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Spironolactone for adult female acne

Submission date	Recruitment status	[X] Prospectively registered
09/10/2018	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
15/10/2018	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
16/09/2024	Skin and Connective Tissue Diseases	

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

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2018-003630-33

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
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

Study type(s)
Treatment

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

Key secondary outcome(s))
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.

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

Healthy volunteers allowed

No

Age group
Adult

Lower age limit
18 years

Sex
Female

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
United Kingdom

England

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
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Imperial College Healthcare NHS Trust
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W2 1NY

Sponsor information

Organisation
University of Southampton

ROR
https://ror.org/01ryk1543

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 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?
Results article	results	17/05/2023	17/05/2023	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
Protocol article		26/08/2021	27/08/2021	Yes	No
HRA research summary			28/06/2023	No	No
Other publications	Qualitative interview study	12/10/2023	12/10/2023	Yes	No
Plain English results			18/05/2023	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes