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Proactive against reactive treatment for lichen sclerosus

Submission date
09/01/2024

Recruitment status
Recruiting

Registration date
08/03/2024

Overall study status
Ongoing

Last Edited
02/12/2025

Condition category
Skin and Connective Tissue Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Lichen sclerosus (LS) is a long-term, itchy and distressing condition affecting vulval skin (the skin around the outside of the vagina). It needs ongoing treatment with steroid creams to manage flares of symptoms. If untreated, it may lead to scarring causing the labia minora (inner lips) to fuse together or the entrance to the vagina to narrow. People with LS are at higher risk of developing vulval cancer. Vulval LS can affect everyone, but most commonly children and women of any age, particularly women who have gone through the menopause and children before puberty. This study will try to find out what is the best way to manage future flares of LS: using a steroid treatment regularly (e.g. twice a week), even when symptoms are controlled OR using a steroid cream only during a flare.

Who can participate?
Female patients with LS aged 5 years and over

What does the study involve?
Participants are randomly allocated to either use their steroid cream twice a week or to only use it if they experience symptoms. The researchers will compare how many people in each group develop LS flares. With the optional consent of the participant/parent/guardian, photographs will be taken at baseline to check if scarring worsens during the trial. The researchers will follow patients for 2 years to gather data. With participants' consent (optional), the researchers will check their medical records at a later stage (after the trial ends) to see how many patients in each treatment group develop cancer. They will conduct an optional qualitative study and interview patients (those who consented to participate in qualitative sub-study) to explore how they feel about the trial and the different ways of treating LS that we are testing. The researchers will also compare the costs and outcomes of the two treatments used in the trial to see if one is better value for money for the NHS. If successful, the study results will be used to change clinical practice for the treatment of patients with LS.

What are the possible benefits and risks of participating?
The study treatment involves topical steroid ointment/cream, which is normally prescribed to patients as their routine care for LS. The only difference between the study treatment and the routine care may be the treatment regimen. It is, therefore, believed that the risk associated

with the study due to the intervention is negligible. Participants will be asked to attend research appointments. Every effort will be made to coincide these appointments with participants' clinical appointments.
Safety data will be collected for the duration of participation and will be reported as per sponsor guidelines. Although the steroid treatment can be safely applied to the whole body in a single dose with minimal risk of adverse reactions, there is however a risk of adverse reactions following long-term use of topical corticosteroid on localised areas of skin (e.g. skin thinning, telangiectasia). These will be monitored during clinical examination at follow-up visits (or at an unscheduled trial visit, as necessary).

Where is the study run from?
Nottingham Clinical Trials Unit (UK)

When is the study starting and how long is it expected to run for?
March 2023 to March 2028

Who is funding the study?
NIHR Health Technology Assessment Programme (UK)

Who is the main contact?
PEARLS study team, PEARLS@nottingham.ac.uk

Contact information

Type(s)
Scientific, Principal investigator

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Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1008267

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
23055, CPMS 61122

Study information

Scientific Title
Proactive against reactive therapy for the prevention of lichen sclerosus exacerbation and progression of disease – a pragmatic, parallel group randomised controlled trial with embedded economic evaluation and process evaluation

Acronym
PEARLS

Study objectives
Primary objective:
Compare the clinical and cost-effectiveness of a twice-weekly topical corticosteroid maintenance strategy (proactive therapy) with as-required treatment (reactive therapy) in the management of vulval lichen sclerosus (LS)

Secondary objectives:
1. Assess the effectiveness of proactive versus reactive use of topical corticosteroids (TCSs) over 24 months in reducing disease progression
2. Assess the clinical effectiveness of proactive versus reactive strategies for the management of vulval LS for up to 24 months
3. Assess the safety of using potent and superpotent TCSs in the vulval area over 24 months
4. Assess the cost-effectiveness of the two treatment strategies
5. Understand the acceptability of reactive and proactive long-term treatment strategies and the barriers and facilitators to continuing with prescribed treatment

Ethics approval required
Ethics approval required

Ethics approval(s)

approved 27/02/2024, South West – Central Bristol Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8197, +44 (0)207 104 8269, +44 (0) 207 104 8061; centralbristol.rec@hra.nhs.uk), ref: 24/SW/0016

Study design
Open randomized controlled parallel-group trial

Primary study design
Interventional

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Vulval lichen sclerosis

Interventions
In the intervention group participants will be asked to apply potent or superpotent topical corticosteroid (TCS) on two non-consecutive days per week even in the absence of symptoms (proactive treatment). In the comparator group participants will be asked to apply potent or superpotent TCS as required to treat a LS flare (reactive treatment).

Eligible patients will be individually allocated in a 1:1 ratio to either proactive or reactive use of TCS. Treatment will be assigned randomly using a minimisation algorithm with a random element, balancing across groups on the recruiting site, age, time since last flare and strength of prescribed TCS.

The choice of TCS will be according to the patient's usual care. PEARLS is a pragmatic trial, and the researchers will test the strategy of proactive vs reactive treatment using the potency of topical corticosteroid recommended by the treating clinician (potent or superpotent). There are several generic names available for these prescribed TCSs and all available brands and forms can be prescribed. The examples of the most commonly prescribed brands/products of the TCS class are:
1. Dermovate ointment - superpotent TCS
2. Elocon® 0.1% w/w ointment - potent TCS

The topical dosage of TCSs for both trial groups will be recommended in Fingertip Units (FTU) depending upon the area affected by LS (typically 0.5-1 FTU). FTU is the amount of topical steroid (ointment or cream) that is applied along an adult's fingertip to the first crease in the finger. One FTU is sufficient to treat an area of skin twice the size of the flat of an adult's hand with the fingers together (i.e. a 'handprint'). FTU is also used to treat an area of skin on a child. The treating physician will advise on the dosage for adults or children.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)

Topical Corticosteroid (TCS)

Primary outcome(s)
Number of flares over 12 months. Flare is defined as the worsening of symptoms requiring increased application of TCS, measured via text/app/email reminders every 2 weeks for 12 months.

Key secondary outcome(s))
Clinical effectiveness:
1. Progression of scarring, assessed by a blinded assessor at 12 and 24 months by comparing the post-randomisation assessment to baseline photographs (if patients consented), or assessed clinically if consent has not been given for photographs:
1.1. Adults: scarring worsened (yes/no).
1.2. Children and adolescents: failure of normal vulval development (clinical assessment) and/or evidence of scarring (yes/no)
2. Vulval Architectural Severity Scale (VASS) at 12 and 24 months post-randomisation, assessed clinically
3. Time to first flare, measured via text/app/email reminders at the point of first flare
4. Clinician global severity assessment of LS using a 5-point ordinal scale at 3, 6, 12, 18 and 24 months. Also assessed by a blinded assessor at 12 and 24 months. This will be measured via clinical assessment.
5. Condition-specific quality of life (QoL) measured at 3, 6, 12, 18 and 24 months using:
5.1. Vulvar Quality Life Index (VQLI) (adults)
5.2. Children's Dermatology Life Quality Index (CDLQI) (adolescents and children)
5.3. Sexual function (adults only) assessed using the Female Sexual Function Index at 12 and 24 months

Safety:
1. Adverse reactions (e.g. stinging, skin thinning) measured throughout the trial by patient-reported symptoms and clinical examination from randomisation over 24 months
2. Development of vulval intraepithelial neoplasia or vulval squamous cell carcinoma at 24 months, measured by clinical assessment and/or medical notes

Treatment acceptability and potential barriers/facilitators to treatment:
1. Acceptability of treatment strategy measured using a Likert scale at 12 and 24 months
2. Adherence to treatment measured using a bespoke questionnaire completed by participants at 3, 6, 12, 18 and 24 months
3. Qualitative interview sub-study at 12 months

Cost-effectiveness:
1. Generic utility instrument to measure QoL at 3, 6, 12, 18 and 24 months with EQ-5D-5L (adolescents and adults) and Child Health Utility Instrument - Nine Dimensions (CHU-9) (children)
2. Resource use including prescription, direct and indirect healthcare and out-of-pocket costs associated with vulval LS at 3, 6, 12, 18 and 24 months, measured via a bespoke questionnaire

Completion date
01/03/2028

Eligibility

Key inclusion criteria

1. Clinical or biopsy confirmed diagnosis of vulval LS
2. Currently controlled disease (asymptomatic with minimal clinical evidence of active disease) at baseline
3. Age ≥5 years
4. Able to give consent/child assent plus parental consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
5 years

Upper age limit
100 years

Sex
Female

Total final enrolment
0

Key exclusion criteria
1. Previous vulval intraepithelial neoplasia (VIN) or vulval squamous cell carcinoma (SCC)
2. Contraindications to topical steroids
3. Concomitant use of other topical anti-inflammatory vulval treatments
4. Using systemic immunosuppressants (for any indication)
5. Using systemic treatment for LS
6. Patients with surgical alteration of vulval skin as part of gender reaffirming surgery, or patients not born with a vulva
7. Pregnant and breastfeeding women

Date of first enrolment
01/04/2024

Date of final enrolment
31/03/2026

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
Axess Sexual Health, Royal Liverpool University Hospital
Mount Vernon St
Liverpool
England
L7 8XP

Study participating centre
Liverpool Women's Hospital
Liverpool Womens Hospital
Crown Street
Liverpool
England
L8 7SS

Study participating centre
Aberdeen Royal Infirmary
Foresterhill Road
Aberdeen
Scotland
AB25 2ZN

Study participating centre
Royal Blackburn Hospital
Haslingden Road
Blackburn
England
BB2 3HH

Study participating centre
The James Cook University Hospital
Marton Road
Middlesbrough
England
TS4 3BW

Study participating centre
St Mary's Hospital
Oxford Road
Manchester
England
M13 9WL

Study participating centre
Market Street Health Centre, Oxleas
16-20 Market Street
Woolwich
London
England
SE18 6QR

Study participating centre
Whipps Cross University Hospital
Whipps Cross Road
Leytonstone
London
England
E11 1NR

Study participating centre
Queen Elizabeth Hospital
Sheriff Hill
Gateshead
England
NE9 6SX

Study participating centre
Florence Nightingale Community Hospital
London Road
Derby
England
DE1 2QY

Study participating centre
Royal Derby Hospital
Uttoxeter Road
Derby

England
DE22 3NE

Study participating centre
Churchill Hospital
Churchill Hospital
Old Road
Headington
Oxford
England
OX3 7LE

Study participating centre
Leicester Royal Infirmary
Infirmary Square
Leicester
England
LE1 5WW

Study participating centre
Nottingham City Hospital
Hucknall Road
Nottingham
England
NG5 1PB

Study participating centre
Princess Royal Hospital
Apley Castle,
Grainger Drive
Apley
Telford
England
TF1 6TF

Study participating centre
East Surrey Hospital
Canada Avenue
Redhill
England
RH1 5RH

Study participating centre
Norfolk and Norwich University Hospital
Colney Lane
Colney
Norwich
England
NR4 7UY

Study participating centre
County Durham and Darlington NHS Foundation Trust
Darlington Memorial Hospital
Hollyhurst Road
Darlington
England
DL3 6HX

Study participating centre
Cumberland Infirmary
Newtown Road
Carlisle
England
CA2 7HY

Study participating centre
Modality Community Gynaecology Service
Nishkam Pharmacy, 21 Soho Road
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B21 9SN

Study participating centre
Hull University Teaching Hospitals NHS Trust
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Study participating centre
Cardiff & Vale University Lhb
Woodland House
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CF14 4HH

Sponsor information

Organisation
Nottingham Clinical Trials Unit

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
The datasets analysed during the current trial will be available upon request from the NCTU (ctu@nottingham.ac.uk), a minimum of 6 months after publication of the main results paper. Access to the data will be subject to review of a data sharing and use request by a committee including the CI and sponsor and will only be granted upon receipt of a data sharing and use agreement. Any data shared will be anonymised which may impact on the reproducibility of published analyses.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet version 2.0	11/11/2025	11/11/2025	No	Yes
Protocol file		05/02/2024	01/08/2024	No	No