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Systemic therapy for vulval erosive lichen planus

Submission date
12/06/2014

Recruitment status
No longer recruiting

Registration date
12/06/2014

Overall study status
Completed

Last Edited
08/11/2018

Condition category
Skin and Connective Tissue Diseases

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
Erosive lichen planus affecting the vulval area causes painful ulcers which last for a long time and are difficult to treat. Very little research has taken place into treatments for erosive lichen planus affecting the female external genital area (vulva) and it is not clear which is the best treatment for people who have severe disease. To find that out, this study compares three most commonly used tablets against an ointment and a short course of steroid tablets. The tablets fine tune or dampen the body's immune system. This is because an overactive immune system is thought to be the cause of erosive lichen planus.

Who can participate?
Adult patients with vulval erosive lichen planus that has not responded well to standard treatment with creams and ointments.

What does the study involve?
Participants are randomly allocated to take one of the four treatments, although some of the treatments require additional tablets to be taken alongside them to prevent side effects. Participants are able to use a moisturising cream and strong steroid ointment alongside the tablet treatment. They are given the treatment for 6 months at first, after which time it can be continued if it has been effective. If it has not been effective, treatment can be changed. This is a decision that is made between the participant and their hospital consultant.

What are the possible benefits and risks of participating?
There are no guaranteed direct benefits because it is not known for sure that the medications help but the information from this study may help to guide doctors in how patients should be treated in the future. Because this study is comparing four commonly used treatments and the study is designed to mimic normal care, there are no additional risks to participants in taking part in this study. The care that participants receive is very similar to the care that they would receive if they were not taking part in the study. Participants are closely monitored as part of their usual care.

Where is the study run from?
The study is run from certain hospital departments in the UK that specialize in treating vulval skin disorders.

When is the study starting and how long is it expected to run for?
June 2014 to April 2016

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

Who is the main contact?
Dr Rosalind Simpson
helpstudy@nottingham.ac.uk

Study website
http://www.nottingham.ac.uk/research/groups/cebd/projects/help-trial/index.aspx

Contact information

Type(s)
Scientific

Contact name
Dr Rosalind Simpson

Contact details
Centre of Evidence Based Dermatology
Kings Meadow Campus
Lenton Lane
Nottingham
United Kingdom
NG7 2NR
-
rosalind.simpson@nottingham.ac.uk

Additional identifiers

EudraCT/CTIS number
2014-000547-32

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
16788

Study information

Scientific Title
A randomised controlled trial of adjunctive systemic therapy for vulval Erosive Lichen Planus

Acronym
hELP

Study objectives
To test whether hydroxychloroquine, methotrexate or mycophenolate mofetil are better than standard care with topical clobetasol propionate 0.05% plus a short course of oral prednisolone in patients with vulval erosive lichen planus that has been refractory to first-line therapy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee Yorkshire and The Humber - Sheffield, 14/04/2014, ref: 14/YH/0046

Study design
Randomised; Interventional; Design type: Not specified

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
http://www.nottingham.ac.uk/research/groups/cebd/documents/researchdocs/help-pis-final-v2-0-31-03-14.pdf

Health condition(s) or problem(s) studied
Topic: Dermatology; Subtopic: Skin (all Subtopics); Disease: Dermatology

Interventions
Participants will be randomised to receive one of the three active interventions or to receive the comparator, clobetasol propionate 0.05% plus oral prednisolone, which is standard care:
1. Hydroxychloroquine, oral administration, up to 6.5 mg/kg lean body weight, maximum dose of 200 mg BD (in conjunction with topical clobetasol propionate 0.05%). Treatment duration 6 months.
2. Methotrexate, oral administration, dose commencing at 5 mg/week and gradually increase as per protocol according to response to a maximum of 25 mg/week (in conjunction with topical clobetasol propionate 0.05%. Treatment duration 6 months.
3. Mycophenolate mofetil, oral administration, dose commence at 500 mg OD and gradually increase as per protocol according to response to a maximum dose of 1.5 g BD (in conjunction with topical clobetasol propionate 0.05%) Treatment duration 6 months.
4. Standard care: Clobetasol propionate 0.05% (standard care), topical application, once daily for 1 month and regimen reduced according to response. Maximum 60 g over 6 months (British Association of Dermatologists guidance for the treatment of lichen sclerosus). Oral prednisolone: an initial 4-week course on a reducing regimen of 20 mg OD for 1 week, reducing by 5 mg per week.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Hydroxychloroquine, methotrexate, mycophenolate mofetil, clobetasol propionate, prednisolone

Primary outcome measure
Current primary outcome measures as of 08/12/2014:
Proportion of participants achieving treatment success at 6 months; Treatment should be classed as successful if both criteria and are met:
1. Patient Global Assessment score of 0 or 1 on a 4-point scale
2. Assessment of improvement from baseline judged by clinical images

Previous primary outcome measures:
Proportion of participants achieving treatment success at 6 months; Treatment should be classed as successful if both criteria and are met:
1. Patient Global Assessment score of 0 or 1 on a 4-point scale
2. Investigator Global Assessment of improvement from baseline judged by clinical images

Secondary outcome measures
Current secondary outcome measures as of 08/12/2014:
1. Reduction in pain/soreness
2. Global assessment of disease assessed through:
2.1. Patient Global Assessment
2.2. Investigator Global Assessment by treating clinician
2.3. Assessment by blinded assessor using clinical images
3. Assessment of other affected mucosal sites by treating clinician
4. Psychological assessment using the Hospital Anxiety and Depression Scale
5. Assessment of sexual function
6. Health-related quality of life – using:
6.1. Skindex-29
6.2. Short Form 36
7. Days of topical steroid use during treatment period
8. Treatment satisfaction – assessed as overall satisfaction plus number of participants continuing treatment post the primary endpoint
9. Adverse events (AEs) reported during the study, and discontinuation of medications due to AEs
10. Average cost of intervention in each treatment group per participant

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Overall study start date
01/06/2014

Completion date
30/04/2016

Eligibility

Key inclusion criteria
Current inclusion criteria as of 08/12/2014:
1. Clinical diagnosis of erosive lichen planus affecting the vulvovaginal region (ELPV)
2. Documented histological examination in the patient's history that excludes malignant/pre-malignant disease. Biopsy should be repeated if clinically indicated prior to consideration of systemic therapy
3. Inadequate disease control despite first-line therapy with clobetasol propionate 0.05% for at least 3 months
4. Moderate or severe disease on Investigator Global Assessment
5. Microbiological swabs negative, or result that is not clinically relevant, at study entry
6. Willing and capable of giving informed consent
7. Willing to have clinical images taken
8. Female aged 18 years or over
9. Use of effective contraceptive methods in females of childbearing age for the duration of treatment
10. For participants receiving methotrexate to use effective contraceptive methods until 6 months after the end of treatment

Previous inclusion criteria:
1. Clinical diagnosis of erosive lichen planus affecting the vulva
2. Histological examination within the past 12 months to exclude alternative diagnoses
3. Inadequate control despite first-line therapy with clobetasol propionate 0.05%
4. Disease severity of moderate-severe on Investigator Global Assessment
5. Negative microbiological swabs at study entry
6. Willing and capable of giving informed consent
7. Willing to have clinical images taken
8. Age >18 years (there is no upper age limit)
9. Use of effective contraceptive methods in females of childbearing age

Target Gender: Female; Upper Age Limit 99 years ; Lower Age Limit 18 years

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
Planned Sample Size: 96; UK Sample Size: 96

Key exclusion criteria
Current exclusion criteria as of 08/12/2014:
1. Cases of lichen sclerosus/lichen planus overlap
2. Received one or more of the trial drugs within the last one month (excluding clobetasol propionate 0.05%)
3. Previous/current diagnosis of malignant disease (skin or internal)
4. History of or current diagnosis of pre-malignant vulval skin or cervical disease
5. Receiving concurrent medications that would preclude the use of any of the trial medications in normal practice
6. History of clinically significant renal or liver impairment or other pre-existing medical conditions that would preclude the use of any of the trial medications in normal practice
7. Administration of a live vaccine (BCG, Measles, Mumps, Rubella, Yellow Fever, Oral Polio, Oral Typhoid) within the last 2 weeks
8. Pregnancy or breast-feeding
9. Known allergy to any of the trial medications

Previous exclusion criteria:
1. Cases of lichen sclerosus/lichen planus overlap
2. Patients taking beta blockers or non-steroidal anti-inflammatory medications
3. Received one or more of the trial drugs within the last month (excluding clobetasol propionate 0.05%)
4. Previous/current diagnosis of malignant disease (skin or internal)
5. Pre-malignant vulval skin or cervical disease
6. Receiving concurrent medications that would preclude the use of any of the trial medications in normal practice
7. History of clinically significant renal or liver impairment or other pre-existing medical conditions that would preclude the use of any of the trial medications in normal practice
8. Administration of a live vaccine (BCG, measles, mumps, rubella, yellow fever, oral polio, oral typhoid) within the last 2 weeks
9. Pregnancy or breastfeeding
10. Known sensitivity to any of the trial medications

Date of first enrolment
15/08/2014

Date of final enrolment

31/07/2015

Locations

Countries of recruitment
England

Scotland

United Kingdom

Wales

Study participating centre
Nottingham University Hospitals NHS Trust
Nottingham City Hospital
Nottingham
United Kingdom
NG5 1PB

Study participating centre
Grampian Health Board
Aberdeen Royal Infirmary
Aberdeen
United Kingdom
AB25 7ZD

Study participating centre
East Lancashire Hospitals NHS Trust
Royal Blackburn Hospital
Blackburn
United Kingdom
BB2 3HH

Study participating centre
Bradford Teaching Hospitals NHS Trust
St Luke's Hospital
Bradford
United Kingdom
BD5 0NA

Study participating centre
Cardiff and Vale University Local Health Board
University Hospital of Wales
Cardiff
United Kingdom
CF14 4XW

Study participating centre
Leeds Teaching Hospital NHS Trust
Chapel Allerton Hospital
Leeds
United Kingdom
LS7 4SA

Study participating centre
Royal Liverpool and Broadgreen University Hospitals NHS Trust
Broadgreen Hospital
Liverpool
United Kingdom
L14 3LB

Study participating centre
Barts Health NHS Trust
Whipp's Cross Hospital
London
United Kingdom
E11 1NR

Study participating centre
Central Manchester University Hospitals NHS Foundation Trust
St Mary's Hospital
Manchester
United Kingdom
M13 9WL

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
Addenbrookes Hospital
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Tayside Health Board, Ninewells Hospital and Medical School
Dundee
United Kingdom
DD1 9SY

Study participating centre
Salford Royal NHS Foundation Trust
Salford Royal Hospital
Salford
United Kingdom
M6 8HD

Sponsor information

Organisation
University of Nottingham (UK)

Sponsor details
Division of Primary Care
Graduate Medical School
London
England
United Kingdom
NG7 2NR

Sponsor type
University/education

ROR
https://ror.org/01ee9ar58

Funder(s)

Funder type
Government

Funder Name
NIHR Doctoral Research Fellowship; Grant Codes: DRF-2012-05-166

Results and Publications

Publication and dissemination plan
Intention to publish approx September 2017 in a peer reviewed journal. Dissemination to take place by presentation at appropriate multidisciplinary conferences.

Intention to publish date
01/09/2017

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. Kim Thomas (kim.thomas@nottingham.ac.uk).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	04/01/2016		Yes	No
Basic results	results	10/03/2017	28/06/2017	No	No
Results article		01/10/2018		Yes	No
HRA research summary			28/06/2023	No	No