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A 24-week trial to compare the efficacy and safety of delgocitinib cream 20 mg/g twice-daily with alitretinoin capsules once daily in adult participants with severe chronic hand eczema

Submission date
21/01/2022

Recruitment status
No longer recruiting

Registration date
09/03/2022

Overall study status
Completed

Last Edited
30/01/2026

Condition category
Skin and Connective Tissue Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Chronic hand eczema (CHE) is a serious inflammatory skin disorder located anywhere on the hands or wrists. It is characterised by erythema (rash), hyperkeratosis (thickening of the outer layer of skin) and oedema (swelling). CHE is generally difficult to treat and presents with periods of flares and remissions. As the currently available treatment options either lack documented treatment effect or are limited by restrictions of long-term use due to safety concerns, there is a high unmet medical need for new topical treatments of moderate to severe CHE, especially for long-term use. New and better treatments would potentially improve the everyday lives of patients with moderate to severe CHE.

This study will compare the effectiveness, safety and affect on general health status and quality of life of delgocitinib cream and alitretinoin capsules for treating patients with CHE. Delgocitinib, an experimental medication, is a pan JAK inhibitor (blocks specific processes, such as immune pathways, in the body's response to conditions like hand eczema). Alitretinoin is the only approved product specifically indicated for treatment of CHE, but it is only indicated for severe CHE and only approved in a few countries worldwide.

Who can participate?
Adults over 18 years, with severe CHE.

What does the study involve?
This study is randomised, which means that which of these two medications participants will receive is chosen at random. A computer will randomly select participant's treatment. Participants will have a 50% chance of receiving any one of these medications. Participants assigned to receive delgocitinib will apply delgocitinib cream to the skin twice a day for 16 weeks Participants assigned to receive Alitretinoin will take Alitretinoin by mouth once a day for 12 weeks. All participants may continue on treatment for up to 24 weeks if the doctor considers that they are benefiting from the treatment.

What are the possible benefits and risks of participating?
There is no guarantee that participants will benefit from the treatment they get during the study. Participants are being asked to take part because the study medication may improve the symptoms of their hand eczema. The information collected in this study may help to make delgocitinib cream available for people with hand eczema in the future.
Delgocitinib cream
Based on data from studies so far, no specific side effects have been confirmed for delgocitinib cream. As for other treatments applied to the skin, participants may experience local skin reactions, for example pain where delgocitinib cream was applied. Since delgocitinib has an effect on the immune system, a risk for local skin infection and acne like lesions could arise from use of delgocitinib cream.
Alitretinoin
As alitretinoin is already approved for the treatment of severe chronic hand eczema, some side effects have been confirmed. Please be aware that some of the side effects can depend on the dose of the medication and may improve by reducing the dose. This will be decided as necessary during study conduct by the study doctor.

Where is the study run from?
Guy's and St Thomas' NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
January 2022 to December 2023

Who is funding the study?
Leo Pharma (Denmark)

Who is the main contact?
Dr Richard Woolf, Richard.Woolf@gstt.nhs.uk

Contact information

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT05259722

Clinical Trials Information System (CTIS)
2021-003543-16

Integrated Research Application System (IRAS)
1004431

Central Portfolio Management System (CPMS)
51060

Protocol serial number
LP0133-1528

Study information

Scientific Title
A 24-week, randomised, assessor-blinded, active-controlled, parallel-group, phase 3, 2-arm trial to compare the efficacy and safety of delgocitinib cream 20 mg/g twice-daily with alitretinoin capsules once daily in adult participants with severe chronic hand eczema

Acronym
DELTA FORCE

Study objectives
1. To compare the efficacy and health-related quality of life of twice-daily topical application of delgocitinib cream with once-daily oral administration of alitretinoin capsules in the treatment of patients with severe CHE.
2. To compare the safety of twice-daily topical application of delgocitinib cream with once-daily oral administration of alitretinoin capsules in the treatment of patients with severe CHE.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 04/03/2022, South Central – Berkshire B Research Ethics Committee (Level 3, Block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT, UK; +44 207 104 8253; berkshireb.rec@hra.nhs.uk), ref: 22/SC/0033

Primary study design
Interventional

Study design
Interventional randomized controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Severe hand eczema

Interventions
Eligible participants will be randomised in a 1:1 ratio to receive 1 of the following treatments:
- Topical administration of delgocitinib cream 20 mg/g, twice-daily until week 16, which may continue up to week 24 depending on clearance status (IGA-CHE score) and clinical benefit
- Oral administration of alitretinoin capsules 30 mg (with an option to reduce to 10 mg during trial conduct), once-daily until week 12, which may continue up to week 24 depending on clearance status (IGA-CHE score) and clinical benefit

Randomisation will be stratified by subtype (hyperkeratotic/non-hyperkeratotic) and region (North America/Europe) and performed online.
For each participant, the trial will last at least 25 weeks and up to 33 weeks, including:
- A screening period of 1 to 4 weeks
- A treatment period of up to 24 weeks
- A safety follow up period of 2 to 5 weeks (1 visit for all participants 2 weeks after last IMP dose, plus a pregnancy follow up visit for women of childbearing potential [WOCBP] treated with alitretinoin 5 weeks after the last IMP dose)

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Delgocitinib, alitretinoin

Primary outcome(s)
Hand Eczema Severity Index (HECSI) score at baseline and week 12

Key secondary outcome(s)
1. HECSI-90 (at least 90% improvement in HECSI score from baseline) at Week 12
2. Investigator’s Global Assessment for chronic hand eczema© treatment success (IGA-CHE TS) at Week 12
3. Change in Hand Eczema Symptom Diary© (HESD) itch score (weekly average) from baseline to Week 12
4. Change in HESD pain score (weekly average) from baseline to Week 12
5. AUC of HECSI-90 from baseline up to Week 24
6. AUC of change from baseline in Dermatology Life Quality Index (DLQI) score up to Week 24
7. Change in HECSI score from baseline to Week 24

8. Number of treatment-emergent AEs from baseline up to Week 26 measured using patient records
9. Number of treatment-emergent SAEs from baseline up to Week 26 measured using patient records
10. Number of AEs leading to IMP discontinuation up to Week 24 measured using patient records

Completion date
05/12/2023

Eligibility

Key inclusion criteria
1. Participant must be at least 18 years of age inclusive, at the time of signing the informed consent
2. Diagnosis of CHE defined as hand eczema that has persisted for more than 3 months or returned twice or more within the last 12 months
3. Disease severity graded as severe at screening and baseline according to IGA-CHE (i.e. an IGA-CHE score of 4)
4. Documented recent history of inadequate response to treatment with TCS (at any time within 1 year before the screening visit) or for whom TCS are documented to be otherwise medically inadvisable
5. Participant is adherent to standard non-medicated skin care including avoidance of known and relevant irritants and allergens
6. Contraceptive use must be consistent with local regulations regarding the methods of contraception for those participating in clinical studies

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
100 Years

Sex
All

Total final enrolment
513

Key exclusion criteria
Participants are excluded from the trial if any of the following criteria apply:
Diagnostic Assessments

1. Concurrent skin diseases on the hands (e.g. tinea manuum).
2. Active atopic dermatitis requiring medical treatment in regions other than the hands and feet.
3. Active psoriasis on any part of the body.
4. Hyperkeratotic hand eczema in combination with a history of psoriasis on any part of the body.
5. Clinically significant infection (e.g. impetiginised hand eczema) on the hands.

Medical Conditions

6. Participants who cannot receive alitretinoin for any of the following reasons:
6.1. Hepatic impairment, defined as alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) values >2×ULN, and/or prothrombin international normalised ratio (INR) >1.5×ULN.
6.2. Renal insufficiency, defined as creatinine clearance <60 mL/min calculated by use of the Cockcroft-Gault formula.
6.3. Uncontrolled hypercholesterolemia, defined as fasting cholesterol >1.5×ULN and/or fasting low-density lipoprotein (LDL) cholesterol >1.5×ULN.
6.4. Uncontrolled hypertriglyceridemia, defined as fasting triglyceridaemia 1.5×ULN.
6.5. Uncontrolled hypothyroidism, defined as thyroid stimulating hormone >1×ULN and/or thyroxine <1×lower limits of normal.
6.6. Hypervitaminosis A, defined as retinol levels >1×ULN (e.g. due to the use of vitamin A supplements containing >2000 IU).
6.7. Known or suspected hypersensitivity either to alitretinoin, to other retinoids or to any of the excipients listed in the applicable alitretinoin label, in particular allergies to peanut or soya, or intolerance to sorbitol or fructose.
6.8. Any other contraindication to receive alitretinoin according to the investigator's judgement.
7. Clinically significant infection within 28 days prior to baseline which, in the opinion of the investigator, may compromise the safety of the participant in the trial, interfere with the evaluation of the IMP, or reduce the participant's ability to participate in the trial. Clinically significant infections are defined as:
7.1. A systemic infection.
7.2. A serious skin infection requiring parenteral (intravenous or intramuscular) antibiotics, antiviral, or antifungal medication.
8. History of any known primary immunodeficiency disorder including a positive human immunodeficiency virus (HIV) test at screening, or the participant taking antiretroviral medications as determined by medical history and/or participant's verbal report.
9. Major surgery within 8 weeks prior to baseline, or planned in-patient surgery or hospitalisation during the trial period.
10. History of cancer except the following:
10.1. Participants who have had basal cell carcinoma, localised squamous cell carcinoma of the skin or in situ carcinoma of the cervix are eligible provided that the participant is in remission and curative therapy was completed at least 12 months prior to screening.
10.2. Participants who have had other malignancies are eligible provided that the participant is in remission and curative therapy was completed at least 5 years prior to screening.
11. Psychiatric disorders within the last year (e.g. depression, depression aggravated, anxiety, aggressive tendencies, mood alterations, psychotic symptoms, suicidal ideation, suicide attempts) or current self-reported depression or mood disturbance.
12. Any disorder that is not stable and could:
12.1. Affect the safety of the participant throughout the trial.
12.2. Impede the participant's ability to complete the trial.
Examples include but are not limited to cardiovascular, gastrointestinal, hepatic, renal, neurological, musculoskeletal, infectious, endocrine, metabolic, haematological, and immunological disorders, and major physical impairment.
13. Any abnormal finding that may:
13.1. Put the participant at risk because of their participation in the trial.

13.2. Influence the participant's ability to complete the trial.
The abnormal finding must be clinically significant and observed during the screening period. Examples include abnormal findings in physical examination, vital signs, electrocardiogram (ECG), haematology, clinical chemistry, or urinalysis.
14. Positive hepatitis B surface antigen (HBsAg) or hepatitis C virus (HCV) antibody serology at screening.
15. Current or recent history of chronic alcohol or drug abuse or any condition associated with poor compliance as judged by the investigator.
Prior/Concomitant Therapy
16. Systemic treatment with immunosuppressive drugs (e.g. methotrexate, cyclosporine, azathioprine), immunomodulating drugs, retinoids, or corticosteroids within 28 days prior to baseline (steroid eyedrops and inhaled or intranasal steroids corresponding to up to 1 mg prednisolone for allergic conjunctivitis, asthma, or rhinitis are allowed).
17. Use of tanning beds, phototherapy (e.g. UVB, UVA1, PUVA), or bleach baths on the hands within 28 days prior to baseline.
18. Previous or current treatment with JAK inhibitors (including delgocitinib/LEO 124249), systemic or topical.
19. Cutaneously applied treatment with immunomodulators (e.g. PDE-4 inhibitors, pimecrolimus, tacrolimus) or TCS on the hands within 14 days prior to baseline.
20. Use of systemic antibiotics or cutaneously applied antibiotics on the hands within 14 days prior to baseline.
21. Other transdermal and cutaneously applied therapy on the hands (except for the use of participant's own emollients) within 7 days prior to baseline.
22. Cutaneously applied treatments in regions other than the hands, which could interfere with clinical trial evaluations or pose a safety concern, within 7 days prior to baseline.
23. Treatment with any marketed biological therapy or investigational biologic agents (including immunoglobulin, anti-IgE, and dupilumab), except vaccines:
23.1. Any cell-depleting agents including but not limited to rituximab: within 6 months prior to baseline, or until lymphocyte count returns to normal, whichever is longer.
23.2. Other biologics: within 3 months or 5 half-lives, whichever is longer, prior to baseline.
24. Treatment with CYP3A4 inhibitors (e.g. ketoconazole), potent CYP2C9 inhibitors (e.g. fluconazole, miconazole, oxandrolone), or potent CYP2C8 inhibitors (e.g. gemfibrozil), CYP2C8 substrates (e.g. amiodarone, paclitaxel, rosiglitazone, repaglinide), simvastatin, or tetracyclines within 7 days prior to screening. Topical treatment with CYP2C9 inhibitors (e.g. fluconazole, miconazole, oxandrolone) on areas of the body other than hands is allowed.
25. Treatment with any marketed therapy that may interfere with the trial objective.
Prior/Concurrent Clinical Trial Experience
26. Previously used alitretinoin or participated in a clinical trial with alitretinoin or delgocitinib.
27. Treatment with any non-marketed drug substance (that is, an agent that has not yet been made available for clinical use following registration) within the last 28 days prior to baseline or 5 half-lives, whichever is the longest.
28. Current participation in any other interventional clinical trial.
Other Exclusions
29. Known or suspected hypersensitivity to any component(s) of the IMPs, including allergies to peanut or soya.
30. Women who are pregnant or lactating.
31. Employees of the trial site or any other individuals directly involved with the planning or conduct of the trial, or immediate family members of such individuals.
32. Participants who are legally institutionalised.
33. Previously randomised in this clinical trial.

Date of first enrolment

10/03/2022

Date of final enrolment
26/05/2023

Locations

Countries of recruitment
United Kingdom

Austria

Canada

France

Germany

Italy

Poland

Spain

Study participating centre
Guys Hospital
Guy's and St Thomas' NHS Foundation Trust
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Study participating centre
Queens Medical Centre
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Derby Road
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Sponsor information

Organisation
Leo Pharma (Denmark)

ROR
https://ror.org/05tzrdd39

Funder(s)

Funder type
Industry

Funder Name
LEO Pharma

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to privacy or ethical restrictions. Anonymized patient-level data that support the findings of this study can be made available to researchers via a secured file transfer protocol upon reasonable request.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		10/05/2025	27/01/2026	Yes	No
HRA research summary			28/06/2023	No	No