CO55

Comparative Efficacy and Safety of Delgocitinib, Alitretinoin and PUVA in Patients with Moderate-to-Severe Chronic Hand Eczema – a Network Meta-Analysis

Ryan Pulleyblank[1], Rie von Eyben[1], Daniela Gonçalves-Bradley[2], Bryony Langford[2], Laura Sawyer[2]

1 LEO Pharma A/S, Ballerup, DK
2 Symmetron Ltd, London, UK

Conclusions

- Amongst patients with moderate-to-severe Chronic Hand Eczema, delgocitinib cream provides significantly greater treatment efficacy than both alitretinoin and PUVA according to the IGA-CHE/PGA 0/1 outcome measure at week 12, and delgocitinib cream provides significantly greater efficacy than alitretinoin according to the HECSI90 outcome measure at week 12.
- Treatment with delgocitinib is significantly less likely to result in treatment discontinuation due to adverse events in comparison with alitretinoin and PUVA.

Objectives

- To conduct network meta-analyses (NMAs) investigating efficacy and safety of treatments for moderate-to-severe Chronic Hand Eczema (CHE) amongst who have not adequately responded to treatment with topical corticosteroids (TCS) or for whom TCS is inappropriate.

Background

- CHE is hand eczema that lasts for 3 months or relapses at least twice a year.[1]
- CHE is a persistent, inflammatory skin disease affecting the hands and wrists, characterised by key symptoms of itch and pain, together with signs such as erythema, scaling, fissures and vesiculation.[2]
- CHE is associated with a substantial burden of illness including strongly impacting patients' physical and psychological quality of life.[3]
- Current therapies indicated for patients with moderate-to-severe CHE where treatment with topical corticosteroids (TCS) is inappropriate or inadequate include psoralen with ultraviolet A (PUVA) phototherapy, oral alitretinoin, and delgocitinib cream.
- No direct evidence of the relative efficacy or safety of delgocitinib vs. PUVA exists.

Methods

Source data

- A systematic literature review (SLR) identified relevant randomized controlled trials (RCTs) assessing safety and efficacy of treatments for moderate to severe CHE.
- The SLR (Oct 2024) was compliant with PRISMA-P guidelines[4] for reporting SLRs and meta-analyses, meeting standards of the National Institute for Health and Care Excellent (NICE) methods guidelines for technology appraisals[5] and the Cochrane Handbook.[6]

Evidence synthesis

- A feasibility assessment was conducted assessing trial comparators, connections, study designs, patient characteristics, and risks from unobserved variables.
- Seven trials were identified (Table 1) for inclusion in NMAs across two efficacy outcomes:
  - Investigator Global Assessment-CHE / Physician Global Assessment: Clear (0) or Almost Clear (1) (IGA-CHE/PGA 0/1);
  - Hand Eczema Severity Index: 90% improvement from baseline (HECSI90);
- and one safety outcome:
  - Discontinuation due to adverse events (DAEs).
- A Bayesian NMA approach was adopted to estimate relative treatment effects of comparators.

Table 1 Overview of trials included in NMAs

Trial ID	Investigational drug and comparator	IGA-CHE/PGA 0/1	HECSI90	DAEs
DELTA 1 (NCT04871711)[7]	Delgocitinib vs. vehicle cream	12/16	12/16	16
DELTA 2 (NCT04872101)[7]	Delgocitinib vs. vehicle cream	12/16	12/16	16
Worm 2022 (NCT03683719)[8]	Delgocitinib vs. vehicle cream	12/16	12/16	16
DELTA FORCE (S) (NCT05259722)[9]	Delgocitinib vs. alitretinoin	12	12	24
BACH (S) (NCT00124475)[10]	Alitretinoin vs. placebo	NR	NR	24
HANDEL (S) (NCT00817063)[11]	Alitretinoin vs. placebo	NR	NR	24
ALPHA (S) (ISRCTN80206075)[12]	Alitretinoin vs. PUVA	12	NR	24

NOTEs: 12/16/24 indicate timepoints trial endpoint was reported in weeks. NR indicates Not Reported. S indicates trial included only severe patients.

Figure 1a Evidence Network: IGA-CHE/PGA 0/1

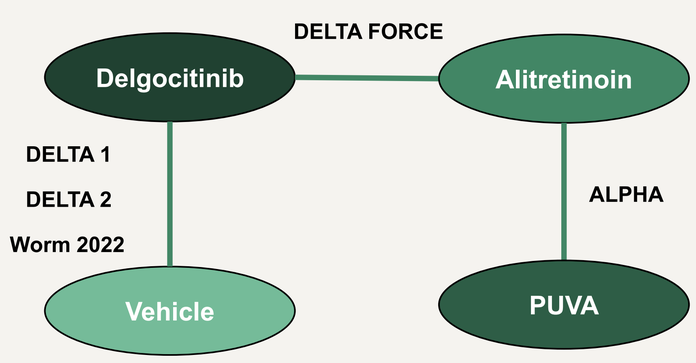

Figure 1b Median Odds Ratios: IGA-CHE/PGA 0/1 at Week 12

Delgocitinib			
1.89 (1.23, 2.93)	Alitretinoin		
2.73 (1.43, 5.25)	1.45 (0.89, 2.37)	PUVA	
2.93 (2.07, 4.23)	1.55 (0.89, 2.74)	1.07 (0.51, 2.25)	Vehicle

NOTE: Brackets indicate the 95% credible interval for FE models. Statistically significant odds ratios are bold.

Figure 2a Evidence Network: HECSI90

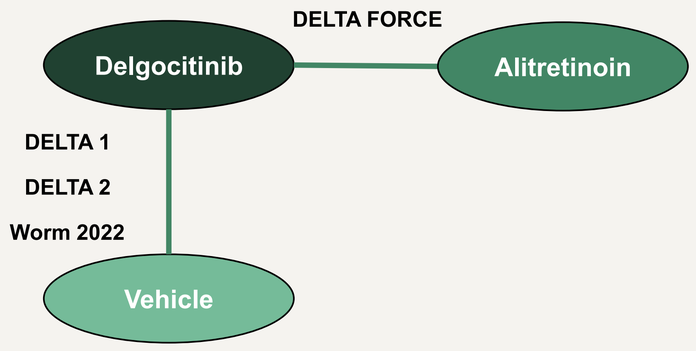

Figure 2b Median Odds Ratios: HECSI90 at Week 12

Delgocitinib		
1.79 (1.23, 2.63)	Alitretinoin	
4.34 (3.02, 6.39)	**2.43 (1.43, 4.16)**	Vehicle

NOTE: Brackets indicate the 95% credible interval for FE models. Statistically significant odds ratios are bold.

Figure 3a Evidence Network: Discontinuation due to AEs

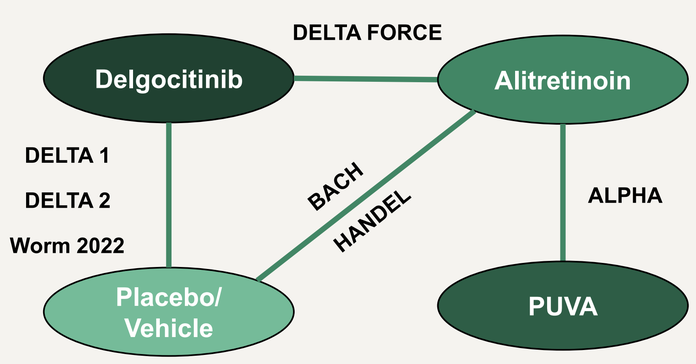

Figure 3b Median Odds Ratios: Discontinuation due to AEs

Delgocitinib			
0.07 (0.02, 0.17)	Alitretinoin		
0.07 (0.02, 0.25)	1.01 (0.40, 2.53)	PUVA	
0.15 (0.05, 0.36)	**2.16 (1.38, 3.49)**	2.16 (0.77, 6.03)	Placebo/ Vehicle

NOTE: Brackets indicate the 95% credible interval for FE models. Statistically significant odds ratios are bold.

Results

- Both fixed-effects (FE) and random-effects models were estimated.
- Considering the sparsity within available evidence networks, fixed-effects analyses were considered most appropriate.

Efficacy Endpoints

- The evidence network and table of median odds ratios for the IGA-CHE/PGA 0/1 endpoint at week 12 are reported in Figures 1 a & b.
  - Patients treated with delgocitinib had significantly higher odds of achieving an IGA-CHE/PGA 0/1 assessment in comparison with both alitretinoin and PUVA, as well as vehicle.
- The evidence network and table of median odds ratios for the HECSI90 endpoint at week 12 are reported in Figures 2 a & b.
  - Patients treated with delgocitinib had significantly higher odds of achieving HECSI90 in comparison with alitretinoin, as well as vehicle.
  - Patients treated with alitretinoin had significantly higher odds of achieving HECSI90 in comparison with vehicle.

Safety Endpoint

- The evidence network and table of median odds ratios for discontinuations due to adverse events are reported in Figures 3 a & b.
  - Patients treated with delgocitinib had significantly lower odds of DAEs in comparison with both alitretinoin and PUVA, as well as placebo/vehicle.
  - Patients treated with alitretinoin had significantly lower odds of DAEs in comparison with placebo/vehicle.

Limitations

- The ALPHA trial's primary treatment efficacy endpoint considered the PGA scale, whereas trials including delgocitinib made use of the similar, but more conservative, IGA-CHE scale. Combining these studies in the IGA-CHE/PGA 0/1 NMA relied on an assumption of sufficient comparability between the IGA-CHE and PGA definitions of both 'clear' (score of 0) and 'almost clear' (score of 1).
- The DELTA FORCE, ALPHA, BACH, and HANDEL trials included only severe patients. Combining studies with both moderate-to-severe, and severe only patient populations required an assumption that baseline severity was not a treatment effect modifier.

Abbreviations: AEs, adverse events; CHE, chronic hand eczema; DAE, discontinuation due to adverse event; FE, fixed-effects; IGA-CHE, Investigator Global Assessment for Chronic Hand Eczema; HECSI, Hand Eczema Severity Index; NICE, National Institute of Care and Health Excellence; NMA, network meta-analysis; NR, not reported; PGA, Physician Global Assessment; PUVA, psoralen ultraviolet A; RCT, randomised controlled trial; SLR, systematic literature review; TCS, topical corticosteroid.

Acknowledgements: Thanks to Chris Wright from LEO Pharma for additional project assistance.

Funding: LEO Pharma A/S, Ballerup, Denmark

Disclosures: **RP** and **RvE** are employees of LEO Pharma A/S. **DGB**, **BL**, and **LS** are employees of Symmetron Ltd, which consults in the life sciences industry.

References: [1] Thyssen JP, et al. 2022. Guidelines for diagnosis, prevention, and treatment of hand eczema. Contact dermatitis; 86:357-378. [2] Lee GR, et al. 2019. Current and emerging therapies for hand eczema. Dermatol Ther; 32:e12840. [3] Grant L, et al. 2020. Development of a Conceptual Model of Chronic Hand Eczema (CHE) Based on Qualitative Interviews with Patients and Expert Dermatologists. Adv Ther; 37(2):692-706. [4] Shamseer L, et al. 2015. Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015: elaboration and explanation. BMJ; 349:g7647. [5] NICE. 2022. Health technology evaluations: the manual. Available at: www.nice.org.uk/process/pmg36. [6] Higgins JPT, et al. 2024. Cochrane Handbook for Systematic Reviews of Interventions version 6.5 (updated August 2024). Cochrane. Available at: www.cochrane.org/handbook. [7] Bissonnette R, et al. 2024. Efficacy and safety of delgocitinib cream in adults with moderate to severe chronic hand eczema (DELTA 1 and DELTA 2): results from multicentre, randomised, controlled, double-blind, phase 3 trials. The Lancet; 404(10451):461-473. [8] Worm M, et al. 2022. The pan-JAK inhibitor delgocitinib in a cream formulation demonstrates dose response in chronic hand eczema in a 16-week randomized phase IIb trial. Br J Dermatol; 187(1), 42–51. [9] Giménez-Arnau AM, et al. 2025. Efficacy and safety of topical delgocitinib cream versus oral alitretinoin capsules in adults with severe chronic hand eczema (DELTA FORCE): a 24-week, randomised, head-to-head, phase 3 trial. The Lancet; 405:1676-1688.

[10] Ruzicka T, et al. 2008. Efficacy and safety of oral alitretinoin (9-cis retinoic acid) in patients with severe chronic hand eczema refractory to topical corticosteroids: results of a randomized, double-blind, placebo-controlled, multicentre trial. Br J Dermatol; 158, 2008:808-817. [11] Fowler J, Graff O, Hamedani A. 2014. A phase 3, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of alitretinoin (BAL4079) in the treatment of severe chronic hand eczema refractory to potent topical corticosteroid therapy. J Drugs Dermatol; 13:1198-1204. [12] Smith IL, et al. 2022. Comparison of ALitretinoin with PUVA as the first-line treatment in patients with severe chronic HAnd eczema (ALPHA): study protocol for a randomised controlled trial. BMJ Open;12(2):e060029.

Presented at the ISPOR Europe 2025, Glasgow, Scotland, UK, 9-12 November 2025