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Comparing treatments for severe chronic hand eczema

Submission date	Recruitment status	[X] Prospectively registered
22/07/2015	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
29/07/2015	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
04/10/2024	Skin and Connective Tissue Diseases	

Plain English summary of protocol

Background and study aims
Hand eczema (HE) is one of the most common skin disorders and can considerably impact the daily life of sufferers. However, there is a lack of reliable evidence to direct clinical practice regarding the most effective treatment for severe HE when steroid creams are not sufficient to control the disease. In particular, there is no reliable information on the effect of treatments with patients suffering from different types of HE. This study will be the first study to directly compare Alitretinoin and immersion PUVA (two commonly available NHS treatments) to see which of these two treatments is most effective in treating which type of hand eczema. It will also examine both the short term and longer term effectiveness of each treatment in terms of both how good the hands heal with the treatment and how long the skin can remain clear once healed.

Who can participate?
Patients aged 18 or older who suffer from severe chronic hand eczema, which has not improved with strong steroid treatment for at least 4 weeks prior to participation.

What does the study involve?
A routine blood sample will be required to assess suitability for the study and to screen for atopy, which is the tendency to develop the classic allergic diseases (atopic dermatitis, allergic rhinitis [hay fever], and asthma). Participants will be randomly allocated to receive either PUVA (where the hands are exposed to ultraviolet [UV] light after they have been soaked in a solution called psoralen) or to take Alitretinoin (a tablet) over a 12-24 week period (depending on how well the hand eczema has responded). During this 12-24 week period, participants will attend clinic every 4 weeks to complete questionnaires about their hands and health, and their hands will be assessed. All participants will be asked to complete a medication diary during this period. Participants will also provide a blood sample to look at skin proteins known to be important in eczema. After this period, participants will receive standard care treatment as required. They will be asked to attend once every 4 weeks until week 36, then once every 8 weeks until week 52. At these visits, participants will complete questionnaires about their hands and health, and their hands will be assessed.

What are the possible benefits and risks of participating?
It is hoped by taking part in this study the participant will respond to treatment and have an increased quality of life. This is in line with what the participant would have experienced if treated according to normal NHS practice, as both treatments are used as standard NHS treatments. This study will help us to understand which of these treatments, if any, is more effective in the short term, and what the long-term benefits of each treatment may be. Taking part in this research study involves time and commitment such as regular hospital visits for treatment and follow-up visits. Although the number of treatment visits will be no more than if the participant receives these treatments outside of a research study setting, the follow-up visits will be in addition. The treatments used as part of the study are currently available as routine standard treatment by the NHS and therefore there are no additional risks beyond those that the participant would be exposed to as part of standard care.

Where is the study run from?
The study will be run from approximately 35-40 hospital dermatology departments across the UK.

When is the study starting and how long is it expected to run for?
The study runs from October 2015 until March 2019. Each person will take part in the study for 12 months. September 2017 is the end of the recruitment phase.

Who is funding the study?
The National Institute for Health Research (NIHR) (UK)

Who is the main contact?
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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2014-004741-27

Protocol serial number
DM14/11351; HTA 12/186/01

Study information

Scientific Title
Comparison of Alitretinoin with PUVA as the first line treatment in patients with severe chronic hand eczema: a randomised controlled trial

Acronym
ALPHA

Study objectives
The aim of this study is to determine the clinical and cost effectiveness of Alitretinoin and PUVA when used in conjunction with concomitant topical corticosteroids, emollients and patient education for the treatment of severe chronic hand eczema (CHE) which is unresponsive to treatment with potent topical corticosteroids alone.

More details can be found at http://www.nets.nihr.ac.uk/projects/hta/1218601
Protocol can be found at http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0005/136994/PRO-12-186-01.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Leeds West research ethics committee, 09/01/2015, ref: 14/YH/1259
2. Amendment approved 18/03/2015

Study design
Prospective multicentre open-label two-arm parallel-group adaptive randomised controlled trial with one planned interim analysis

Primary study design

Interventional

Study type(s)
Treatment

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

Interventions
A maximum of 780 consenting participants with severe CHE will be randomised on a 1:1 basis to receive either Alitretinoin (30 mg per day) or the phototherapy Psoralen with UV-A treatment (PUVA) (twice weekly) in conjunction with concomitant topical corticosteroids, emollients and patient education. PUVA therapy will involve photosensitising of hands by immersion in a dilute solution of Meladinine®, before exposure of hands to UV-A light.

The trial is an adaptive design with a planned interim analysis to re-estimate the sample size, which may lead to fewer than the required 780 participants, although a minimum of 500 participants will be recruited.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
1. Alitretinoin 2. Meladinine® 0.75% solution

Primary outcome(s)
Disease activity of the index hand, quantified using the HECSI tool, at 12 weeks post planned start of treatment

Key secondary outcome(s))
1. Disease activity of the index hand, quantified using the HECSI tool, at 24 and 52 weeks post planned start of treatment
2. Disease activity of the index hand, quantified using the mTLSS tool, at 24 and 52 weeks post planned start of treatment
3. Disease activity of the index hand, quantified using the PGA tool at 24 and 52 weeks post planned start of treatment
4. Time to relapse of the index hand (HECSI score >75% baseline HECSI score of the index hand)
5. Time in remission of the index hand (defined by the period of time when patient is classed as clear/almost clear until the disease is scored as ‘mild’ or higher on the PGA scale and participants have been using topical corticosteroids daily for the previous 7 or more days)
6. Patient reported outcome using the DLQI tool, over the 52 weeks post planned start of treatment
7. Patient reported outcome using the PBI-HE over the 52 weeks post planned start of treatment
8. PeDeSi over the 52 weeks post planned start of treatment
9. Cost-effectiveness over the 52 weeks post planned start of treatment

(added 08/11/2019: Participants randomised from 1st October will complete follow up at week 24 [not week 52])

Completion date
31/12/2021

Eligibility

Key inclusion criteria
1. Patients aged ≥18 years at the time of signing the Informed Consent Form
2. Patients suffering from uncontrolled, severe CHE defined as the presence of both of the following criteria:
2.1. PGA score of severe
2.2. Resistance to treatment with potent topical corticosteroids for ≥ 4 weeks prior to the point of eligibility screening
3. Avoidance strategies for known contact allergens are in place for at least a two-week period prior to randomisation
4. Patient has provided written informed consent
5. Patient is expected to comply with treatment and protocol schedule

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
441

Key exclusion criteria
Skin related:
1. Patients who have a clinically suspected infection (fungal, bacterial or viral) as cause for dermatitis of the hands
2. Patients with known clinically relevant allergic contact dermatitis of the hands unless they had made a reasonable effort to avoid the contact allergen
3. Patients suffering from atopic eczema covering more than 10% of body surface (excluding hands)
4. Patients who have skin conditions worsened by the sun i.e., do not tolerate UV light (e.g., lupus erythematosus, porphyria)

Treatment related:
1. Patients who have received phototherapy/photochemotherapy in the last 3 months prior to randomisation
2. Patients who have received systemic vitamin A derivatives or other systemic

immunosuppressants e.g. methotrexate or biologics treatment for HE in the last 3 months prior to randomisation
3. Patients who have received Ciclosporin A or systemic glucocorticoid steroid treatment for HE in the last 4 weeks prior to randomisation.
4. Patients receiving topical calcineurin antagonist treatment within 1 week prior to randomisation.
5. Patients receiving concomitant treatment with tetracyclines, or medication with potential for drug-drug interaction with Alitretinoin (e.g. CYP3A4 inhibitor ketoconazole) that cannot be suspended or switched to an acceptable alternative
6. Patients receiving concomitant treatment with relevant photosensitisers, when this treatment cannot be suspended for the duration of the intervention or switched to an acceptable alternative
7. Patients with a history of melanoma skin cancer, or patients with a history of non-melanoma skin cancer depending on history, location and “severity” of the non-melanoma skin cancer based on experience from routine practice
8. Patients who have received prior treatment with arsenic agents or ionising radiation in the treatment area (e.g. hands)

General:
1. Women who are lactating or of child bearing potential (WCBP, Appendix 1) with:
1.1. Positive pregnancy test (absence of pregnancy will be confirmed with a negative pregnancy test before randomisation)
1.2. Unwilling to follow pregnancy prevention program measures* (see below) whilst receiving treatment and after the last dose of protocol treatment as indicated in the relevant SmPC
2. Patients with hepatic insufficiency (alanine aminotransferase and/or aspartate aminotransferase > 2.5 times the upper limit of normal), known severe renal insufficiency, uncontrolled hyperlipidaemia (for all of the following: triglycerides, cholesterol and/or LDL cholesterol) or uncontrolled hypothyroidism in the 12 week period prior to randomisation
3. Patients with known hypersensitivity to peanut, soya or vitamin A derivatives or with rare hereditary fructose intolerance as determined by patient history
4. Patients currently suffering from hypervitaminose A as directed by clinical symptoms or patient history
5. Patients previously participated in the ALPHA trial

*Rigorous contraception for women of childbearing potential is required 1 month before treatment, during the treatment period and 1 month after cessation of treatment as per usual standard practice.

Date of first enrolment
01/10/2015

Date of final enrolment
31/12/2020

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
Leeds Teaching Hospital NHS Trust
Musculo Skeletal office, 2nd floor
Chapel Allerton Hospital
Chapeltown road
Leeds
United Kingdom
LS7 4SA

Study participating centre
St Woolos Hospital
Aneurin Bevan UHB
131 Stow Hill
Newport
United Kingdom
NP20 4SZ

Study participating centre
Whipps Cross Hospital
Barts Health NHS Trust
Junction 9, Lower Ground Floor
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Leytonstone
London
United Kingdom
E11 1NR

Study participating centre
Royal London Hospital
Barts Health NHS Trust
5 Walden Street
London
United Kingdom
E1 2EF

Study participating centre

Nottingham University Hospitals NHS Trust
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QMC
Nottingham
United Kingdom
NG7 2UH

Study participating centre
The James Cook University Hospital
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TS4 3BW

Study participating centre
Royal Cornwall Hospital
Royal Cornwall Hospitals NHS Trust
Truro
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TR1 3HD

Study participating centre
Royal Devon and Exeter NHS Foundation Trust
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EX2 5DW

Study participating centre
Guy's Hospital
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Norfolk & Norwich University Hospitals NHS Foundation Trust
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Study participating centre
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KY12 OSU

Study participating centre
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Study participating centre
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NN1 5BD

Study participating centre
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Study participating centre
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Royal Liverpool & Broadgreen University Hospitals NHS Trust
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Study participating centre
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Study participating centre
St Lukes Hospital
Bradford Teaching Hospitals NHS Foundation Trust
Little Horton Ln

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BD5 0NA

Study participating centre
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Sponsor information

Organisation
University of Leeds

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

Current IPD sharing statement as of 02/08/2022:
De-identified individual participant data datasets generated and/or analysed during the current study will be available upon request from the Clinical Trials Research Unit, University of Leeds (contact CTRU-DataAccess@leeds.ac.uk in the first instance). Data will be made available at the end of the trial, i.e. usually when all primary and secondary endpoints have been met and all key analyses are complete. Data will remain available from then on for as long as CTRU retains the data.

CTRU makes data available by a 'controlled access' approach. Data will only be released for legitimate secondary research purposes, where the Chief Investigator, Sponsor and CTRU agree that the proposed use has scientific value and will be carried out to a high standard (in terms of scientific rigour and information governance and security) and that there are resources available to satisfy the request. Data will only be released in line with participants' consent, all applicable laws relating to data protection and confidentiality, and any contractual obligations to which the CTRU is subject. No individual participant data will be released before an appropriate agreement is in place setting out the conditions of release. The agreement will govern data retention, usually stipulating that data recipients must delete their copy of the released data at the end of the planned project.

The CTRU encourages a collaborative approach to data sharing and believes it is best practice for researchers who generated datasets to be involved in subsequent uses of those datasets. Recipients of trial data for secondary research will also receive data dictionaries, copies of key trial documents and any other information required to understand and reuse the released datasets.

The conditions of release for aggregate data may differ from those applying to individual participant data. Requests for aggregate data should also be sent to the above email address to discuss and agree suitable requirements for release.

Previous IPD sharing statement:
The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository at the Clinical Trials Unit in Leeds.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/10/2024	04/10/2024	Yes	No
Protocol article		23/02/2022	12/08/2022	Yes	No
Basic results	version 1.0		07/03/2024	No	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes