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First in woman safety and ease of use assessment of 400 mg progesterone Callavid in women with luteal phase progesterone insufficiency

Submission date
15/11/2025

Recruitment status
Recruiting

Registration date
11/02/2026

Overall study status
Ongoing

Last Edited
17/08/2026

Condition category
Nutritional, Metabolic, Endocrine

[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
This is a Phase I, first-in-human randomised control trial to assess the safety of a new vaginal 400 mg progesterone drug-device combination product called 400 mg progesterone Callavid.

Who can participate?
Women aged 18 to 45 years who have had at least one miscarriage and have luteal phase progesterone insufficiency

What does the study involve?
400 mg Progesterone Callavid and 400 mg Cyclogest are used vaginally twice a day for 7 days in each round.
Participants are randomly allocated to one of two groups.
Group 1: Participants use Callavid first for 2-hour wear before crossing over to use Cyclogest. In the third round, participants receive Callavid again but for 3-hour wear.
Group 2: Participants use Cyclogest first before crossing over to use Callavid for 2 hour wear. In the third round, participants receive Callavid again but for 3-hour wear.

What are the possible benefits and risks of participating?
Known common side effects of vaginally administered progesterone are vaginal discharge, bloating and breast tenderness, and mood changes (more rare). In some people, taking progesterone can alter the length of the menstrual cycle, though this is not very common.
Potential risks of contact with the device component of the novel drug-device combination IMP 400 mg progesterone Callavid have been extensively assessed in the Biological Evaluation Plan and will be thoroughly analysed within the Biological Evaluation Report, which will be submitted by the sponsor to MHRA and REC for review. The drug formulation uses established active and excipient ingredients, the safety profile of which are detailed in the IMPD.
If the novel drug-device combination IMP 400 mg progesterone Callavid delivers less progesterone than does the standard of care Cyclogest 400 mg reference IMP, then the patient

may have a lower probability of successfully conceiving during the single affected menstrual cycle.
During the interview, participants may become embarrassed or upset by some of the question topics. We have drafted a distress protocol to enable the researchers to help anyone who may need it.
Attending hospital for 6 hours on up to 6 occasions throughout the trial represents a burden for participants. We have attempted to minimise this by offering compensation as well as childcare costs, if required.

Where is the study run from?
University Hospitals Coventry and Warwickshire NHS Trust (UK)

When is the study starting and how long is it expected to run for?
January to December 2026

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

Who is the main contact?
freedomstudyoffice@uhcw.nhs.uk

Contact information

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Public

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT07136922

Integrated Research Application System (IRAS)
1008895

Central Portfolio Management System (CPMS)
58662

Protocol serial number
SQ641924

Study information

Scientific Title
First in woman safety and ease of use assessment of 400 mg progesterone Callavid in women with luteal phase progesterone insufficiency

Acronym
FREEDOM

Study objectives
Primary objective:
To establish the safety of 400 mg progesterone Callavid, a new drug-device combination product that is delivered vaginally.

Secondary objectives:
1. To explore the usability and acceptability to patients of 400 mg progesterone Callavid, and Cyclogest 400 mg (standard care)
2. To assess the delivery of vaginal progesterone into the blood using 400 mg progesterone

Callavid with 2-hour wear (round 1 or 2) and 3-hour wear (round 3), and Cyclogest 400 mg (standard care)

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 03/02/2026, Health and Social Care Research Ethics Committee B (Business Services Organisation Unit 4, Lissue Industrial Estate West Rathdown Walk Moira Road, Lisburn, BT28 2RF, United Kingdom; +44 28 9536 1400; RECB@hscni.net), ref: 25/NI/0165

Primary study design
Interventional

Study design
Open randomized controlled cross over trial

Study type(s)
Safety, Not Specified

Health condition(s) or problem(s) studied
Women who have had at least one miscarriage and have luteal phase progesterone insufficiency

Interventions
IMP is 400 mg Progesterone Callavid used vaginally 2 x day for 7 days in each round.
Comparator is 400mg Cyclogest used vaginally 2 x day for 7 days in each round.

Arm 1: Callavid 2-hour first , Cyclogest second, Callavid 3-hour third
Participants are randomised to use Callavid first for 2-hour wear before crossing over to use Cyclogest. In the third round, participants receive Callavid again but for 3-hour wear.

Arm 2: Cyclogest first, Callavid 2-hour second, Callavid 3-hour third
Participants are randomised to use Cyclogest first before crossing over to use Callavid for 2 hour wear. In the third round, participants receive Callavid again but for 3-hour wear.

Randomisation will be conducted by UHCW Pharmacy.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Callavid (progesterone) , Cyclogest (progesterone)

Primary outcome(s)
Any grade of adverse event (AE), specifically allergy, gastrointestinal (bloating, constipation), neurological (headache, drowsiness, euphoria), according to Common Terminology Criteria for Adverse Events (CTCAE), up to 24 hours after the last dose at each trial round

Key secondary outcome(s)
1. Level of fear/anxiety measured by PROMIS short 4-item anxiety-fear instrument completed on day 1 and day 7 during rounds 1, 2 and 3 of treatment
2. Acceptability measured using questionnaires on day 1 and 7 of each round
3. Usability and acceptability measured with semi-structured interviews post round 2
4. Serum progesterone levels measured using blood test at 0, 3 and 6 hours after the first dose on day 1 and the 13th dose on day 7 for each round of treatment

Other exploratory questions:
1. Progesterone leakage measured using day 1 and day 7 pads for Cyclogest users, and liner and scaffold for 400 mg progesterone Callavid users, for each round of the trial
2. Progesterone levels in leakage material measured using mass spectrometry after 2 and 3 hours of wear (product stored before sending to a third party for analysis)
3. Any leakage beyond the Callavid liner recorded in diary at morning and evening

Completion date
31/12/2026

Eligibility

Key inclusion criteria
1. Female sex
2. Clinical diagnosis of luteal phase insufficiency on the basis of one of the following:
2.1. Spotting before first day of heavy menstrual bleeding
2.2. Short time between ovulation and menstruation
2.3. Symptoms of progesterone insufficiency
3. Aged 18 – 45 years
4. Experienced at least one previous miscarriage

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
45 Years

Sex
Female

Total final enrolment
0

Key exclusion criteria
1. Positive pregnancy test
2. Currently breastfeeding

3. Allergies or contraindications to excipients/ progesterone pessaries
4. Current or history of previous condition where hormone treatments are contraindicated, e.g. breast cancer
5. Individuals who lack capacity to consent to the trial
6. Individuals who have an inability to comply with the trial procedures (e.g. cannot attend hospital for trial visits)
7. Inability to understand English

Date of first enrolment
01/04/2026

Date of final enrolment
31/12/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University Hospital Coventry
Clifford Bridge Road
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Sponsor information

Organisation
Calla Lily Clinical Care Ltd

ROR
https://ror.org/025n38288

Funder(s)

Funder type

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date