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A trial looking at metformin for early prostate cancer patients undergoing surgery

Submission date
22/07/2026

Recruitment status
No longer recruiting

Registration date
17/09/2026

Overall study status
Ongoing

Last Edited
23/07/2026

Condition category
Cancer

[ ] 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
Prostate cancer is a common cancer in men. At present the only risk factors known for developing prostate cancer are age, family history and ethnic origin. There is evidence that having a condition called metabolic syndrome may increase your risk of getting prostate cancer. Metabolic syndrome is a group of conditions including high blood pressure, high blood fats, high blood sugar and obesity.
Metformin is a drug that is commonly used in the treatment of diabetes and can be used to treat parts of the metabolic syndrome. It has been suggested that metformin can reduce the risk of getting prostate cancer and may also help to treat it more successfully. However, it is unknown today why metformin may have a positive effect on prostate cancer treatment. In this study we want to investigate how metformin affects prostate cancer tissue in order to further understand how it might be having its anti-cancer effect.

Who can participate?
You can participate if you are aged over 18 years, have been diagnosed with localised prostate cancer via biopsy in the last 6 months, are choosing to have surgery as your treatment, and have had no previous treatment for prostate cancer. You must be willing to take tablets via mouth, and your blood test results must be within normal ranges. You cannot take part if you are diabetic already or have any severe long-term medical conditions that the researchers would deem it unsafe for you to take part (such as heart failure or severe liver disease). You cannot have another cancer diagnosis and must be willing to use barrier protection if you are sexually active.

What does the study involve?
If you agree to join the study you will be asked to give your written consent. You will then be randomly assigned (by a computer) to either receive metformin tablets or placebo (dummy) tablets for the period prior to your radical prostatectomy.
You will return for three extra visits, a screening and baseline visit and one the week before your surgery, in addition to your standard visits to check on how you are tolerating the tablets. We will try, where possible, to fit this with your routine pre-operative assessment visit to minimise your visits to the hospital. We will only be able to reimburse you for any additional visits in exceptional circumstances.

You will be seen by a member of the trial team when you are in the hospital having your surgery. You will stop the tablets the evening prior to your surgery and will not have to take any additional medications afterwards. The drug is only available in the study and would not be provided on completion of the study.
The tissue from your initial prostate biopsy, which provided your original diagnosis of prostate cancer, will be retrieved from the laboratory and, alongside some tissue from your radical prostatectomy, will be securely sent to Cornell University, Ithaca, New York, USA, for assessment of the molecular markers we are investigating. Afterwards, it will be kept in the KHP Cancer Biobank at Guy's Hospital.
You will have one trial follow-up visit, which will be scheduled alongside your post-operative outpatient clinic 8-10 weeks after your surgery. You will then need no further trial follow-up and will continue on with standard care as you would have, had you not been on the trial.
At each of the visits described above, some of your medical details will be recorded by the researchers. In addition, your height, weight, waist circumference, routine observations (blood pressure, pulse, blood sugar and oxygen saturations), and some blood tests will also be taken.
You will receive a diary to keep a note of when you take your tablets.
At the screening and pre-surgery visit, a small amount of blood may be taken at some hospitals to be stored for potential future projects, subject to these receiving the correct ethical approvals. Your research team will inform you if this is the case at your hospital or not.
To take part in the trial, if you are able to father a child, you must agree to use barrier protection, in the form of a condom, for the duration of the trial and for 16 weeks after the last study drug administration.
Participants should avoid drinking alcohol while partaking in the study

What are the possible benefits and risks?
If you take part in the study, you may help scientists and doctors understand how metformin acts against prostate cancer.
It is important for you to realise that the research study is designed to increase knowledge and understanding of metformin and prostate cancer, and so you yourself will most unlikely benefit from taking part in it.
Metformin is a widely used drug in the treatment of diabetes and is very well tolerated and safe. However, it may cause some side effects. It is not possible to predict if you will have some, all or none of these or how severe they will be. The most common side effect is stomach upset and/or diarrhoea, but this can be limited by starting the drug at a lower dose and increasing it over the first few days. You will receive clear verbal and written instructions on how to do this. If you do experience these side effects, we can manage them by reducing your dose or occasionally giving extra medication. If your dose has to be reduced you would continue on in the study but your data may only be used in the safety analysis and not included in the final data analysis. This is because we want to ensure everyone, in the main analysis, has had the same dose of metformin if possible.
A serious but rare side effect is lactic acidosis, which is when the blood becomes too acidic. This is rare with a frequency somewhere between one in a thousand and one in ten thousand but you would need to come in to hospital to treat it. However, it tends to occur when you have other medical problems and so you will be unable to take part in this trial if you have other serious health problems which could increase the risk of lactic acidosis.

Where is the study run from?
This study is being conducted by the clinical teams at Guy's and St Thomas' NHS Foundation Trust in collaboration with the King's College London (KCL) and the King's Health Partners (KHP) Cancer Biobank, based at Guy's Hospital (UK)

When is the study starting and how long is it expected to run for?
The study is starting in 2015 and is expected to run for 11 years.

Who is funding the study?
The project is funded by the JP Moulton Charitable Trust and the TOUR charity

Who is the main contact?
Dr Sarah Rudman

Contact information

Type(s)
Principal investigator

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Additional identifiers

Integrated Research Application System (IRAS)
151495

Study information

Scientific Title
METformin And Longevity (METAL): a window of opportunity study investigating biological effects of metformin in localised prostate cancer

Acronym
METAL

Study objectives

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 31/03/2015, NRES Committee London - Fulham (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, United Kingdom; +44 (0)207 104 8000; nrescommitee.london-fulham@nhs.net), ref: 15/LO/0290

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Blinded (masking used)

Control
Placebo

Assignment
Parallel

Purpose
Basic science, Treatment

Study type(s)

Health condition(s) or problem(s) studied
Prostate cancer

Interventions
Participants with a confirmed diagnosis of prostate cancer, who meet the inclusion criteria and none of the exclusion criteria, will provide informed consent and enter screening. Once eligibility is confirmed, they will then be randomised to receive oral blinded doses of either 2 g of metformin or a placebo. Patients will be randomised using block randomisation with randomly varying block sizes. Randomisation will be performed via a web-based independent randomisation service. The metformin administered is a 500 mg tablet, which is the standard form, with a visually matching placebo.

Participants will start the study drug (metformin 2 g or placebo) and continue the drug for 4 weeks +/- 1 week (dependent on the scheduling of their radical prostatectomy surgery). To limit side effects, a dose escalation will occur, with participants taking 2 mg by day 5 onwards. Dose escalation will occur with the placebo also.

Study safety visits will take place on Day 21 and Day 28 (with flexibility due to the surgery date).

Intervention Type
Drug

Phase
Phase IV

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

Primary outcome(s)
1. Markers of the FASN/AMPK pathway in prostate tissue measured using immunohistochemistry (IHC) at pre-surgery (biopsy tissue) and post-surgery (prostatectomy tissue)

Key secondary outcome(s)
1. Markers of proliferation (ki-67) in prostate tissue measured using IHC at pre-surgery (biopsy tissue) and post-surgery (prostatectomy tissue)

2. FASN/AMPK-associated markers in benign and malignant prostate tissue measured using IHC at the end of the study

3. Metformin levels in prostate tissue measured using mass-spectrometry or similar techniques at pre-surgery (biopsy tissue) and post-surgery (prostatectomy tissue)

4. Safety of metformin in this non-diabetic patient cohort measured using assessment of adverse events and laboratory evaluations at the end of the study

5. Surgical toxicity measured using time between biopsy and surgery, peri-operative bleeding, infection, rectal injury and length of hospital stay at the end of the study

Completion date
06/02/2027

Eligibility

Key inclusion criteria
1. Aged 18 years or older and willing and able to provide signed informed consent.
2. Histologically confirmed adenocarcinoma of the prostate with a maximal tumour length of greater or equal to 6 mm on core biopsy
3. No previous treatment for prostate cancer (including surgery, any hormone therapy, radiotherapy or cryotherapy)
4. Prostate biopsy within 6 months from screening
5. Radical prostatectomy is the scheduled treatment of choice
6. Eastern Cooperative Oncology Group (ECOG) Performance status less than or equal to 0-1
7. Adequate organ function, defined as follows:
7.1. Haemoglobin >10.0 g/dl
7.2. Absolute neutrophil count >1.5 x 10e9/l
7.3. Platelet count >100 x 10e9/l
7.4. Renal function, eGFR >60 ml/min

7.5. AST and/or ALT <2.5 x ULN
7.6. Total bilirubin <1.5 x ULN
8. Able to swallow the drug and comply with study requirements

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
100 Years

Sex
Male

Total final enrolment
96

Key exclusion criteria
1. Patients with a current or historical diagnosis of type 1 or 2 diabetes and/or have ever received metformin
2. Patients with hypersensitivity to any of the components of the metformin or placebo tablet
3. History of or conditions associated with lactic acidosis such as shock or pulmonary insufficiency, alcoholism (acute or chronic), and conditions associated with hypoxaemia
4. Patients with chronic liver disease, severe cardiovascular impairment, cardiac failure, recent myocardial infarction, severe peripheral vascular disease or renal impairment (eGFR <60 ml/min as measured by Cockcroft-Gault)
5. Patients with acute severe disorders, for example infections with fever, pancreatitis, trauma, dehydration or reduced diet (<1000 kcal or 4200 kJ per day)
6. Other active malignancy over the last five years that has required systemic therapy, excluding:
6.1. Adjuvant therapy in the curative setting
6.2. Non-melanoma skin cancer
6.3. Superficial transitional cell carcinoma (CIS-T1)
7. Current enrolment in an investigational drug or device study or participation in such a study within 30 days of signing consent
8. Any subjects who is able to father a child and does not agree to use barrier protection, in the form of a condom, for the duration of the trial and for 16 weeks after the last study drug administration

Date of first enrolment
22/08/2015

Date of final enrolment
06/02/2020

Locations

Countries of recruitment
United Kingdom

England

Wales

Study participating centre
Guy's and St Thomas' Hospitals
Trust Offices
Guy's Hospital
Great Maze Pond
London
England
SE1 9RT

Study participating centre
The Royal Marsden Hospital
Fulham Road
London
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SW3 6JJ

Study participating centre
Royal Gwent Hospital
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NP20 2UB

Sponsor information

Organisation
Guy's and St Thomas' NHS Foundation Trust

ROR
https://ror.org/00j161312

Organisation
King's College London

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type

Funder Name
Jon Moulton Charity Trust

Alternative Name(s)
The Jon Moulton Charity Trust

Funding Body Type
Private sector organisation

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

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available