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Investigating the use of obafistat on metabolic health in women with polycystic ovary syndrome

Submission date
03/06/2026

Recruitment status
Recruiting

Registration date
21/09/2026

Overall study status
Ongoing

Last Edited
21/09/2026

Condition category
Nutritional, Metabolic, Endocrine

[ ] 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
Polyendocrine metabolic ovarian syndrome (PMOS, previously known as polycystic ovary syndrome or PCOS) affects 10% of all women, and it usually co-exists with increased levels of 'male hormones' (also termed androgens) and poor response to sugar-regulating hormones (also termed insulin resistance). Women with PMOS are at increased risk of metabolic complications such as diabetes, fatty liver disease, high blood pressure and heart disease. The risk of these metabolic complications increases with increasing levels of androgens.
Adipose (fat) tissue is an important organ that converts androgens into their active form. The enzyme that activates the androgens is named aldoketoreductase type 1C3, or AKR1C3 for short. The AKR1C3 enzyme has been found to be increased in women with PMOS, leading to increased androgens in blood and fat tissue. Inhibiting the activity of the AKR1C3 enzyme is therefore a potential treatment option to lower the concentration of active androgens in women with PMOS.
In this study, we aim to study the use of a medication called obafistat (an inhibitor of the AKR1C3 enzyme) in women with PMOS. As it is a relatively new drug, we aim to investigate its safety, how it is processed in your body (termed pharmacokinetics) and what the medicine does to your body (i.e., how it can lower your androgen levels, termed pharmacodynamics). In addition, we also want to investigate if obafistat can be beneficial in metabolic health by measuring androgens and other markers of metabolic health in blood, saliva, urine and fat tissues.

Who can participate?
Women aged 18-42 years (inclusive) with PMOS

What does the study involve?
Once eligible, participants will be asked to have an intrauterine system inserted (Jaydess®) at least 8 weeks before their first dosage of study drug. Participants will be randomly allocated to be treated with obafistat (AKR1C3 inhibitor) or placebo. Participants will be dosed once daily for a period of 8 weeks and will attend a series of inpatient and outpatient visits concluded by an end of study visit.

What are the possible benefits and risks of participating?
The development of the previous steroidal AKR1C3 inhibitor (BAY1128688) was terminated due to hepatotoxicity; however, obafistat is believed not to carry an increased risk for hepatotoxicity for the reasons outlined in the protocol. As for other investigational drugs at this stage of development, liver function will be monitored closely (baseline, after 2 weeks of treatment, 4 weeks of treatment, after 8 weeks of treatment and 4 weeks after the last dose) alongside other safety parameters. Furthermore, as this is a dose escalation study, the decision for progression to the higher doses will be done after the careful assessment of the safety, tolerability, pharmacokinetics and pharmacodynamics of obafistat by the trial steering committee.
With drugs that oppose androgen action, which includes AKR1C3 inhibitors, there is a theoretical risk of teratogenicity, especially with a male foetus, due to possible undervirilisation associated with reduced androgen action. To ensure highly effective contraception, the AKROPAT trial will only recruit women who are willing to have an intrauterine system as a method for highly effective contraception for the duration of study. We will also only recruit women who are not planning pregnancy within 6 months of study end.
Other potential risks for the trial relate to its conduct. Some participants find inserting a cannula for taking blood uncomfortable. This procedure will be performed by experienced staff. Taking a fat sample (biopsy) can cause some mild discomfort. It may also leave a small scar initially that should disappear after a couple of weeks. Insertion of microdialysis and the cannula can cause pain, but we will use local anaesthetic to numb the area. We will use sterile techniques for all the procedures to minimise the risk of infection. We will reduce the risk of bleeding and bruising by pressing firmly on the site for 5 minutes after the procedure has been performed. Finally, some participants may find insertion or removal of the IUS painful. To minimise this, the procedure will be performed by experienced staff.

Where is the study run from?
Imperial College London (UK)

When is the study starting and how long is it expected to run for?
March 2026 to December 2028

Who is funding the study?
1. Wellcome Trust (UK)
2. Medical Research Council (UK)

Who is the main contact?
Aaron Clarke, Akropat@imperial.ac.uk

Contact information

Type(s)
Public

Contact name
Mr Aaron Clarke

Contact details
- Imperial College London, 5th floor Roderic Hill Building, South Kensington Campus, Prince Consort Rd
London
United Kingdom

SW7 2AZ
-
Akropat@imperial.ac.uk

Type(s)
Principal investigator

Contact name
Prof Wiebke Arlt

Contact details
MRC Laboratory of Medical Sciences, Du Cane Rd, Hammersmith Hospital
London
United Kingdom
W12 0HS
+44 (0)20 020 3313 8070
w.arlt@imperial.ac.uk

Type(s)
Scientific

Contact name
Dr Eka Melson

Contact details
MRC Laboratory of Medical Sciences, Room 6.01, Institute of Medical Sciences, Hammersmith Hospital, UKRI MRC, Du Cane Rd
London
United Kingdom
W12 0HS
-
e.melson@lms.mrc.ac.uk

Additional identifiers

Integrated Research Application System (IRAS)
1013397

Sponsor's protocol code number
172268

Study information

Scientific Title
AKROPAT: AKR1C3 as a mediator of metabOlic risk in women with Polycystic ovary syndrome and Androgen excess phenoType

Acronym
AKROPAT

Study objectives
The primary objective of this study is the assessment of the safety of obafistat in women with PCOS

Secondary objectives:
1. To study the pharmacokinetics of obafistat
2. To study the effect of obafistat on serum androgens (male hormones) in women with PCOS
3. To study the effect of obafistat on metabolic health in women with PCOS

Ethics approval required
Ethics approval required

Ethics approval(s)
Not yet submitted

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Blinded (masking used)

Control
Placebo

Assignment
Single

Purpose
Safety

Study type(s)
Safety, Other

Health condition(s) or problem(s) studied
Polycystic ovary syndrome

Interventions
The AKROPAT trial is a placebo-controlled randomised dose escalation study whereby we aim to treat 44 women with polyendocrine metabolic ovarian syndrome (previously known as polycystic ovary syndrome [PCOS]) with obafistat (AKR1C3 inhibitor) or placebo. Once eligible, participants will be asked to have an intrauterine system inserted (Jaydess®) at least 8 weeks prior to their first dosage of study drug. This 8-week window has been put in place to avoid bias that may arise from the effects of placing a low-dose levonorgestrel (LNG)-containing intrauterine system in place prior to treatment. After this window participants will be electronically randomised onto one of two arms, obafistat vs placebo, using a purposely built system, Sealed Envelope. Being that this is a double-blinded study, neither the investigators nor the participant will know which arm they have been allocated to.

Participants will be dosed once daily for a period of 8 weeks, whereby they will attend a series of inpatient and outpatient visits concluded by an end of study visit.

AKROPAT is a dose escalation study whereby patients will be sequentially randomised into 4 different cohorts of increasingly higher dosages of obafistat, starting at 4 mg once daily and escalating to a maximum dosage of 40 mg once daily. After each cohort an interim analysis will be performed to review safety as well as pharmacokinetic and pharmacodynamic analyses to determine if it is appropriate to move up to the next dosing level.

Once allocation to the escalation cohorts has concluded (or if data from the interim analysis shows that dose escalation to a higher cohort is not recommended), the study will move to the expansion phase whereby all further patients will be dosed at the recommended dose as determined by the dose escalation phase of the study.

Intervention Type
Drug

Phase
Phase I

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

Primary outcome(s)
Number of treatment-emergent adverse events (TEAEs, whether considered drug-related by the investigator or not) collected throughout the trial until the end of follow-up period

Key secondary outcome(s)
1. Percentage of participants achieving greater than 30% reduction in morning serum concentrations of biologically active 11-oxygenated androgens (11-hydroxytestosterone and 11-ketotestosterone) measured using liquid chromatography-mass spectrometry (LC-MS/MS) at Baseline, 8 weeks
2. Plasma concentration of obafistat including area under the curve (AUC) and maximum concentration (Cmax) measured using liquid chromatography-mass spectrometry (LC-MS/MS) at Baseline, 8 weeks

Exploratory outcomes:
3. Serum multi-steroid profile including classic and 11-oxygenated androgens measured using liquid chromatography-mass spectrometry (LC-MS/MS) at Baseline, 8 weeks
4. Salivary androgen concentrations (androstenedione, testosterone, 11OHA4, 11KT) measured using liquid chromatography-mass spectrometry (LC-MS/MS) at Baseline, 8 weeks
5. Urinary androgen metabolite concentrations measured using liquid chromatography-mass spectrometry (LC-MS/MS) at Baseline, 8 weeks
6. Serum sex hormone binding globulin concentrations measured using electrochemiluminescence immunoassays (ECLIA) at Baseline, 8 weeks
7. Serum Anti-Müllerian hormone concentrations measured using electrochemiluminescence immunoassays (ECLIA) at Baseline, 8 weeks
8. Serum luteinising hormone and follicle-stimulating hormone concentrations measured using chemiluminescent microparticle immunoassay (CMIA) at Baseline, 8 weeks
9. Anthropometric measures (height, weight, waist circumference, body mass index and waist-height ratio) measured using validated Tanita bioimpedance machine at Baseline, 8 weeks

10. Body composition including total fat mass, total lean mass and total body water measured using bioimpedance analysis at Baseline, 8 weeks
11. Abdominal fat distribution, liver fat and fibrosis measured using magnetic resonance imaging (MRI) at Baseline, 8 weeks
12. Glycated haemoglobin (HbA1c) levels measured using chemiluminescent microparticle immunoassay (CMIA) at Baseline, 8 weeks
13. Fasting lipid profile (total cholesterol, HDL cholesterol, triglycerides and calculated LDL cholesterol) measured using enzymatic assay at Baseline, 8 weeks
14. Metabolomic profile measured using liquid chromatography-mass spectrometry (LC-MS/MS) at Baseline, 8 weeks
15. Markers of insulin resistance (HOMA-IR, Matsuda index, Gutt insulin sensitivity index, AdipoIR, HIRI, MISI) measured using 2-hour oral glucose tolerance test at Baseline, 8 weeks
16. Adipose tissue interstitial concentrations of androgens and metabolites (glycerol, glucose, pyruvate and lactate) measured using subcutaneous adipose tissue microdialysis at Baseline, 8 weeks
17. Adipose tissue venous concentrations of androgens and metabolites including non-esterified fatty acids measured using adipose tissue vein cannulation at Baseline, 8 weeks
18. Adipose tissue gene expression profiles measured using single-nuclei RNA sequencing on 10X Genomics Chromium Single Cell 3' Gene Expression platform with Illumina sequencing at Baseline, 8 weeks
19. High-sensitivity C-reactive protein concentrations measured using immunoturbidimetric assay at Baseline, 8 weeks
20. Whole blood inflammatory cytokine concentrations (TNF-alpha, IL-6, IL-1beta, IL-10, IFN-alpha, IFN-gamma) measured using blood test following in vitro stimulation with pathogen mimics at Baseline, 8 weeks
21. Severity of androgen excess symptoms (hirsutism, acne, alopecia) measured using modified Ferriman-Gallwey score and clinical assessment at Baseline, 8 weeks
22. Anxiety and depression severity measured using Hospital Anxiety and Depression Scale (HADS) at Baseline, 8 weeks
23. Health-related quality of life measured using PCOS Quality of Life Questionnaire (PCOSQ) and Short Form-36 (SF-36) at Baseline, 8 weeks

Completion date
30/12/2028

Eligibility

Key inclusion criteria
1. Women aged 18-42 years (inclusive), with a documented diagnosis of PCOS based on the international 2023 guideline for PCOS (20). Two out of three of the 2023 International Guidelines for PCOS below will need to be fulfilled:
1.1. Clinical (excess hair growth, acne or alopecia) AND/OR biochemical hyperandrogenism (total T or free T above the female reference range)
1.2. Irregular menstrual cycles (oligomenorrhoea; <21 or >35 days or <8 cycles per year) OR absence of menstrual cycle (amenorrhoea)
1.3. Polycystic ovarian morphology on ultrasound [follicle number per ovary (FNPO) ≥20 in at least one ovary or ovarian volume ≥10 ml) AND/OR serum anti-mullerian hormone (AMH) above the female reference range.
2. BMI in the obesity range (obesity defined as BMI ≥ 30 kg/m²; ≥ 27.5 kg/m² in Asian, Chinese, Middle Eastern, Black African or African-Caribbean women).
3. Serum concentration of 11-Ketotestosterone above the upper quartile of the female

reference range (reference range to be determined)
4. Negative urine pregnancy test at screening and baseline visit and prepared to use a highly effective method of contraception during the study period and for up to 6 months after treatment (please see 'contraception' section below).
5. Willingness and ability to provide informed consent before any trial activity.
6. Participants from all ethnicities who are English speakers.

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
42 Years

Sex
Female

Total final enrolment
0

Key exclusion criteria
1. Other conditions associated with androgen excess and/or irregular/absent menstrual cycle, e.g., non-classical 21-hydroxylase deficiency, androgen-secreting tumour, functional hypothalamic amenorrhoea, Cushing's syndrome, adrenal tumour, hyperprolactinaemia, thyroid dysfunction, primary ovarian insufficiency, perimenopause or menopause (determined by serum FSH level at the postmenopausal range).
2. Confirmed type 1 or 2 diabetes or maturity-onset diabetes of the young (MODY). Impaired fasting glucose or impaired glucose tolerance are permitted.
3. Pregnancy, breastfeeding or intention to become pregnant within six months after the last dose of intervention.
4. Participants who are on any of the following medications within 3 months of screening and for the duration of the trial:
4.1. Any medication that will impact on insulin sensitivity (e.g., metformin, other hypoglycaemic agent, GLP-1 receptor agonists or GLP-1 and GIP receptor agonists, myoinositol, etc)
4.2. Anti-androgen therapy (e.g., spironolactone, flutamide, finasteride, etc)
4.3. Clomiphene citrate or oestrogen modulators such as letrozole
4.4. GnRH modulators such as leuprolide
4.5. Minoxidil
4.6. Any regular medications that would affect serum androgens and metabolic parameters, such as glucocorticoids.
4.7. Hormonal contraceptives (e.g. birth control pills, hormone-releasing implants; for intrauterine system, please see the 'contraception' section below).
4.8. Any essential co-medications preventing administration of obafistat (see IB for drug classes with interaction potential – including drugs metabolised by CYP2C9, CYP2C19 and CYP2B6).
4.9. Involvement in another clinical trial with an investigational medicinal product (CTIMP) within the past 8 weeks.

4.10. Presence or history of any neoplasm that are requiring treatment or under surveillance
4.11. Confirmed clinical diagnosis of excessive and compulsive drinking of alcohol or history of previous alcohol abuse.
4.12. Moderate to severe renal impairment (creatinine clearance [CrCl] ≤ 60 ml/min or estimated glomerular filtration rate [eGFR] ≤60 ml/min/1.73 m²).
4.13. Severe hepatic insufficiency and/or significant abnormal liver function defined as total bilirubin >2x upper limit of normal (ULN), ALT > 3ULN and/or alkaline phosphatase (ALP) >2 x ULN.
4.14. History of a major surgical procedure involving the stomach or small intestine which could affect absorption as judged by the investigator or history of an eating disorder.
4.15. Previous bilateral oophorectomy or bilateral salpingo-oophorectomy.
5. Shift workers who work outside the hours of 06:00AM to 06:00PM (including irregular or rotation shift work), as this will impact on the circadian steroid and androgen production.

Date of first enrolment
15/03/2026

Date of final enrolment
31/05/2028

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
NIHR Imperial Clinical Research Facility, Imperial College Healthcare NHS Trust
Imperial Centre for Translational and Experimental Medicine, Hammersmith Hospital Campus, Du Cane Road
London
England
W12 0HS

Sponsor information

Organisation
Imperial College London

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type

Funder Name
Wellcome Trust

Alternative Name(s)
Wellcome, WT

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

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