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An international multicentre controlled clinical trial to evaluate high dose RIFApentine and a QUINolone in the treatment of pulmonary tuberculosis

Submission date
01/05/2007

Registration date
03/07/2007

Last Edited
03/11/2014

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Infections and Infestations

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

Plain English summary of protocol
http://www.ctu.mrc.ac.uk/research_areas/study_details.aspx?s=49

Contact information

Type(s)
Scientific

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Additional identifiers

Study information

Scientific Title

Acronym
RIFAQUIN

Study objectives
1. Rifapentine (a rifamycin) and moxifloxacin (a quinolone) given together, will shorten the length of treatment for tuberculosis to four months and/or simplify treatment administration, i. e., given once or twice a week rather than daily
2. Doubling the dose of rifapentine will reduce the overall relapse rates and eliminate rifamycin resistance in those Human Immunodeficiency Virus (HIV) positive patients who may relapse
3. Laboratory experiments suggest that replacing isoniazid with moxifloxacin could strengthen the treatment. We are also assessing whether, by substituting moxifloxacin for isoniazid, it is possible to simplify, and even reduce the duration of, the continuation phase of treatment

Please note that, as of 07/10/2008, the start date of this trial has been updated from 31/07 /2008 to 15/08/2008.

Please note that as of 29/04/2008 this trial record was updated. All changes can be found in the relevant section under this update date. Please also note that the anticipated start and end dates of this trial have also been updated, the previous dates were:
Anticipated start date: 31/07/2007
Anticipated end date: 31/07/2009

Please note, as of 26/10/2011 updates have been made to the trial record in accordance with an amendment to the protocol. These can be found under this date of update in the relevant fields below. The anticipated end date has been extended. The previous date was 31/07/2010.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London-Surrey Borders Research Ethics Committee (ref: 07/Q0806/58). The most recent ethics approval for version 1.5 of the protocol was given on 17/03/2008.

The protocol will also be submitted to the Medical Ethics Committee of each of the participating clinical site and/or country and enrolment to the study will start only after receiving the written agreement of the relevant body(ies).

Study design
Multicentre randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Pulmonary tuberculosis

Interventions
Control regimen:
Two months of daily ethambutol (E), isoniazid (H), rifampicin (R), and pyrazinamide (Z) followed by four months of daily isoniazid and rifampicin (2EHRZ/4HR).

Study regimen one:
Two months of daily ethambutol, moxifloxacin (M), rifampicin, and pyrazinamide followed by two months of twice weekly moxifloxacin and rifapentine (2EMRZ/2P2M2).

Study regimen two:
Two months of daily ethambutol, moxifloxacin, rifampicin, and pyrazinamide followed by four months of once weekly moxifloxacin and rifapentine (2EMRZ/4P1M1).

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Ethambutol, isoniazid, rifampicin, pyrazinamide, moxifloxacin

Primary outcome(s)
1. Combined rate of failure at the end of treatment and relapse, measured at 18 months
2. Presence of Rifamycin Monoresistance (RMR) in relapse cultures of HIV infected patients, measured at 5, 6, 7, 8, 9, 10, 11, 12, 15, 18 months on the four-month arm and 7, 8, 9, 10, 11, 12, 15, 18 months on the six-month arm, plus at any unscheduled visit
3. Occurrence of serious adverse events at any time during chemotherapy, recorded as they present themselves throughout the course of the trial

Added 26/10/2011: Please note, Patients will be followed up for 18 months from the commencement of chemotherapy. Follow-up visits will occur monthly until 12 months then at 15 and 18 months. However, follow-up will be stopped 12 months after the last patient has been randomised into the study; thus patients randomised in the final 6 months will have reduced follow-up.

Key secondary outcome(s))
1. Sputum culture results at two months after the initiation of chemotherapy, measured at all visits
2. Rate of completion of chemotherapy according to the protocol, measured at all visits
3. Number of observed doses of chemotherapy ingested, measured at all visits
4. Any adverse events, recorded as they present themselves throughout the course of the trial

Completion date
30/11/2012

Eligibility

Key inclusion criteria

1. Newly diagnosed pulmonary tuberculosis
2. Two sputum specimens positive for tubercle bacilli on direct smear microscopy
3. Either no previous anti-tuberculosis chemotherapy, or less than two weeks of previous chemotherapy
4. Aged 18 years and over
5. A firm home address that is readily accessible for visiting and be intending to remain there during the entire treatment and follow up period
6. Willing to agree to participate in the study and to give a sample of blood for HIV testing

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Not Specified

Key exclusion criteria
1. Has any condition (except HIV infection) that may prove fatal during the study period
2. Has Tuberculous (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-Retroviral Treatment (ART) at diagnosis
8. Has a history of prolonged QTc syndrome or current or planned therapy with quinidine, procainamide, amiodarone, sotalol, disopyramide, ziprasidone, or terfenadine during the intensive phase of TB therapy
9. Haemoglobin less than 7g/l
10. Aspartate Aminotransferase (AST) or Alanine Aminotransferase (ALT) greater than five times the upper range
11. Creatinine clearance of less than 30 mls/min
12. Has a history of seizures
13. Is HIV positive with a CD4 count of less than 200/mm^3
14. Weight less than 35 kg
Added 26/10/2011:
15. Already receiving anti anti-retroviral therapy (ART)

Date of first enrolment
15/08/2008

Date of final enrolment
30/11/2012

Locations

Countries of recruitment
United Kingdom

England

Botswana

Mozambique

South Africa

Zambia

Zimbabwe

Study participating centre
Centre for Infection
London
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Sponsor information

Organisation
St. Georges Hospital Medical School (UK)

ROR
https://ror.org/040f08y74

Funder(s)

Funder type
Government

Funder Name
European and Developing Countries Clinical Trials Partnership (EDCTP) (The Netherlands)

Alternative Name(s)
The European & Developing Countries Clinical Trials Partnership, The European & Developing Countries Clinical Trials Partnership (EDCTP), European and Developing Countries Clinical Trials, Le partenariat Europe-Pays en développement pour les essais cliniques, A Parceria entre a Europa e os Países em Desenvolvimento para a Realização de Ensaios Clínicos, EDCTP

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
Netherlands

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	01/08/2012		Yes	No
Results article	results	23/10/2014		Yes	No