

Metformin treatment for diabetes prevention in Africa

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|----------------------------------------|----------------------------------------------------------------|---------------------------------------------------------------------------------------------------|
| Submission date 08/03/2019 | Recruitment status No longer recruiting | <input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol |
| Registration date 22/03/2019 | Overall study status Completed | <input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results |
| Last Edited 18/07/2023 | Condition category Nutritional, Metabolic, Endocrine | <input type="checkbox"/> Individual participant data |

Plain English summary of protocol

Background and study aims

The numbers of people with type 2 diabetes in Africa are rising rapidly. We are looking for ways to prevent people who have already have raised blood sugar (called prediabetes), from going on to develop diabetes.

We will test a drug called metformin in HIV infected persons with pre-diabetes to see what effect, if any, it has on blood glucose. If the drug is able to lower their blood sugar levels, and appears to be safe, we hope to go on to test whether the drug can stop or delay a person developing diabetes in a subsequent large trial. Metformin has been tested for this purpose in high-income countries, but not in Africa among those who are on HIV treatment. The study will be conducted in Tanzania.

Who can participate?

Adults over the age of 18, who are HIV-infected and have been stable on treatment for HIV-infection for a minimum of 6 months.

What does the study involve?

We will screen people in HIV treatment programmes to identify those who are prediabetic. If they agree to take part in the study, we will allocate them at random to one of two groups. The first group will receive a slow-release preparation of metformin which only needs to be taken once a day; and the second group will receive a placebo that looks like the metformin and also is taken once a day. Neither the patient or the doctors will know who is receiving the drug and who is receiving the placebo (this is called a randomised double-blind placebo-controlled trial). Each participant will be followed up for 12 months, and at the end we will assess blood sugar levels in those who received metformin compared to those who received the placebo.

What are the possible benefits and risks of participating?

The benefits of participating are that the study will provide information on a possible prevention strategy for those that are at risk of developing diabetes. There are risks associated with taking metformin. A proportion of people who take this drug experience side effects, particularly of the gastro-intestinal system like nausea, abdominal pain, vomiting and diarrhoea, although these

symptoms should decrease with time. There are also more serious side effects like the development of a condition called lactic acidosis, but is very rare and unlikely to occur. We will be monitoring the study closely.

Where is the study run from?

From 4 hospitals in Dar es Salaam, the Hindu Mandal Hospital, Amana Hospital, Temeke Regional Referral Hospital, and Mwananyamala Hospital. All are in Tanzania

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

April 2019 to October 2021

Who is funding the study?

The National Institute for Health Research (NIHR).

Who is the main contact?

Prof Shabbar Jaffar at LSTM (Shabbar.jaffar@lstmed.ac.uk).

Contact information

Type(s)

Scientific

Contact name

Prof Shabbar Jaffar

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Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number

ClinicalTrials.gov number

Nil known

Secondary identifying numbers

Protocol version 14

Study information

Scientific Title

A randomised placebo-controlled double-blind phase II trial to determine the effects of metformin versus placebo on glycaemia in HIV-infected persons with pre-diabetes in Tanzania.

Acronym

META

Study objectives

Metformin significantly reduces progression to diabetes in prediabetic HIV infected persons on antiretroviral therapy compared to Placebo.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Liverpool School of Tropical Medicine (LSTM) Research Ethics Committee; reference (17-078)
National Institute of Medical Research and the Ministry of Health, Community Development, Gender, Elderly and Children.
Tanzania Food and Drug Authority

Study design

Randomised placebo-controlled double-blind trial.

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Prevention

Participant information sheet

Not available in web format, please use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied

Prediabetes in person who are on HIV treatment

Interventions

The intervention will be Metformin hydrochloride slow-release preparation, 2000 mg per day, compared with a matching placebo. The treatment will only be taken once a day. Participants who are HIV infected and on treatment, found to be prediabetic on screening, will be randomised using permuted block randomisation with varying block sizes chosen at random using the SAS software.

Intervention Type

Drug

Phase

Phase II

Drug/device/biological/vaccine name(s)

Metformin hydrochloride, slow release preparation

Primary outcome measure

Glycaemia at 12 months as ascertained by the oral glucose tolerance test.

Secondary outcome measures

Current secondary outcome measures as of 20/05/2020:

1. Changes in glycaemia from baseline as ascertained by the oral glucose tolerance test at 6 and 12 months
2. Incidence of adverse events assessed using patient notes at 12 months
3. Rates of retention in care assessed using patient notes at 12 months
4. Estimated adherence to study drugs assessed using patient notes at 12 months

Previous secondary outcome measures:

1. Changes in glycaemia from baseline as ascertained by the oral glucose tolerance test
2. Incidence of adverse events assessed using patient notes at 12 months
3. Rates of retention in care assessed using patient notes at 12 months
4. Estimated adherence to study drugs assessed using patient notes at 12 months

Overall study start date

01/04/2019

Completion date

26/10/2021

Eligibility**Key inclusion criteria**

1. HIV-positive on antiretroviral therapy (ART) for at least 6 months and considered stable on treatment (i.e. in regular attendance for care).
2. BMI>30 combined with either impaired fasting glucose (6.1 to 6.9 mmol/L) and/or impaired glucose tolerance at 2 hours (7.0 to 11.10 mmol/L)
3. BMI≤30 combined with either impaired fasting glucose (6.3 to 6.9 mmol/L) and/or impaired glucose tolerance at 2 hours (9.0 to 11.10 mmol/L)
4. Planning to remain in the area for > 6-months
5. Written informed consent

Participant type(s)

Patient

Age group

Adult

Sex

Both

Target number of participants

360

Total final enrolment

364

Key exclusion criteria

1. Pregnant women
2. Renal disease or renal dysfunction (eGFR<45)
3. Signs and symptoms of any form of acute metabolic acidosis including lactic acidosis and diabetic ketoacidosis
4. Other acute conditions with:
 - 4.1 the potential to alter renal function including: dehydration, severe infection or shock
 - 4.2 the potential to cause tissue hypoxia including decompensated heart failure, respiratory failure, recent myocardial infarction, shock
5. Congestive heart failure requiring pharmacological treatment
6. Clinical evidence of liver disease
7. Evidence of alcoholism or acute alcohol intoxication
8. Known hypersensitivity to metformin or any excipients associated with the preparation (in this case: Magnesium stearate, sodium carboxymethylcellulose, hypromellose)
9. Other acute conditions requiring hospital admission.

Date of first enrolment

05/11/2019

Date of final enrolment

24/07/2020

Locations**Countries of recruitment**

Tanzania

Study participating centre**Hindu Mandal Hospital**

Chusi Street
Dar es Salaam
Tanzania

-

Study participating centre**Amana Hospital**

Uhuru Street
Dar es Salaam

Tanzania

-

Study participating centre

Temeke Regional Referral Hospital

Temeke Street

Dar es Salaam

Tanzania

-

Study participating centre

Mwanyanamala Hospital

61665 Kinondoni

Dar es Salaam

Tanzania

-

Sponsor information

Organisation

Liverpool School of Tropical Medicine

Sponsor details

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Sponsor type

University/education

Website

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ROR

<https://ror.org/03svjbs84>

Funder(s)

Funder type
Government

Funder Name
National Institute for Health 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

Publication and dissemination plan
We plan to publish one paper in a high impact peer-reviewed journal shortly after the end of the trial. The paper will include the main efficacy findings.

Intention to publish date
30/06/2022

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? |
|---------------------------------|---------|--------------|------------|----------------|-----------------|
| Results article | | 18/07/2023 | 18/07/2023 | Yes | No |