# The role of isoniazid medication in preventing progression to active tuberculosis disease in persons with latent tuberculosis: The effect on the body's immune system

<b>Submission date</b> 17/09/2015	<b>Recruitment status</b> No longer recruiting	<ul><li>☐ Prospectively registered</li><li>☐ Protocol</li></ul>
Registration date 30/09/2015	Overall study status Completed	<ul><li>Statistical analysis plan</li><li>[X] Results</li></ul>
<b>Last Edited</b> 26/10/2015	Condition category Infections and Infestations	☐ Individual participant data

#### Plain English summary of protocol

Background and study aims

Tuberculosis (TB) is a highly contagious bacterial infection. It is generally spread by breathing in tiny droplets released into the air by an infected person coughing or sneezing. TB usually affects the lungs, but it can also affect other areas of the body such as the bones, brain and kidneys. When a person is suffering from active TB, they are visibly unwell and can spread the infection to others. Many people however have latent TB, where the bacteria remain in an inactive state in the body. A person with latent TB has no symptoms and cannot spread the infection to others. Without treatment, the infection can become active at any time, and so monitoring people with latent TB is a vital part of controlling the spread of TB in general. Isoniazid is an antibacterial medication which has been used for many years to treat active TB infections. This drug is also commonly used to prevent active TB developing in people who have come into contact with an infected person. The aim of this study is the way that isoniazid preventative treatment (IPT) affects the body in people with latent TB, and if it can increase immunity to TB in general.

## Who can participate?

Healthy people above 5 years of age, who are living with someone diagnosed with active TB.

#### What does the study involve?

Participants are randomly allocated into two groups. The first group receive isoniazid tablets for six months as well as attending monthly clinic visits. The second group attend monthly clinic visits only. All participants are tested for latent TB infection using a blood test at the start of the study, and then again after six months.

What are the possible benefits and risks of participating?

Participants benefit from receiving a free blood test to screen them for TB and HIV, as well as education about the medication they may be taking so that they are fully prepared for any possible side effects. Risks of participating are minimal, including pain or bruising from blood tests, as well as finding the interviews tiring.

Where is the study run from?

- 1. Kitebi Health Center III (Uganda)
- 2. Kisenyi Health Center IV (Uganda)

When is the study starting and how long is it expected to run for? May 2011 to January 2012

Who is funding the study?

- 1. Seventh Framework Programme (Belgium)
- 2. Wellcome Trust (UK)

Who is the main contact? Dr Irene Andia-Biraro

# Contact information

#### Type(s)

Scientific

#### Contact name

Dr Irene Andia-Biraro

#### **ORCID ID**

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#### Contact details

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# Additional identifiers

**Protocol serial number** N/A

# Study information

#### Scientific Title

The effect of isoniazid preventive therapy on immune responses of household contacts with latent tuberculosis infection

#### Study objectives

Household contacts of active tuberculosis patients with latent tuberculosis infection would present with mixed Th1/Th2 cytokine profiles and treatment of the latently infected people with

isoniazid would reverses the immune equilibrium from Th2 responses back to Th1 immune dominance.

#### Ethics approval required

Old ethics approval format

## Ethics approval(s)

- 1. The Makerere University College of Health Sciences Ethical Review Board, 10/09/2009, ref: 2009-140
- 2. Uganda National Council for Science and Technology, 16/09/2009, ref: HS 676

#### Study design

Redomised controlled trial nested within a cohort study

#### Primary study design

Interventional

## Study type(s)

Treatment

## Health condition(s) or problem(s) studied

Latent tuberculosis infection

#### **Interventions**

Household contacts that were eligible for the study were randomized to receive either isoniazid preventive therapy (IPT) and monthly visits or monthly visits only. Household contacts in the IPT arm were offered self-administerd isoniazid (5mg/kg to a max of 300mg) plus pyridoxine 25mg daily for six months.

#### **Intervention Type**

Drug

#### **Phase**

Not Applicable

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

Isoniazid

#### Primary outcome(s)

1. Net cytokine responses measured from Quantiferon supernatants using an 11-analyte Bio-Plex human cytokine bead array consisting of IFN-γ, IL-2, TNF-α, IL-4, IL-5, IL-13, IL-10, IL-17a, IL-17f, IL-21, and IL-22, among the household contacts at the end of six-months follow up 2. Mtb specific antibody concentrations to purified protein derivative (PPD), culture filtrate protein 10 (CFP-10), early secreted antigenic target 6 (ESAT-6) antigens using an in-house IgG ELISA assay, among the household contacts at the end of six-months follow up

# Key secondary outcome(s))

- 1. The spontaneous cytokine responses measured from Quantiferon supernatants using an 11-analyte Bio-Plex human cytokine bead array consisting of IFN-γ, IL-2, TNF-α, IL-4, IL-5, IL-13, IL-10, IL-17a, IL-17f, IL-21, and IL-22 at the end of six-months follow up
- 2. Any side effects due to IPT found during clinical assessment at each monthly clinic visit or

reported as they occur

- 3. Any changes in TST and QFN test reactions between baseline and at the end of six-months follow up
- 4. Incidence of active TB acquired during the course of the six-months follow up

## Completion date

20/10/2014

# **Eligibility**

#### Key inclusion criteria

Household contacts exposed to patients with sputum smear positive tuberculosis that are:

- 1. Above the age of 5 years
- 2. HIV negative
- 3. Tested positive on both the tuberculin skin test and the QuantiFERON®-TB Gold In-Tube® test (Cellestis GmbH (Europe), Hannover, Germany; QFN)

## Participant type(s)

Other

#### Healthy volunteers allowed

No

#### Age group

Mixed

#### Sex

All

#### Key exclusion criteria

Household contacts excluded if they have:

- 1. Signs and symptoms of active tuberculosis
- 2. Liver disease
- 3. Epilepsy

# Date of first enrolment

01/05/2011

#### Date of final enrolment

31/01/2012

# **Locations**

#### Countries of recruitment

Uganda

#### Study participating centre

#### Kitebi Health Center III

Kampala Uganda 041

Study participating centre Kisenyi Health Center IV Kampala Uganda 041

# Sponsor information

## Organisation

College of Health Sciences, Makerere University

#### **ROR**

https://ror.org/03dmz0111

# Funder(s)

# Funder type

Research organisation

#### **Funder Name**

Wellcome Trust Strategic Award through the Makerere University-Uganda Virus Research Institute Infection and Immunity Research Training Programme (MUII)

#### **Funder Name**

Seventh Framework Programme

## Alternative Name(s)

EC Seventh Framework Programme, European Commission Seventh Framework Programme, EU Seventh Framework Programme, European Union Seventh Framework Programme, FP7

# **Funding Body Type**

Government organisation

# **Funding Body Subtype**

National government

# Location

# **Results and Publications**

Individual participant data (IPD) sharing plan

# IPD sharing plan summary

Available on request

**Study outputs** 

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	22/10/2015		Yes	No