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A clinical trial to see if LPRI-424 is safe and works for Polycystic Ovary Syndrome compared to a placebo for 9 months

Submission date
19/07/2022

Recruitment status
No longer recruiting

Registration date
14/09/2022

Overall study status
Completed

Last Edited
21/12/2022

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
The test medicine (LPRI-424) is being given to women with polycystic ovary syndrome (PCOS) to see if there is a change in hair growth when given for 9 months. This is being tested against a placebo and the hair growth is being measured by a tool called the Adapted Modified Ferriman-Gallwey (mFG) score. This score is used by Doctors to see how much hair growth there is for those suffering with polycystic ovary syndrome.

Who can participate?
Women aged 14 to 40 years diagnosed with PCOS.

What does the study involve?
Not provided at time of registration

What are the possible benefits and risks of participating?
Benefits:
Improvement of PCOS symptoms in particular of hirsutism. Information learned from the trial may help other patients with hirsutism in the future.
Risks:
The main burden for subjects would be the E-Diary completion each day. The burden is minimised by taking less than 3 minutes to complete and the subjects being compensated for their time/compliance with the E-Diary. The amount of compensation will be given within the patient information sheet. Subjects will not be allowed any permanent hair removal during the trial, they can only use shaving as a method of hair removal. If the subject chooses to shave areas of their bodies, they must do so 15 days prior to the mFG score being tested to ensure the same standardised assessment of hair growth is done. This burden will be minimised by providing compensation to those patients who comply and complete the trial.
Other risks and burdens include blood withdrawals, where the subject may get injection-site pain /discomfort. To mitigate this risk only a trained, experienced and delegated member of the study site team will perform blood withdrawals. The subjects will also have gynaecological examinations and intravaginal ultrasounds, this is an intrusive examination and the experience

will be minimised by a trained and experienced member of the site team performing the assessments.

Where is the study run from?
Chemo Research S.L. (Spain)

When is the study starting and how long is it expected to run for?
September 2020 to November 2023

Who is funding the study?
Chemo Research S.L. (Spain)

Who is the main contact?
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Additional identifiers

EudraCT/CTIS number
2021-002178-17

IRAS number
1006162

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
LPRI-424/304, IRAS 1006162, CPMS 47924

Study information

Scientific Title
A multicentre, phase III, double-blind, randomised clinical trial to assess the efficacy and safety of LPRI-424 (dienogest 2.00 mg / ethinyl estradiol 0.02 mg) in the treatment of polycystic ovary syndrome (PCOS) versus placebo during 9 cycles

Study objectives
Primary objective:
To demonstrate the efficacy of LPRI-424 on hirsutism, measured by an adapted modified Ferriman-Gallwey (mFG) score based on the investigator decision against placebo

Secondary objective:
To assess the safety of LPRI-424, bleeding pattern and health-related quality of life

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/09/2022, Wales REC 5 (Health and Care Research Wales Support and Delivery Centre, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, UK; no telephone number provided; Wales.REC5@wales.nhs.uk), ref: 22/WA/0230

Study design
Interventional double blind randomized placebo controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Excess of body hair in women with polycystic ovarian syndrome (PCOS)

Interventions
Duration of treatment: 9 sequential cycles of 28 days (252 days in total)

Dose and mode of administration:
a) Test product: LPRI-424 tablets (dienogest [DNG] 2 mg / ethinyl estradiol [EE] 0.02 mg), film-coated tablets, oral administration. Each blister contains 28 tablets. One treatment cycle consists of 24 active white tablets followed by 4 green placebo tablets.
The tablets will be taken once daily at approximately the same time each day.
b) Reference therapy: LPRI-424 tablets matching placebo tablets, film-coated tablets, oral administration. Each blister contains 28 tablets. One treatment cycle consists of 24 white placebo tablets followed by 4 green placebo tablets.
The tablets will be taken once daily at approximately the same time each day.

Follow-up activity for both arms:
• Document concomitant medication
• Vital signs (blood pressure, heart rate, respiration rate, body temperature), height only in adolescent subjects, body weight, waist circumference
• Gynaecological examination
• Urine pregnancy test
• Check for Adverse events

Randomisation process: Online tool

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
dienogest 2.00 mg, ethinyl estradiol 0.02 mg

Primary outcome measure
Hirsutism is measured using a modified Ferriman-Gallwey score (mFG) based on the investigator's decision at baseline, treatment cycle 6 (day 20+/- 7 of medication cycle) and at the end of treatment.

Secondary outcome measures
Changes in laboratory parameters from baseline to trial termination
1. Adverse events (AEs)
2. Vital signs
3. Clinical laboratory parameters
4. Physical examination
5. Electrocardiogram (ECG)
6. Gynaecological examination
7. Cervical cytology

8. Changes in weight and waist
9. Change in bleeding pattern from baseline
10. Number of subjects with prolonged bleeding/spotting >10 days
11. IP acceptability based on IP satisfaction and wellbeing
12. Changes in quality of life based on the Polycystic Ovarian Syndrome Questionnaire (PCOSQ) from baseline

Overall study start date
01/09/2020

Completion date
30/11/2023

Eligibility

Key inclusion criteria
At Visit 1a (Screening) and at Visit 1b (IP Dispensation), subjects must meet ALL of the following criteria:
1. Two years postmenarcheal women of any ethnic origin between 14 and 40 years (inclusive at the time of enrolment), not seeking pregnancy.
Female subjects at risk of pregnancy aged between 14 and 17 years (inclusive) provided that:
a. Applicable national, state and local laws allow subjects in this age group to consent/assent to receive contraceptive services,
b. All applicable laws and regulations regarding the informed consent/assent of the subjects to participate in clinical trials are observed.
2. Diagnosed with PCOS according to the following criteria:
a. Presence of hirsutism measured using an adapted mFG with a cut-off value of ≥7 (at V1a only based on patient's history or interview; to be determined only at Visit 1b)
and
b. Presence of one of the following criteria:
1. Oligomenorrhea (≤6 menses per year) while not using hormonal contraceptives
2. Polycystic ovaries defined as presence of 12 or more follicles measuring 2 - 9 mm throughout the entire ovary or an ovarian volume ≥10 cm^3 determined by ultrasound. This criterion applies only for subjects aged ≥16 years due to the high incidence of multi-follicular ovaries in young subjects.
(Ovarian cyst are any fluid filled structure >30 mm in diameter that persisted for more than 2 cycles and enlarged follicles are any structure similar to an ovarian cyst that did not persist).
3. Informed consent form (ICF)/assent form signed voluntarily before any study-related procedure is performed; indicating that the subject understands the purpose of and procedures required for the study and is willing to participate in the study.
4. Body Mass Index (BMI): 18 kg/m^2≤ BMI <35 kg/m^2
5. At screening, maximum systolic blood pressure (median value of 3 values) ≤140 mm Hg and diastolic blood pressure (median value of 3 values) ≤90 mm Hg.
6. Haematology and chemistry parameters, heart rate (HR) and electrocardiogram (ECG) within reference range, or showing no clinically relevant deviations, as judged by the investigator.
7. Willing to use trial medication for nine 28-day cycles.
8. Is consenting to use reliable nonhormonal contraceptive methods (condoms, female or male sterilisation or sexual abstinence) during the study from screening until the final examination visit.
9. Must be willing to avoid the use of all hair removal or growth procedures and products apart from shaving during the trial and not to shave the hairs for a period of 14 days before the

modified adapted mFG score will be determined during study participation.
10. Has a good physical and mental health as determined on the basis of medical history and general physical examination performed at screening.
11. Willing to adhere to the prohibitions and restrictions specified in the protocol and being able to comply with the use of the trial medication or the use of the trial diary.
12. Agrees to not participate in any other clinical trials during the course of this trial.

Participant type(s)
Patient

Age group
Mixed

Sex
Female

Target number of participants
367

Key exclusion criteria
Subjects are to be excluded from the trial for ANY ONE of the following reasons:
1. Pregnancy or wish for pregnancy.
2. Breastfeeding women.
3. Current smoker with age ≥36 years and/or with BMI >30 kg/m² (at the time of trial enrolment)
4. Abnormal finding on pelvic, breast or intravaginal ultrasound examination (or transabdominal ultrasound examination for adolescents) that in the investigator's opinion contraindicates participation in the trial.
5. Women ≥21 years of age with a Papanicolaou (pap) smear reading low-grade squamous intraepithelial lesion (LSIL) or higher at screening (or 6 months prior to screening date). Subjects with atypical squamous cells of undetermined significance (ASC-US) can be
included if they are negative for high-risk Human papilloma virus (HPV) strains. Subjects <21 years of age do not require a Pap smear.
6. Poorly controlled diabetes (HgbA1c >6.5%). Treatment with metformin is allowed only if it is expected to remain stable during the trial (defined as a stable dose for at least 3 months before V1a).
7. Anaemia (haemoglobin <10 g/dL).
8. Subjects with disorders other than PCOS, that can result in menstrual irregularity and hyperandrogenism
9. Known contraindication or hypersensitivity to ingredients or excipients of the IP, including:
9.1. Presence or risk of a venous thromboembolism (VTE)
9.2. Presence or risk of an arterial thromboembolism (ATE)
9.3. Presence or history of pancreatitis, if it is associated with severe hypertriglyceridemia
9.4. Presence or history of liver diseases in which liver function has not returned to normal (also Dubin-Johnson and Rotor syndrome)
9.5. Current or previous liver tumours
9.6. Known or suspected sex hormone-dependent malignant tumours
9.7. Undiagnosed vaginal bleeding
9.8. Unexplained amenorrhoea
9.9. Concomitant use of medicinal products containing ombitasvir/paritaprevir/ritonavir or dasabuvir
10. Uncontrolled chronic concomitant diseases (i.e., not on a stable treatment dose for at least 2

months at the time
11. Severe Covid-19 disease or less than 3 months after hospitalisation due to a Covid-19 disease.
12. Evidence or history of alcohol, medication or drug abuse (within the last 12 months prior to consent/assent).
13. Known or suspected human immunodeficiency virus (HIV) and/or hepatitis infection at screening.
14. Previous intake of hormonal contraceptives within the last 3 months prior consent/assent or concomitant intake of hormonal contraceptives
15. Previous or concomitant intake of 5a-reductate inhibitors (e.g. flutamide) or similar inhibitors
16. Long-term treatment (longer than 7 consecutive days within a month prior to V1b) of any medication that might interfere with the efficacy of hormonal contraceptives
17. Prohibited medication include the use of oestrogens, progestogens, strong microsomal enzyme-inducing drugs (intensive and moderate frequency).
18. Other prohibited medications include antiandrogens, insulin sensitizers or drugs that might interfere with blood pressure regulation, lipid profile or carbohydrate metabolism within the last 6 months prior to consent/assent.
19. Administration of human chorionic gonadotropin (hCG) or intake of co-medication containing hCG within a month prior to V1b.
20. Inositol treatment within the last 3 months prior to consent/assent.
21. Evidence or history of clinically significant psychiatric illness or suicide risk.
22. Planned surgery during the anticipated time of participation in this trial requiring withdrawal of an oral contraceptive.
23. Participation in any other trial of an investigational drug or device parallel to the current trial or less than 90 days before consent/assent, or previous participation in a clinical trial with LPRI-421 or LPRI-424, or previous participation in the current trial including dispensed trial medication.
24. Subject is a member of the investigator’s or sponsor’s staff or a relative or family member thereof.
25. Any condition that, in the opinion of the investigator, may jeopardize protocol compliance or the scientific integrity of the trial.

Date of first enrolment
01/11/2021

Date of final enrolment
31/01/2023

Locations

Countries of recruitment
Czech Republic

Hungary

Lithuania

Poland

Serbia

Slovakia

Spain

Ukraine

United Kingdom

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
Chemo Research S.L.

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Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
Chemo Research S.L.

Results and Publications

Publication and dissemination plan

Peer reviewed scientific journals
Submission to regulatory authorities
The study results will be posted on a public repository

Intention to publish date
30/11/2024

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be 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?
HRA research summary			28/06/2023	No	No