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Low-dose isotretinoin versus standard-dose isotretinoin to treat severe acne in young people – the Acne-ID study

Submission date
26/04/2024

Recruitment status
Recruiting

Registration date
15/08/2024

Overall study status
Ongoing

Last Edited
19/08/2026

Condition category
Skin and Connective Tissue Diseases

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

Plain English summary of protocol

Background and study aims
Although many teenagers experience acne, around 1 in 10 people get severe acne that can also scar the skin. Having acne on your face and body as a young person can affect your confidence, sometimes leading to low mood and anxiety. There is an effective treatment for severe acne called isotretinoin, which is a licenced drug.Although isotretinoin works well at clearing acne, most people who take it experience side effects and some people will experience more than one. One way to potentially reduce these side effects is to give a lower dose of isotretinoin possibly over a longer period of time. We want to be sure a lower dose possibly taken for longer clears acne as effectively as the standard dose and find out if people are happy to take the tablets for a longer period of time. It is also possible that if the acne is not fully treated at a lower dose, it may come back after stopping treatment sooner than normal, so we also need to check that out. This trial involves two groups of patients. One group will take the dose of isotretinoin usually prescribed (standard dose) and the other a lower dose. Patients will not get to choose which group you go into. Due to how isotretinoin works, there is a possibility that the dose may change throughout the treatment course.

Who can participate?
Young people aged 12-24 years with severe acne who have not previously been treated with isotretinoin. Patients will only be approached to join the trial once the joint decision between patient and doctor has been made to start isotretinoin.

What does the study involve?
This study will compare the advantages and disadvantages of two different doses of isotretinoin for people with severe acne – a lower dose, possibly taken for a longer time, or a dose usually prescribed (standard dose) over a shorter duration. The researchers will be comparing how effective the two different doses are at treating acne and we will record side effects and other measures such as how patients feel their acne has changed, how the acne is affecting their life, satisfaction with treatment and any changes in mood.

What are the possible benefits and risks of participating?
Following the new MHRA guidance around isotretinoin, many activities such as blood tests, monitoring of side effects and the Pregnancy Prevention Program have been confirmed as part of usual care. This is a pragmatic trial and the researchers are closely following the usual care pathway. Patients will only be approached to join the trial once a joint decision between the patient and clinician has been reached to begin oral isotretinoin. There are no additional visits for participants, these will follow the pattern of usual care visits.
Isotretinoin is a long-standing treatment for acne and as such participants will have no greater risk than standard
care. If participants experience side effects, these will be assessed as part of their usual clinic visits and the clinician will manage their treatment accordingly, as per standard care. If a participant triggers a response of concern in the questionnaire within one month of stopping isotretinoin, participants will be sign-posted to their GP/urgent care.
In follow-up the questionnaires have been reduced to minimise the time burden on participants. All trial data has been considered so that the researchers are only asking what is needed for the trial.
A small number of participants will be asked to take part in qualitative interviews about isotretinoin (around 30 participants), however this will be optional.
Due to the risks associated with isotretinoin in patients of childbearing potential, patients will be asked to take part in the Pregnancy Prevention Programme (if relevant) as per the MHRA Acknowledgement of Risk form. This will be discussed as part of usual care/isotretinoin education, and it is clearly stated in the PIS that participants must not become pregnant whilst on isotretinoin.

Where is the study run from?
Queens Medical Centre, Nottingham (UK)

When is the study starting and how long is it expected to run for?
April 2024 to August 2028

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

Who is the main contact?
Acne-id@nottingham.ac.uk

Contact information

Type(s)
Scientific, Principal investigator

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Scientific

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Additional identifiers

Integrated Research Application System (IRAS)
1009472

Protocol serial number
24010

Study information

Scientific Title
Investigating the benefits and harms of reduced daily dose oral isotretinoin in the treatment of acne: a parallel group, assessor blind, non-inferiority, multicentre randomised controlled trial, with an internal pilot

Acronym
ACNE-ID

Study objectives
Primary objective:
To investigate whether a low-dose isotretinoin strategy is non-inferior to standard-care dose for clearance of acne at the end of treatment.

Secondary objectives:
1. To investigate the benefits and harms of a low-dose isotretinoin strategy compared to standard-care dose in relation to side effects, satisfaction with treatment, quality of life, and acne recurrence
2. To establish the health economic implications of the two isotretinoin dosing strategies

(technical efficiency)
3. To develop a clinical support tool to aid shared decision-making when initiating isotretinoin treatment

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 02/08/2024, East Midlands, Nottingham 2 REC (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, United Kingdom; +44 (0)207 104 8009; nottingham2.rec@hra.nhs.uk), ref: 24/EM/0111

Primary study design
Interventional

Study design
Open randomized controlled parallel-group non inferiority trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Acne

Interventions
This trial is a comparison of two dosing strategies.

Low-dose strategy (intervention):
Oral isotretinoin 0.25 mg/kg/day (within a range of 0.2-0.3 mg/kg/day). At 6 months, if there has been insufficient improvement, the dose can be increased to <0.5 mg/kg/day. Low-dose strategy may have a longer treatment duration (anticipated 6-12 months).

Standard-dose strategy (comparator)
Oral isotretinoin ≥0.5 mg/kg day and dose titration up to 1 mg/kg/day over 1-2 months, unless clinically contraindicated. Aim for a minimum of 0.7 mg/kg/day. The typical treatment duration for the standard-dose strategy is 6 months.

The end of the treatment course for each strategy will be when the first of the following criteria is met:
1. Participants have no new inflammatory lesions for a minimum of 4 weeks; this is a shared decision between the participant and a health professional or
2. A maximum cumulative dose of 150 mg/kg is reached or
3. A total of 12 months duration on the medication or
4. A participant and/or clinician decision to stop isotretinoin even when there has not been a satisfactory outcome e.g. due to side effects
5. A participant becomes pregnant

Participants who reach 150 mg/kg/day cumulative dose or 12 months duration of treatment and continue to have new inflammatory lesions will be treated according to routine clinical care.

Intervention Type

Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Isotretinoin

Primary outcome(s)
The proportion of participants achieving clearance of acne, defined as “clear or almost clear” at the end of their treatment course. Treatment success (clearance of acne) is defined as ‘clear or almost clear’, assessed using a blinded Investigator Global Assessment (IGA) using the Comprehensive Acne Severity Scale (CASS). The end of the active treatment period is defined as:
1. When participants have no new inflammatory lesions for a minimum of 4 weeks; this is a shared decision between the participant and a health professional or
2. A maximum cumulative dose of 150 mg/kg is reached or
3. A total of 12 months duration on the medication (whichever happens sooner) or
4. A participant and/or clinician decision to stop isotretinoin even when there has not been a satisfactory outcome (e.g. because of side effects)

Key secondary outcome(s)
1. Blinded investigator assessed acne severity, assessed using Investigator Global Assessment (IGA) using the Comprehensive Acne Severity Scale (CASS) at baseline,1, 3, 5-6, 8-10 months and end of treatment
2. Time to treatment success (clearance of acne) defined as “clear or almost clear” using the Comprehensive Acne Severity Scale (CASS) at the end of their treatment course.
3. Patient-reported acne severity assessed using the Patient Global Assessment (PGA) - baseline then monthly until end of treatment, and monthly in the follow-up phase
4. Patient-reported change in acne assessed using bespoke question at month 3 and end of treatment
5. Tolerability of side effects, assessed using the Modified British Association of Dermatologists side effect questionnaire – monthly until the end of treatment, then 1 month and 12 months in the follow-up phase
6. Acne health related quality of life assessed using the Acne Specific Quality of Life Questionnaire (Acne-QoL) at baseline, 3, 6, 9 months and end of treatment course
7. Patient satisfaction with treatment assessed using the Treatment Satisfaction Questionnaire for Medicine (TSQM) at month 3 and end of treatment course
8. Referral for a mental health assessment and/or cessation of isotretinoin due to concerns with mood, collected from medical notes at 1, 3, 5-6, 8-10 months and end of treatment course, or at any other time in the active treatment phase
9. Referral for a mental health assessment and/or dose reduction of isotretinoin, collected from medical notes, at 1, 3, 5-6, 8-10 months and end of treatment course, or at any other time in the active treatment phase
10. Patient-reported depression score assessed using Patient Health Questionnaire (PHQ-9/9a) monthly until the end of treatment and 1 month after stopping treatment
11. Patient-reported anxiety score assessed using the General Anxiety Disorder (GAD-7) questionnaire monthly until the end of treatment and 1 month after stopping treatment
12. Recurrence in acne within 12 months of stopping oral isotretinoin, assessed using a bespoke question monthly in the follow-up phase for those participants who achieved acne clearance by the end of their isotretinoin treatment
13. Time to recurrence in acne, assessed using patient report via bespoke question via remote

follow-up questionnaire
14. Personal costs measured using bespoke questionnaire monthly until the end of treatment, and monthly in the follow-up phase
15. Health care resource use measured using a bespoke questionnaire monthly until the end of treatment course, and monthly in the follow-up phase

Completion date
30/08/2028

Eligibility

Key inclusion criteria
Current inclusion criteria as of 22/08/2025:

1. Age 12 years to 24 years.
2. Acne of the face +/- trunk.
3. Meets the MHRA definition of severe forms of acne (including acne at risk of permanent scarring).
4. Able to give consent or child assent with parental consent
5. Clinical decision to start treatment with oral isotretinoin
6. Medicines and Healthcare products Regulatory Agency (MHRA) risk acknowledgment form completed by the treating clinician
7. Willing to be randomised to either treatment group
8. Willing and able to complete the trial questionnaires

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Previous inclusion criteria:

1. Clinical diagnosis of severe acne (including acne at risk of scarring) of the face +/- trunk
2. Acne that has failed to respond to at least one 12-week minimum course of oral antibiotics in combination with a topical treatment
3. Age ≥12 years to <25 years
4. Able to give consent or child assent with parental consent
5. Clinical decision to start treatment with oral isotretinoin
6. Medicines and Healthcare products Regulatory Agency (MHRA) risk acknowledgment form completed by the treating clinician
7. Willing to be randomised to either treatment group
8. Willing and able to complete the trial questionnaires

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
12 Years

Upper age limit
24 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Contraindication to isotretinoin as per clinician assessment in routine care (e.g. severe mood concerns on screening, refusal to sign the Acknowledgement of Risk Form and enter the Pregnancy Prevention Programme if has childbearing potential (pregnant, or breastfeeding or Intention to become pregnant), concomitant medications with an interaction with isotretinoin)
2. Acne fulminans, acne conglobata or other acne subtype unsuitable for higher dose strategy
3. Previously been treated with oral isotretinoin
4. Known allergy or sensitivity to isotretinoin or any of its excipients

Date of first enrolment
01/12/2024

Date of final enrolment
31/03/2027

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
Queens Medical Centre, Nottingham University Hospital
Derby Road
Nottingham
England
NG7 2UH

Study participating centre
Ashford Hospital
Ashford Hospital
Kings Avenue

Ashford
England
TN23 1LX

Study participating centre
Harrogate & District NHS Foundation Trust
Strayside Wing
Harrogate District Hospital
Lancaster Park Road
Harrogate
England
HG2 7SX

Study participating centre
Norfolk & Norwich Hospital Laboratory
Norfolk & Norwich Uni Hospital
Colney Lane
Colney
Norwich
England
NR4 7UY

Study participating centre
University Hospital Southampton NHS Foundation Trust
Southampton General Hospital
Tremona Road
Southampton
England
SO16 6YD

Study participating centre
Epsom and St Helier University Hospitals NHS Trust
St Helier Hospital
Wrythe Lane
Carshalton
England
SM5 1AA

Study participating centre
Chesterfield Royal Hospital NHS Foundation Trust
Chesterfield Road

Calow
Chesterfield
England
S44 5BL

Study participating centre
Pinderfields General Hospital
Aberford Road
Wakefield
England
WF1 4DG

Study participating centre
University Hospitals Bristol and Weston NHS Foundation Trust
Bristol Royal Infirmary
Marlborough Street
Bristol
England
BS2 8HW

Study participating centre
Hull University Teaching Hospitals NHS Trust
Hull Royal Infirmary
Anlaby Road
Hull
England
HU3 2JZ

Study participating centre
London North West University Healthcare NHS Trust
Northwick Park Hospital
Watford Road
Harrow
England
HA1 3UJ

Study participating centre
Brighton and Sussex University Hospitals NHS Trust
Royal Sussex County Hospital
Eastern Road
Brighton

England
BN2 5BE

Study participating centre
East Lancashire Teaching Pct
NHS East Lancashire
Walshaw House
Regent Street
Nelson
England
BB9 8AS

Study participating centre
Barts Health NHS Trust
The Royal London Hospital
80 Newark Street
London
England
E1 2ES

Study participating centre
Royal Infirmary of Edinburgh
51 Little France Crescent
Old Dalkeith Road
Edinburgh
Lothian
Scotland
EH16 4SA

Study participating centre
Musgrove Park Hospital
Musgrove Park
Taunton
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TA1 5DA

Study participating centre
Yeovil
Yeovil District Hospital
Higher Kingston
Yeovil

England
BA21 4AT

Study participating centre
Royal Derby Hospital
Uttoxeter Road
Derby
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DE22 3NE

Study participating centre
South Tees Hospitals NHS Foundation Trust
James Cook University Hospital
Marton Road
Middlesbrough
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TS4 3BW

Study participating centre
Guy's and St Thomas' Hospitals
Trust Offices
Guy's Hospital
Great Maze Pond
London
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SE1 9RT

Study participating centre
Chelsea and Westminster Hospital NHS Foundation Trust
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369 Fulham Road
London
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SW10 9NH

Study participating centre
Leicester Royal Infirmary
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LE1 5WW

Study participating centre
Torbay and South Devon NHS Foundation Trust
Torbay Hospital
Newton Road
Torquay
England
TQ2 7AA

Study participating centre
Northern Care Alliance NHS Foundation Trust
Salford Royal
Stott Lane
Salford
England
M6 8HD

Study participating centre
Sheffield Teaching Hospitals NHS Foundation Trust
Northern General Hospital
Herries Road
Sheffield
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S5 7AU

Study participating centre
Sheffield Teaching Hospitals NHS Foundation Trust
Northern General Hospital
Herries Road
Sheffield
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S5 7AU

Study participating centre
Bedfordshire Hospitals NHS Foundation Trust
Lewsey Road
Luton
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LU4 0DZ

Study participating centre
Buckinghamshire Healthcare NHS Trust
Amersham Hospital
Whielden Street
Amersham
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HP7 0JD

Study participating centre
NHS Borders
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TD6 9DB

Sponsor information

Organisation
University of Nottingham

ROR
https://ror.org/01ee9ar58

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 full trial protocol and all study documentation is available on request. The datasets analysed during this trial will be available to researchers upon request from the NCTU (ctu@nottingham.ac.uk), a minimum of 12 months after publication of this 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 de-identified which may impact on the reproducibility of published analyses. All requests for data should be sent to the Nottingham Clinical Trials Unit'

The datasets containing individual participant data analysed during the Acne-ID trial will be available upon request from the NCTU (ctu@nottingham.ac.uk) a minimum of 12 months after publication of this main results paper. Access to the data will be subject to review of a data sharing and use request by a committee including the Chief Investigator and Sponsor and will only be granted upon receipt of a data sharing and use agreement. Any data shared will be pseudo-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	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes