusion study (OFM) in pigs. Four probes at each of two application sites were inserted within the dermis of two pigs. A single dose of delgocitinib cream formulation was applied to the skin surface (10 mg/cm2) of the application sites and OFM samples were collected in 3-hour intervals for 12 hours.

Results: In the PPMRS, 74 adults with CHE were included, of those 54% were female and 79% were 18-54 years. Overall, 49% of the patients had been diagnosed with CHE for ≥15 years (23% for 10-14 years), with 77% reporting CHE impacted their lives to a "moderate" or "very large" extent. The treatment features being considered most important by patients were quick absorption (58%), not being sticky (43%), and not being greasy (42%). One of the light cream samples performed the best according to perception of consistency/feel (62%), application (77%), and appearance (69%), and was the most preferred product overall among the 5 samples. Based on these results, this formulation was selected to further guide development of delgocitinib cream. Demographic factors, e.g., age, disease history, spot/whole hand application, and impact on quality of life, did not influence product preference. In the OFM, it was shown that delgocitinib distributed into the dermis. The mean (standard deviation) OFM concentration based on the area under the curve (AUC) over the 12 hours sampling time was 121 (102) nM.

Conclusion: Delgocitinib cream is well-suited to patients with CHE, as it was developed based on preferences of patients with CHE and was shown to deliver the active substance to the site of inflammation within the dermis. The cream was developed without skin penetration enhancers which may contribute to the negligible systemic exposure seen in later clinical delgocitinib studies.