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Evaluation of high dose rifampicin toxicity in pulmonary tuberculosis

Submission date	Recruitment status
12/10/2010	No longer recruiting
Registration date	**Overall study status**
09/11/2010	Completed
Last Edited	**Condition category**
20/09/2017	Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
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 pulmomary 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

Secondary study design

Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a patient information sheet

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

Secondary outcome measures
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

Overall study start date
01/10/2010

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

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
300

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. Asparate 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-age) x weight x 1.23 x (0.85 if female))/Creat[micromol/l)
11. Has glucose in urine
12. Is HIV positive with a CD4 count of less than 350/mm3
13. Weight < 35kg

Date of first enrolment

01/10/2010

Date of final enrolment
01/10/2012

Locations

Countries of recruitment
Bolivia

England

India

Nepal

United Kingdom

Study participating centre
St George's University of London
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Sponsor information

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Sponsor type
University/education

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

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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	sub-study results	24/04/2017		Yes	No