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Treatment with delgocitinib cream is associated with a reduction of *Staphylococcus aureus* density and pain in patients with mild to severe Chronic Hand Eczema

Tove Agner^{*1}, Derya Aytan-Aktug², James Greig², Daniel Elenius Madsen², Line Brok Nørreslet^{1, 3}

¹Department of Dermatology, Bispebjerg Hospital, University of Copenhagen, Copenhagen, Denmark

²LEO Pharma A/S, Ballerup, Denmark

³Department of Dermatology and Allergy Centre, Odense University Hospital, Odense, Denmark

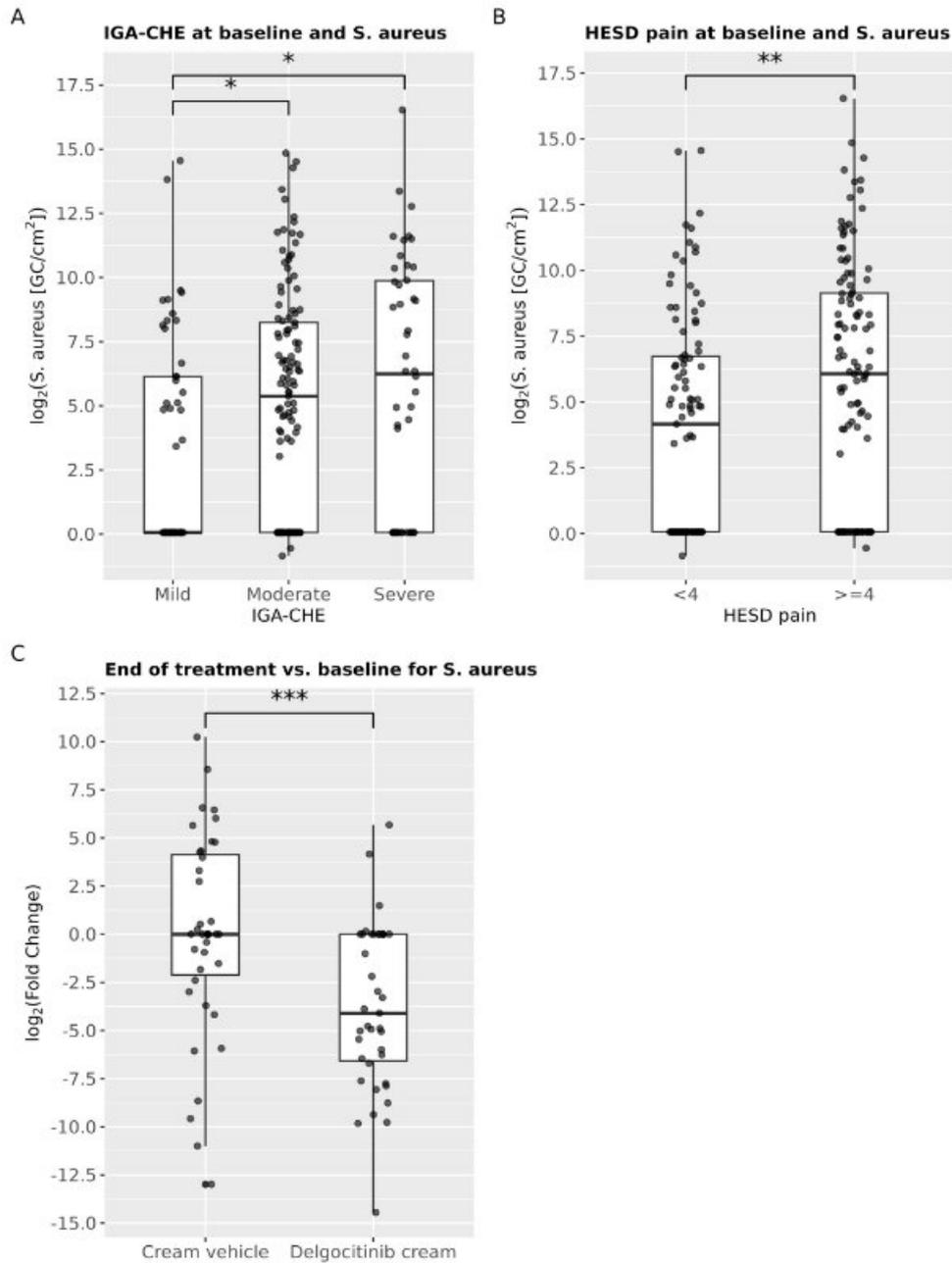
Introduction & Objectives: Chronic Hand Eczema (CHE) is a multifactorial inflammatory skin disease related to skin barrier dysfunction and immune cell dysregulation. Pain is one of the most common and burdensome symptoms of CHE, negatively affecting patients' quality of life. More than 50% of patients with moderate to severe CHE are colonized with *Staphylococcus aureus* (*S. aureus*). The severity of CHE has been shown to be associated with an increase in *S. aureus* colonization and a change in the composition of the microbiome has been reported. In a phase 2b dose-ranging trial, the twice-daily application of delgocitinib cream, a pan-Janus kinase inhibitor, for 16 weeks was efficacious and had a favourable safety profile in adults with mild to severe CHE. Here, we report changes in *S. aureus* density in patients with CHE who were treated with delgocitinib cream. In addition, we investigated the correlation between *S. aureus* density and pain.

Materials & Methods: In a phase 2b dose-ranging trial (NCT03683719), 258 adult patients with mild to severe CHE were randomised 1:1:1:1 to delgocitinib cream 1, 3, 8, 20 mg/g, or cream vehicle twice-daily for 16 weeks. Eligibility criteria included mild to severe disease according to the Investigator's Global Assessment for CHE (IGA-CHE) and a recent history of inadequate response or contraindication to topical corticosteroids. The Hand Eczema Symptom eDiary (HESD) captured patient-reported worst severity of pain over the past 24 hours on an 11-point numeric rating scale (from 0=no pain to 10=severe pain). From each patient (N=220), a representative lesional (n=216) and/or non-lesional (n=217) skin area of approximately 2 cm x 5 cm on the dorsal hand, wrist, or fingers was swabbed before start of treatment (i.e., baseline) and at the end of treatment (Week 16). The number of *S. aureus* gene-copy numbers was quantified by qPCR, by targeting the *femA* gene, and calculated per cm² of skin (*S. aureus* density). The Spearman's rank correlation coefficient test was used to assess the correlation between *S. aureus* density and disease severity (IGA-CHE), as well as between *S. aureus* density* and* HESD pain.

Results: In all patients, *S. aureus* density was higher in lesional compared with nonlesional CHE skin at baseline ($P<0.001$). In lesional CHE skin samples, positive correlations were found between disease severity (IGA-CHE) and *S. aureus* density at baseline ($P<0.05$), as well as between HESD pain and *S. aureus* density at baseline ($P<0.01$) (Figure). From the end of treatment to baseline, a positive correlation was observed between *S. aureus* density and HESD pain ($P<0.001$). Patients treated with delgocitinib cream at a dose of 20 mg/g showed a larger reduction in *S. aureus* gene-copy numbers* from baseline to Week 16 compared with cream vehicle ($P<0.001$).

Conclusion: In patients with mild to severe CHE, *S. aureus* density was positively correlated to disease severity as well as HESD pain. Treatment with delgocitinib cream at a dose of 20 mg/g for 16 weeks was associated with a significant reduction in *S. aureus* density.

Figure. Correlations between (A) IGA-CHE at baseline and *S. aureus* density, (B) HESD pain at baseline and *S. aureus* density, and (C) the end of treatment and baseline for *S. aureus* density.



* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

\log_2 -transformed gene-copy numbers/cm² or fold changes in \log_2 -transformed gene-copy numbers/cm² are displayed on the y-axis.

CHE, Chronic Hand Eczema; GC/cm², gene-copy numbers per cm²; HESD, Hand Eczema Symptom eDiary; IGA-CHE, Investigator's Global Assessment for Chronic Hand Eczema; \log_2 , \log_2 -transformed value; *S. aureus*, *Staphylococcus aureus*.

