The impact of moderate to severe Chronic Hand Eczema and the effect of improved clinical symptoms on work productivity loss: data from the DELTA 1 and DELTA 2 phase 3 trials

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Objectives

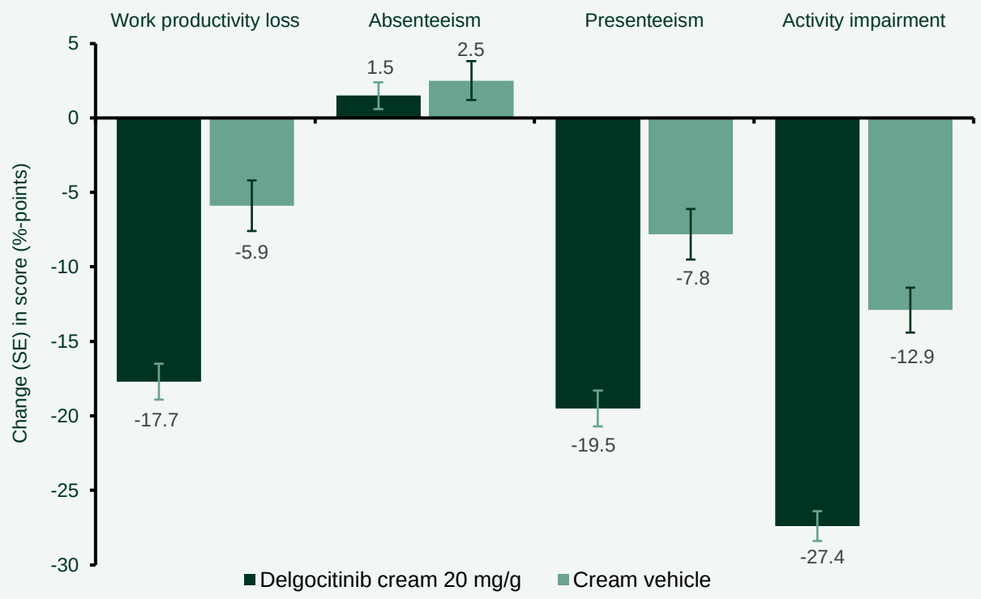
- To assess the effects of twice-daily treatment with delgocitinib cream 20 mg/g versus cream vehicle on work productivity loss and leisure time activity impairment in patients with moderate to severe CHE enrolled in two pivotal phase 3 trials.
- To investigate the association between clinical response and changes in work productivity loss and activity impairment.

Results

Changes in work productivity loss and activity impairment: delgocitinib cream versus cream vehicle

- Twice-daily application of delgocitinib cream 20 mg/g was associated with greater improvements than cream vehicle in work productivity loss, presenteeism, and activity impairment at 16 weeks **(Figure 1)**. Changes in absenteeism were not different between groups, which may have been due to the low rate of absenteeism at baseline.

Figure 1. Changes in work productivity loss and activity impairment at 16 weeks



	Work productivity loss	Absenteeism	Presenteeism	Activity impairment
Difference (95% CI), p-value	−11.8 (−15.9, −7.6) p<0.001	−1.0 (−4.0, 2.1) p=0.523	−11.6 (−15.7, −7.6) p<0.001	−14.5 (−18.0, −11.0) p<0.001

Data are LS mean change (SE) in %-points. Greater reductions in scores represent a greater improvement in status. Changes in WPAI:CHE (composite estimand) from baseline to week 16 were modelled by ANCOVA with study ID, treatment, region, baseline IGA-CHE score and baseline value as independent variables. Observed data collected prior to or on the visit of permanent discontinuation of study treatment or initiation of rescue treatment were included. Missing data and data collected after permanent discontinuation of study treatment or initiation of rescue treatment were considered non-response by using worst observation carried forward (including the baseline value).

Association between changes in work productivity loss and activity impairment by clinical response

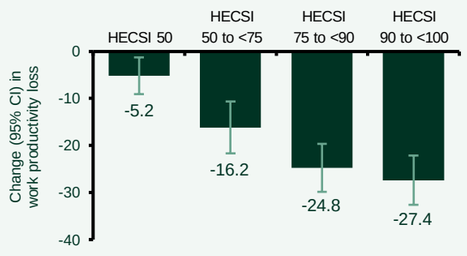
- When analysed by clinical response to delgocitinib cream 20 mg/g, a greater HECSI response was associated with a greater decrease in work productivity loss score and activity impairment from baseline to week 16 **(Figure 2).** A similar pattern was seen in the cream vehicle group.

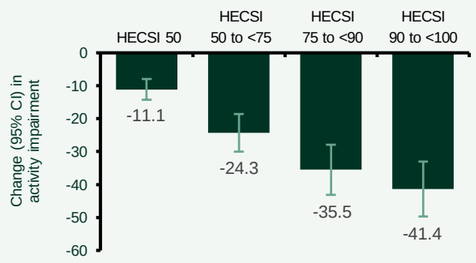
Figure 2. Changes in work productivity loss and activity impairment by HECSI response

Patients with response, n (%):

	HECSI <50	HECSI 50 to 75	HECSI 75 to <90	HECSI 90 to <100
Delgocitinib cream 20 mg/g	209 (32.8%)	114 (17.9%)	122 (19.1%)	116 (18.2%)
Cream vehicle	196 (61.1%)	58 (18.1%)	33 (10.3%)	27 (8.4%)

Delgocitinib cream 20 mg/g:





	HECSI 50	HECSI 50 to <75	HECSI 75 to <90	HECSI 90 to <100	HECSI 50	HECSI 50 to <75	HECSI 75 to <90	HECSI 90 to <100
Cream vehicle:	0.5	-8.6	-11.0	-28.2	-2.7	-18.1	-32.8	-41.0

Data are LS mean change (95% CIs) in %-points. Greater reductions in scores represent a greater improvement in status. Data for patients with HECSI 100 are not reported due to low patient numbers in the cream vehicle group (delgocitinib cream, n=77; cream vehicle, n=7). Changes in WPAI:CHE (composite estimand) from baseline to week 16 were modelled by ANCOVA with study ID, treatment, region, baseline IGA-CHE score and baseline value as independent variables. Observed data collected prior to or on the visit of permanent discontinuation of study treatment or initiation of rescue treatment were included. Missing data and data collected after permanent discontinuation of study treatment or initiation of rescue treatment were considered non-response by using worst observation carried forward (including the baseline value).

Conclusions

- CHE is associated with work productivity loss and leisure time activity impairment in adults with moderate to severe CHE.
- Treatment with twice-daily delgocitinib cream 20 mg/g was associated with greater improvements in work productivity and leisure time activity than cream vehicle; improvements in work productivity were largely driven by reduced presenteeism.
- Clinical response as assessed by HECSI was associated with improved work productivity and leisure time activity, with greater clinical response associated with greater improvements.

Background

- Hand eczema is a heterogenous, fluctuating inflammatory disease of the hands and wrists that has a substantial impact on patients' daily lives and physical functioning. The lifetime prevalence of hand eczema has been estimated as 14.5% in the general population[1], and substantially higher in certain high-risk occupations, especially those involving wet-work.[2] Hand eczema that has persisted for >3 months or returned twice or more within the last 12 months is considered chronic.[2]
- CHE represents a significant economic burden, especially its impact on people's ability to work. A recent systematic review estimated that up to 57% of patients with CHE took sick leave.[3] Presenteeism (working while sick) is also frequent and may result in even greater productivity loss and higher long-term costs than absence due to sickness.[4,5]
- To date, there are no topical treatments specifically approved for moderate to severe CHE that provide effective short- and long-term disease control.
- Delgocitinib is a first-in-class topical pan-JAK inhibitor that provided significant improvements in clinician-assessed and patient-reported efficacy outcomes at 16 weeks compared to cream vehicle in patients with CHE, and is well tolerated.[6,7]

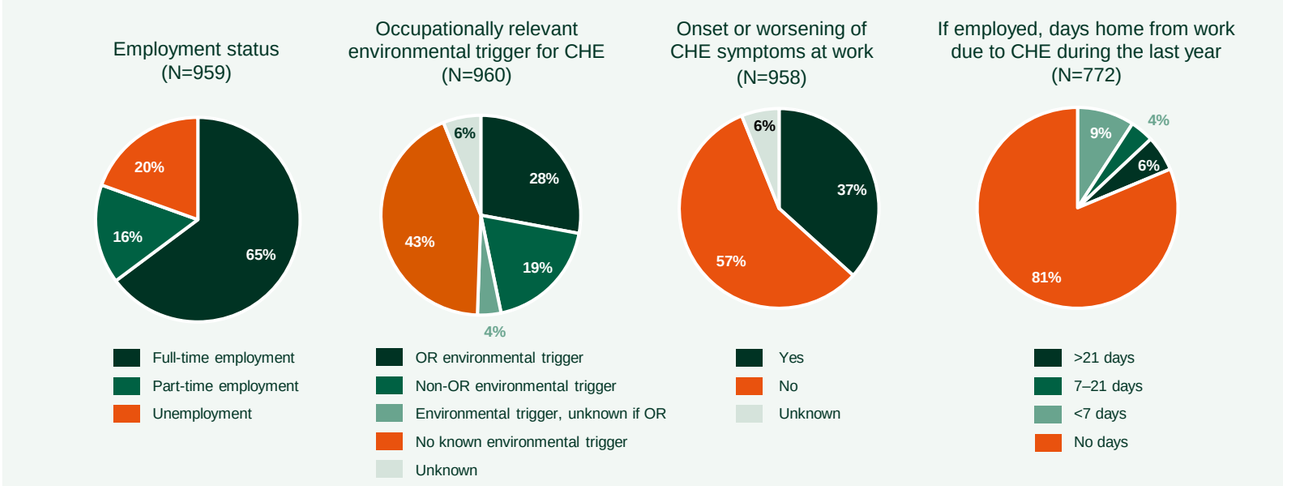
Methods

- DELTA 1 (NCT04871711) and DELTA 2 (NCT04872101) were phase 3 trials of identical design. In both trials, adult patients with moderate to severe CHE were randomised (2:1) to double-blind treatment with delgocitinib cream 20 mg/g or cream vehicle twice daily for 16 weeks.
- Data were pooled from both trials and changes in work productivity loss (in employed patients only) and activity impairment were assessed using the Work Productivity and Activity Impairment (WPAI):CHE questionnaire that measures the effect of overall health and specific symptoms on productivity at work and regular activity outside of work during the previous 7 days, including work time missed due to CHE (absenteeism), impairment while working with CHE (presenteeism), overall CHE-related work productivity loss (absenteeism and presenteeism combined), and CHE-related activity impairment. Scores are expressed as a percentage of impairment, with higher scores indicating greater impairment.
- The association between treatment response as measured by relative change in HECSI and work productivity loss and activity impairment at 16 weeks were assessed in a *post-hoc* analysis.
- Baseline data on the impact of CHE on the ability of patients to work were also collected via a questionnaire at the first trial visit.

Baseline Characteristics

- Overall, 80.5% patients (n=772) were employed full-time or part-time. An environmental CHE trigger was reported by 51.5% (n=485) of patients; of these, over half (55.3%, n=268) considered the trigger to be occupationally relevant. Thirty-percent of patients (n=287) reported wet-work exposure. Of those employed,18.7% (n=144) reported days off work due to CHE in the last year **(Figure 2).**

Figure 2. CHE employment-related characteristics at baseline



- Across the two trials, 639 patients were randomised to delgocitinib cream 20 mg/g and 321 to cream vehicle. Most patients were white (90%), female (64%), with moderate baseline disease severity (72%) **(Table 2)**.

Table 2. Baseline characteristics

	Delgocitinib cream 20 mg/g (n=639)	Cream vehicle (n=321)
Age, years, mean (SD)	44.8 (14.5)	42.7 (14.2)
Female sex, n (%)	406 (63.5)	212 (66.0)
Duration of CHE, years, mean (SD)	9.6 (11.0)	10.0 (11.2)
HECSI score, mean (SD)	71.1 (43.0)	72.5 (47.3)
Work productivity loss score, %, mean (SD)	44.3 (28.2)	42.7 (26.7)
Absenteeism score, %, mean (SD)	6.7 (19.6)	5.9 (19.8)
Presenteeism score, %, mean (SD)	43.0 (27.4)	41.7 (26.0)
Activity impairment score, %, mean (SD)	53.3 (25.2)	52.3 (26.1)

References

1. Quaade AS, *et al. Contact Dermatitis*. 2021;84:361–74; 2. Thyssen JP, *et al. Contact Dermatitis*. 2022;86:357–78; 3. Armstrong A, *et al. Am J Clin Dermatol*. 2022;23:287–300.
4. Oosterhaven JAF, *et al. Contact Dermatitis*. 2018;79:10–19; 5. Collins JJ, *et al. J Occup Environ Med*. 2005;47:547–57; 6. Bissonnette R, *et al.* Presented at the EADV Annual Meeting, 11–14 October 2023, Berlin, Germany; 7. Schliemann S, *et al*. Presented at the EADV Annual Meeting, 11–14 October 2023, Berlin, Germany.

Disclosures

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Abbreviations

CHE, Chronic Hand Eczema; CI, confidence interval; HECSI, Hand Eczema Severity Index; IGA-CHE, Investigator's Global Assessment for Chronic Hand Eczema; JAK, Janus kinase; LS, least squares; OR, occupationally relevant; SE, standard error; WPAI:CHE, Work Productivity and Activity Impairment: Chronic Hand Eczema.

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