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Metformin in non-diabetic women with endometrial cancer

Submission date	Recruitment status	[_] Prospectively registered
20/12/2011	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
22/05/2012	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
29/01/2019	Cancer	

Plain English summary of protocol

Background and study aims

Endometrial cancer, or cancer of the lining of the womb, has become the most common cancer of the reproductive tract in British women. Obese women are at increased risk of the disease and are also more likely to die from it. The recent obesity epidemic means that more women than ever before are developing the disease. Endometrial cancer can usually be cured by surgery but for obese or elderly women, surgery may be dangerous. It also leaves a woman infertile. There is an urgent need to prevent this cancer and to develop effective non-surgical treatments. Metformin is one of the drugs used to treat diabetes. Recently, its role in the treatment of cancer has been explored. Diabetics who take metformin for many years are less likely to develop and die from cancer than those who do not. They are also more likely to respond well to chemotherapy if cancer does develop. Metformin has been shown to slow down the growth of breast, prostate, colon and endometrial cancers in the laboratory. Early studies in breast cancer patients have had promising results but metformin has never been tested in patients with endometrial cancer before.

This study will test metformin in patients with atypical endometrial hyperplasia (pre-cancer) and endometrial cancer. Women with atypical endometrial hyperplasia or endometrial cancer will receive metformin for one to four weeks while they wait for their surgery. The effects of metformin will then be assessed by comparing the characteristics of the endometrial tumour, taken at diagnosis, with those of the tumour removed at surgery. We will look at how fast the cells are multiplying and the proportion of cells undergoing cell death, and try to determine whether metformin affects key cancer pathways. It is hoped that the results of this small study will inform the design of a larger one.

Who can participate?

Non-diabetic women, aged 18 years or more who have recently been diagnosed with atypical endometrial hyperplasia or type I endometrial cancer.

What does the study involve?

Women taking part in the study will take metformin tablets twice a day for one to four weeks while they wait for their hysterectomy (Metformin Group). Other women taking part in the study will receive no treatment with metformin (Control Group). Both groups of women will have blood samples and a sample of the lining of the womb (endometrial biopsy) taken at recruitment

and at hysterectomy. Those women who took metformin will be asked to report their experiences of taking the tablets by filling out a questionnaire.

What are the possible risks and benefits of participating?
There will be no direct benefit to those taking part. But there should be benefits in future for women with endometrial cancer because this study will help us decide whether metformin is useful in the treatment of this disease.
The main risk of taking metformin is mild tummy upset, nausea or diarrhoea, but this is usually short-lived. Women can not drink alcohol while they are on metformin tablets. Rarely, patients taking metformin have become very unwell because of and allergic reaction (anaphylaxis) or kidney failure (lactic acidosis). Participants will be closely monitored to prevent this happening and tablets will be stopped immediately and appropriate medical treatment started if there are any concerns.

Where is the study run from?
St Marys Hospital, Tameside Hospital and the Royal Oldham Hospital in Greater Manchester (UK).

When is the study starting and how long is it expected to run for?
The study will start mid 2012 and is likely to run for two to three years.

Who is funding the study?
1. Central Manchester University Hospitals NHS Foundation Trust - Experimental Medicine Scheme Grant (2011)
2. Wellbeing of Women Research Training Fellowship (2012)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
METFORM01

Study information

Scientific Title
Proof of mechanism pre-surgical window trial of metformin in non-diabetic women with endometrial carcinoma: a feasibility study

Study objectives
Metformin reduces cellular proliferation in type 1 endometrial cancer.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North West Haydock Research Ethics Committee, 19/08/2011, ref: 11/NW/0442

Study design
Non-randomised controlled pre-surgical window study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Type 1 or endometrioid adenocarcinoma of the endometrium

Interventions
Current interventions as of 06/09/2013:
Metformin Group
Participants in the Metformin group will receive 850 mg metformin hydrochloride twice daily by mouth for one to four weeks between recruitment into the trial and surgery for endometrial cancer. They will discontinue their metformin the night before surgery. They will be asked to complete a tolerability of metformin treatment questionnaire two weeks after surgery. They do not require any other follow up as a result of participation in this study.

Control Group
Participants in the Control group will NOT receive Metformin during the one to four week period between recruitment and surgery. They do not require any follow up after their surgery.

Previous interventions:

Metformin Group
Participants in the Metformin group will receive 850mg metformin hydrochloride twice daily by mouth for two to four weeks between recruitment into the trial and surgery for endometrial

cancer. They will discontinue their metformin the night before surgery. They will be asked to complete a tolerability of metformin treatment questionnaire two weeks after surgery. They do not require any other follow up as a result of participation in this study.

Control Group
Participants in the Control group will NOT receive Metformin during the two to four week period between recruitment and surgery. They do not require any follow up after their surgery.

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
Test for Ki-67

Key secondary outcome(s))
Test for:
1. Phospho-H3
2. Cleaved caspase-3 and cleaved PARP
3. AKT, phosphorylated AKT
4. ERK1,2, phosphorylated ERK 1,2
5. PTEN, strathmin
6. Phosphorylation status of key signal transduction molecules (mTOR pathway)
7. Insulin receptor/phosphorylated insulin receptor
8. Fasting serum glucose, insulin, IGFBP-1 and C-peptide levels
9. Tolerability of metformin treatment

Completion date
02/01/2015

Eligibility

Key inclusion criteria
Current inclusion criteria as of 06/09/2013:
1. Biopsy-proven atypical endometrial hyperplasia or type 1 endometrial carcinoma
2. Scheduled for surgical treatment in 1 or more weeks time
3. Written informed consent to participate in the trial
4. Females aged 18 years or older

Previous inclusion criteria:
1. Biopsy-proven type 1 endometrial carcinoma
2. Scheduled for surgical treatment in 2 or more weeks time
3. Written informed consent to participate in the trial
4. Females aged 18 years or older

Participant type(s)
Patient

Healthy volunteers allowed

No

Age group
Adult

Lower age limit
18 years

Sex
Female

Key exclusion criteria
Current exclusion criteria as of 06/09/2013:
1. Already receiving metformin treatment
2. Type 1 or 2 diabetes mellitus on drug treatment
3. Renal or hepatic impairment
4. Unable to comply with treatment protocol

Previous exclusion criteria:
1. Already receiving metformin treatment
2. Type 1 or 2 diabetes mellitus
3. Renal or hepatic impairment
4. Unable to comply with treatment protocol

Date of first enrolment
03/01/2012

Date of final enrolment
02/01/2015

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
NIHR Clinical Lecturer in Gynaecological Oncology
Manchester
United Kingdom
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Sponsor information

Organisation
Central Manchester University Hospitals NHS Foundation Trust (UK)

ROR
https://ror.org/00he80998

Funder(s)

Funder type
University/education

Funder Name
University of Manchester (UK)

Alternative Name(s)
University of Manchester in United Kingdom, University of Manchester UK, The University of Manchester, UoM

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Funder Name
Central Manchester University Hospitals NHS Foundation Trust, Experimental Medicine Scheme Grant (UK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	02/02/2016	29/01/2019	Yes	No

HRA research summary	28/06/2023	No	No