

# Evaluation of high dose rifampicin toxicity in pulmonary tuberculosis

<b>Submission date</b> 12/10/2010	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
<b>Registration date</b> 09/11/2010	<b>Overall study status</b> Completed	<input type="checkbox"/> Protocol
<b>Last Edited</b> 20/09/2017	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

**Contact name**  
Dr Amina Jindani

**Contact details**  
St George's University of London  
Infection and Immunity Research Centre  
Cranmer Terrace  
London  
United Kingdom  
SW17 0RE  
+44 (0)20 8725 2810  
ajindani@sgul.ac.uk

## Additional identifiers

**Protocol serial number**  
Version 2.1

## Study information

**Scientific Title**  
An international multicentre controlled clinical trial to evaluate the toxicity of high dose rifampicin in the treatment of pulmonary tuberculosis (RIFATOX)

## Acronym

RIFATOX

## Study objectives

The current treatment of tuberculosis involves taking drugs daily for 6 or 8 months. Although the drugs are free to patients in low income countries, this still involves a substantial cost, in terms of time and administration, to both the patient and the treatment services. If the length of treatment could be shortened to 3, or even, 4 months, this would be of great benefit to the patients and the treatment services. A shorter treatment could also result in greater cure rates and, perhaps, a reduction in the emergence of resistance to the drugs.

One of the drugs given in treatment is called rifampicin. Laboratory experiments suggest that increasing the dose of rifampicin results in a greater killing of the tubercle bacillus both in liquid suspensions and in animals.

This trial assesses whether giving an increased dose of rifampicin to patients receiving the standard treatment for tuberculosis is safe and does not result in greater bad effects from the higher dose. If it is found to be safe, another trial would be carried out to see if the increased dose can increase the elimination of the tubercle bacillus from the lungs and if so, whether, eventually, the treatment can be shortened to 3, or even, 4 months.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

1. UK:

1.1. The Oxford Tropical Research Ethics Committee (OXTREC), 02/08/2010, ref: 31-01

1.2. The St. George's University of London R&D Office, 20/09/2010, ref: 10.005

2. Bolivia:

2.1. The Ministry of Health and Sports (Ministerio de Salud y Deportes), April 2010, ref: MSD /DESP./0733/2010

2.2. The Commission for Ethics of Investigations (Comision de Ethica de la Investigation), 19/07 /2010

3. Nepal:

The National Health Research Council, 15/04/2010, ref: 1192

4. India:

Approval pending at time of registration

## Study design

Open-label three-arm trial

## Primary study design

Interventional

## Study type(s)

Treatment

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

Infectious Diseases; Tuberculosis

## Interventions

All patients enrolled will receive treatment for 6 months. The duration of the study will be the first 4 months of treatment. For the last 2 months of treatment, the patients will be transferred to the National Treatment Programme to complete 6 months.

Control Regimen : 2 months of daily ethambutol, isoniazid, rifampicin, and pyrazinamide followed by 4 months of daily isoniazid and rifampicin (2EHRZ/4HR)A.

Study Regimen 1: The regimen as above but with an increase in the dose of rifampicin to 15mg /kg body weight daily for the first 4 months. (2EHR15Z/2HR15/2HR)B For the first 4 months, the dose of rifampicin will be 15mg/kg.

Study Regimen 2: The regimen as above but with an increase in the dose of rifampicin to 20mg /kg body weight daily for the first 4 months. (2EHR20Z/2HR20/2HR)C For the first 4 months, the dose of rifampicin will be 20mg/kg.

## **Intervention Type**

Drug

## **Phase**

Not Applicable

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

Ethambutol, isoniazid, rifampicin, pyrazinamide

## **Primary outcome(s)**

Occurrence of grade 3 or 4 adverse events at any time during chemotherapy

## **Key secondary outcome(s)**

1. Culture conversion at the end of 8 weeks of chemotherapy
2. Per protocol analysis of the primary outcome.
3. Any adverse event graded according to the modified Division of Aids (DAIDS) criteria
4. Rate of completion of chemotherapy according to the protocol
5. Number of observed doses of chemotherapy ingested

## **Completion date**

01/10/2012

# **Eligibility**

## **Key inclusion criteria**

1. Newly diagnosed pulmonary tuberculosis
2. Two sputum specimens positive for tubercle bacilli on direct smear microscopy
3. No previous anti-tuberculosis chemotherapy
4. Aged 18 years and over
5. A firm home address that is readily accessible for visiting and be intending to remain there or within the recruitment area for the entire treatment period
6. Agree to participate in the study and to give a sample of blood for HIV testing
7. Pre-menopausal women must be using a barrier form of contraception or be surgically sterilised or have an interuterine contraceptive device (IUCD) in place for the duration of the treatment phase

## **Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Sex**

All

**Key exclusion criteria**

1. Has any condition (except HIV infection) that may prove fatal during the study period
2. Has TB meningitis
3. Has pre-existing non-tuberculous disease likely to prejudice the response to, or assessment of, treatment e.g. insulin-dependent diabetes, liver or kidney disease, blood disorders, peripheral neuritis
4. Is female and known to be pregnant, or breast feeding
5. Is suffering from a condition likely to lead to uncooperative behaviour such as psychiatric illness or alcoholism
6. Has contraindications to any medications in the study regimens
7. Requires anti-retro viral treatment (ART) at diagnosis
8. Haemoglobin <7g/l
9. Aspartate Aminotransferase (AST) or Alanine Aminotransferase (ALT) > 5 times the upper limit of normal (ULN) for that laboratory
10. Creatinine clearance of < 30mls/min  
Calculated as  $((140 - \text{age}) \times \text{weight} \times 1.23 \times (0.85 \text{ if female})) / \text{Creat}[\text{micromol/l}]$
11. Has glucose in urine
12. Is HIV positive with a CD4 count of less than 350/mm<sup>3</sup>
13. Weight < 35kg

**Date of first enrolment**

01/10/2010

**Date of final enrolment**

01/10/2012

**Locations****Countries of recruitment**

United Kingdom

England

Bolivia

India

Nepal

**Study participating centre**  
**St George's University of London**  
London  
United Kingdom  
SW17 0RE

## **Sponsor information**

**Organisation**  
St George's University of London (UK)

**ROR**  
<https://ror.org/040f08y74>

## **Funder(s)**

**Funder type**  
University/education

**Funder Name**  
St. George's, University of London

**Alternative Name(s)**  
St. George's

**Funding Body Type**  
Private sector organisation

**Funding Body Subtype**  
Universities (academic only)

**Location**  
United Kingdom

## **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?
<a href="#">Results article</a>	sub-study results	24/04/2017		Yes	No
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes