

Spironolactone for adult female acne

Submission date 09/10/2018	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 15/10/2018	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 16/09/2024	Condition category Skin and Connective Tissue Diseases	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Background and study aims

Spironolactone reduces hormones called androgens, which increase grease production and cause changes in follicles in the skin, making them prone to acne. This study will measure whether spironolactone helps adult women with persistent acne that would normally be treated with oral antibiotics. If shown to be effective, spironolactone could reduce the use of antibiotics for acne, be cheaper than antibiotics, and would be more suitable for long-term use than other treatments taken by mouth (oral treatments).

Who can participate?

Adult women with acne

What does the study involve?

Participants will be randomly allocated to one of two groups. In addition to usual care, participants will take either spironolactone tablets or dummy tablets (placebo) once a day for 24 weeks.

During the first 12 weeks, participants may continue using topical treatments (creams, gels or lotions) as usual but not oral treatments for acne (apart from the contraceptive pill if they are already using it and have been on it for 3 months or more). The study will run for 52 weeks, but participants will be able to use all other treatments as usual after the first 24 weeks (apart from oral antibiotics, which may be used from 12 weeks onwards). After 24 weeks all participants and their GPs will be informed which tablets the participant received in the study. Participants in both arms may ask their GP to prescribe it. We will assess the result of the study by asking participants to complete a standardised questionnaire about acne.

What are the possible benefits and risks of participating?

Participants may see an improvement in their acne and avoid needing to use antibiotics or Roaccutane (isotretinoin), and will be helping to further our knowledge of how to treat adult female acne. This will benefit other women with the same condition in the future. However, a possible risk is that the study treatment may not control the participant's acne, and there may be some side effects. There could be risks to a participant's child if they become pregnant and remain on spironolactone. Participants will need to attend 3 clinic visits, provide a couple of blood samples and answer some questionnaires, which they would not do if they were not taking part in the study.

Where is the study run from?

The study is being run from 5 dermatology clinics in hospitals in the UK:

1. Harrogate and District NHS Foundation Trust (lead site)
2. University Hospitals Bristol NHS Foundation Trust, Bristol Royal Infirmary, Bristol Dermatology Centre
3. Poole Hospital NHS Foundation Trust
4. Portsmouth Hospitals NHS Trust, St Marys Hospital
5. Epsom and St Helier University Hospitals NHS Trust
6. University Hospitals Birmingham NHS Foundation Trust
7. Swansea Bay University Health Board
8. Cardiff and Vale University Health Board
9. Nottingham University Hospitals NHS Trust
10. Imperial College Healthcare NHS Trust

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

April 2018 to August 2022

Who is funding the study?

National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme (UK)

Who is the main contact?

Dr Susanne Renz, safa@soton.ac.uk

Study website

<https://www.southampton.ac.uk/safa/>

Contact information

Type(s)

Scientific

Contact name

Dr Miriam Santer

Contact details

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Type(s)

Scientific

Contact name

Dr Alison Layton

Contact details

Harrogate & District NHS Foundation Trust
Lancaster Park Road
Harrogate
United Kingdom
HG2 7SX

Type(s)

Public

Contact name

Dr Fay Chinnery

Contact details

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Additional identifiers

EudraCT/CTIS number

2018-003630-33

IRAS number**ClinicalTrials.gov number**

Nil known

Secondary identifying numbers

HTA 16/13/02

Study information

Scientific Title

Spironolactone for Adult Female Acne: a pragmatic multicentre double-blind randomised superiority trial to investigate the clinical and cost-effectiveness of spironolactone for moderate or severe persistent acne in women

Acronym

SAFA

Study objectives

The clinical effectiveness of adding spironolactone to standard topical treatment is greater than placebo and standard topical treatment, for moderate or severe persistent facial acne in adult women.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 10/01/2019, Wales REC 3 (Health and Care Research Wales Support and Delivery Centre, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff CF11 9AB; Tel: +44 (0)29 2078 5741; Email: corinne.scott@wales.nhs.uk; helen.williams19@wales.nhs.uk), REC ref: 18/WA/0420

Study design

Interventional multi-centre double-blind randomized placebo-controlled superiority trial

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied

Acne

Interventions

Participants will be randomised to a patient pack which will contain either spironolactone or the placebo in a 1:1 ratio using an Interactive Web Response System (IWRS). Participants will be stratified by centre and by baseline severity (IGA <3 versus IGA ≥3). Participants will remain blinded and receive treatment for 24 weeks, followed by an unblinded follow-up to 52 weeks. At the baseline, all participants will be given either spironolactone (50 mg) or a placebo, with one tablet to be taken once daily for 6 weeks.

At the 6 week visit, all participants have a 6 week dose escalation review, where either the dose will be kept at 50 mg (one tablet to be taken once daily for a further 6 weeks), or will be increased to 100 mg (two tablets to be taken once daily for a further 6 weeks).

At the 12 week visit, all participants will have a 12 week dose escalation review. Based on their current prescription, the dose will be kept at 50 mg (one tablet to be taken once daily for a further 12 weeks), or will be increased to 100 mg (two tablets to be taken once daily for a further 12 weeks).

All participants will complete their course of study drug at 24 weeks.

Participants who meet the eligibility criteria (as determined by the inclusion and exclusion criteria) for the study and for whom written consent has been obtained will be individually randomised (1:1 ratio) to either the active or the placebo treatment using an Interactive Web Response System (IWRS).

Intervention Type

Drug

Phase

Phase III

Drug/device/biological/vaccine name(s)

Spironolactone

Primary outcome measure

Quality of life, assessed using the Acne-QoL symptom subscale score at 12 weeks

Secondary outcome measures

1. Quality of life, assessed using the Acne-QoL symptom subscale score at 6 and 24 weeks
2. Emotional effect of the impact of facial acne, assessed using the role-emotional subscale of the Acne-QoL at 6, 12 and 24 weeks
3. Impact of facial acne on a respondent's intersocial relationships, assessed using the role-emotional subscale of the Acne-QoL at 6, 12 and 24 weeks
4. Self-perception of facial acne, assessed using the role-emotional subscale of the Acne-QoL at 6, 12 and 24 weeks
5. Participant self-assessed improvement, recorded on a 6-point Likert scale (with baseline photograph to assist recall) at 6, 12 and 24 weeks
6. Description of individual's acne, assessed by the treating clinician using the Investigator's Global Assessment at 6 and 12 weeks, adjusted for baseline variables
7. Description of individual's acne, assessed by the individual themselves using the Participant's Global Assessment at 6, 12 and 24 weeks, adjusted for baseline variables
8. Participant satisfaction with study treatment at 24 weeks (asked prior to unblinding), assessed using a 6-point Likert scale
9. Health-related quality of life, assessed using the EQ-5D-5L at 6, 12 and 24 weeks
10. Cost and cost-effectiveness, assessed using:
 - 10.1. eCRF (case report form) regarding the intervention at the baseline and 6, 12, 24 and 52 weeks
 - 10.2. Participant questionnaires regarding wider NHS resource use at the baseline and 6, 12, 24 and 52 weeks
 - 10.3. EQ-5D-5L at the baseline and 6, 12, 24 and 52 weeks
 - 10.4. Quality adjusted life years (QALYs), assessed using the EQ-5D-5L at the baseline and 6, 12, 24 and 52 weeks

The primary economic evaluation will be an Incremental cost utility analysis from an NHS perspective, as this enables the cost effectiveness to be compared across a range of health conditions and interventions such that decision makers can use the information to inform prioritisation of health care.

A detailed Health Economic Analysis Plan will be written and reviewed prior to the trial database being locked.

Overall study start date

01/04/2018

Completion date

31/08/2022

Eligibility

Key inclusion criteria

1. Female
2. Aged 18 years or over
3. Facial acne with symptoms present since at least 6 months
4. Acne of sufficient severity to warrant treatment with oral antibiotics, as judged by the study clinician
5. Women of childbearing potential at risk of pregnancy must be willing to use their usual hormonal or barrier method of contraception for the first 6 months of the study
6. Willing to be randomised to either study arm
7. Willing and able to give informed consent
8. Sufficient English to carry out primary outcome Acne-QoL (which has not been validated in other languages)

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Female

Target number of participants

398

Total final enrolment

410

Key exclusion criteria

Current exclusion criteria as of 20/01/2020:

1. Hereditary problems of galactose intolerance, lactase deficiency or glucose-galactose malabsorption
2. Acne grade 0-1 using the Investigator's Global Assessment (i.e. clear or almost clear)
3. Currently using any of the following:
 - 3.1. Potassium-sparing diuretic
 - 3.2. ACE inhibitor
 - 3.3. Angiotensin II receptor blocker
 - 3.4. Digoxin
4. Started, stopped or changed long-term (lasting more than 2 weeks) hormonal contraception, co-cyprindiol or other hormonal treatment within the past 3 months
5. Planning to start, stop or change long-term (lasting more than 2 weeks) hormonal contraception, co-cyprindiol or other hormonal treatment within the next 3 months
6. Pregnant/breastfeeding
7. Intending to become pregnant in the next 6 months
8. Androgen-secreting adrenal or ovarian tumour

9. Cushing's syndrome
10. Congenital adrenal hyperplasia
11. Oral antibiotic treatment (lasting longer than a week) for acne within the past month
12. Oral isotretinoin treatment within the past 6 months
13. Has ever used spironolactone

Blood tests will also be performed at baseline to determine participants' serum potassium level and estimated glomerular filtration rate (eGFR). Participants may start the trial IMP before the test results are known.

STOPPING CRITERIA

Participants may commence treatment before blood test results are known, but if there is an abnormality (serum potassium level is above the upper limit of the reference range for the laboratory processing the sample, or the eGFR is below 60 ml/min/1.73m²), the participant must be contacted within 5 working days by telephone and told to stop taking the IMP. Participant will be considered a screen failure.

Previous exclusion criteria:

1. Serum potassium above the upper limit of the reference range for the laboratory processing the test (measured at the baseline clinic visit)
2. eGFR below 60 ml/min/1.73m²
3. Hereditary problems of galactose intolerance, lactase deficiency or glucose-galactose malabsorption
4. Acne grade 0-1 using the Investigator's Global Assessment (i.e. clear or almost clear)
5. Currently using any of the following:
 - 5.1. Potassium-sparing diuretic
 - 5.2. ACE inhibitor
 - 5.3. Angiotensin II receptor blocker
 - 5.4. Digoxin
6. Started, stopped or changed long-term (lasting more than 2 weeks) hormonal contraception, co-cyprindiol or other hormonal treatment within the past 3 months
7. Planning to start, stop or change long-term (lasting more than 2 weeks) hormonal contraception, co-cyprindiol or other hormonal treatment within the next 3 months
8. Pregnant/breastfeeding
9. Intending to become pregnant in the next 6 months
10. Androgen-secreting adrenal or ovarian tumour
11. Cushing's syndrome
12. Congenital adrenal hyperplasia
13. Oral antibiotic treatment (lasting longer than a week) for acne within the past month
14. Oral isotretinoin treatment within the past 6 months

Added 25/04/2019:

15. Has ever used spironolactone

Date of first enrolment

15/06/2019

Date of final enrolment

31/08/2021

Locations

Countries of recruitment

England

United Kingdom

Wales

Study participating centre

Harrogate and District NHS Foundation Trust

Lancaster Park Road

Harrogate

United Kingdom

HG2 7SX

Study participating centre

Poole Hospital NHS Foundation Trust

Longfleet Road

Poole

United Kingdom

BH15 2JB

Study participating centre

Portsmouth Hospitals NHS Trust

St Marys Hospital, Milton Road

Portsmouth

United Kingdom

PO3 6AD

Study participating centre

University Hospitals Bristol NHS Foundation Trust

Bristol Royal Infirmary, Bristol Dermatology Centre

Bristol

United Kingdom

BS6 7EL

Study participating centre

Queen Elizabeth Hospital

University Hospitals Birmingham NHS Foundation Trust

Mindelsohn Way

Birmingham
United Kingdom
B15 2GW

Study participating centre

St Helier Hospital

Epsom and St Helier University Hospitals NHS Trust
Wrythe Lane
Carshalton
United Kingdom
SM5 1AA

Study participating centre

Singleton Hospital

Sketty Lane
Swansea
United Kingdom
SA2 8QA

Study participating centre

University Hospital of Wales

Dermatology Department
Cardiff
United Kingdom
CF14 4XW

Study participating centre

Queen's Medical Centre

Centre of Evidence Based Dermatology
Room 3082
Opp ward C51
C floor South Block
Nottingham
United Kingdom
NG7 2UH

Study participating centre

St Mary's Hospital

Dermatology department
Mint wing
Imperial College Healthcare NHS Trust

Praed St
Paddington
London
United Kingdom
W2 1NY

Sponsor information

Organisation

University of Southampton

Sponsor details

B28/2027
Highfield
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United Kingdom
SO17 1BJ

Sponsor type

University/education

ROR

<https://ror.org/01ryk1543>

Funder(s)

Funder type

Government

Funder Name

Health Technology Assessment Programme

Alternative Name(s)

NIHR Health Technology Assessment Programme, HTA

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Results and Publications

Publication and dissemination plan

The study will be reported and disseminated via peer-reviewed scientific journals, internal reports and conference presentations.

We will send participants a summary of the study results, unless they have told us they prefer not to receive this. The summary will also be available on the Southampton Clinical Trial Unit SAFA website to members of the public.

The findings will also be published in updates to participants and through contacts with patient groups. Existing networks (email lists and social media) will be used to maximise impact.

No identifiable personal data will be published.

Intention to publish date

01/05/2023

Individual participant data (IPD) sharing plan

The data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	results	26/08/2021	27/08/2021	Yes	No
Results article		17/05/2023	17/05/2023	Yes	No
Plain English results			18/05/2023	No	Yes
HRA research summary			28/06/2023	No	No
Other publications	Qualitative interview study	12/10/2023	12/10/2023	Yes	No
Results article	Health economic evaluation	11/12/2023	18/12/2023	Yes	No
Results article		01/09/2024	16/09/2024	Yes	No