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Controlled comparison of two moxifloxacin containing treatment shortening regimens in pulmonary tuberculosis

Submission date	Recruitment status	[X] Prospectively registered
25/01/2007	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
20/03/2007	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
10/04/2019	Infections and Infestations	

Plain English summary of protocol
http://www.ctu.mrc.ac.uk/research_areas/study_details.aspx?s=29

Study website
http://www.remoxtb.org

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

NCT00864383

Secondary identifying numbers
N/A

Study information

Scientific Title
Controlled comparison of two moxifloxacin containing treatment shortening regimens in pulmonary tuberculosis

Acronym
REMoxTB

Study objectives
1. In treatment-naïve adults with active pulmonary Tuberculosis (TB) treated with eight weeks of moxifloxacin, isoniazid, rifampicin and pyrazinamide (i.e. a standard regimen where moxifloxacin is substituted for ethambutol), followed by nine weeks of moxifloxacin, isoniazid and rifampicin, followed by nine weeks of placebo, the proportion of patients who experience treatment failure or disease relapse in the twelve months following treatment completion will not be inferior to that observed in patients who are treated with a standard regimen (eight weeks of ethambutol, isoniazid, rifampicin and pyrazinamide followed by eighteen weeks of isoniazid plus rifampicin).
2. In treatment-naïve adults with active pulmonary TB treated with eight weeks of ethambutol, moxifloxacin, rifampicin and pyrazinamide (i.e. a standard regimen where moxifloxacin is substituted for isoniazid), followed by nine weeks of moxifloxacin and rifampicin followed by nine weeks of placebo, the proportion of patients who experience treatment failure or disease relapse in the twelve months following treatment completion will not be inferior to that observed in patients who are treated with a standard regimen (eight weeks of ethambutol, isoniazid, rifampicin and pyrazinamide followed by eighteen weeks of isoniazid plus rifampicin).

Ethics approval required
Old ethics approval format

Ethics approval(s)
University College London (UCL) Research Ethics Committee, 05/04/2006, ref:0670/001.
Each trial site will apply to the appropriate institutional research ethics committee, approval must be granted before recruitment commences at that site.

Study design
Multicentre randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

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

Interventions
Regimen one - control regimen:
Eight weeks of chemotherapy with ethambutol, isoniazid, rifampicin and pyrazinamide plus the moxifloxacin placebo, followed by nine weeks of isoniazid and rifampicin plus the moxifloxacin placebo, followed by nine weeks of isoniazid and rifampicin only.

Regimen two:
Eight weeks of chemotherapy with moxifloxacin, isoniazid, rifampicin and pyrazinamide plus the ethambutol placebo, followed by nine weeks of moxifloxacin, isoniazid and rifampicin, followed by nine weeks of the isoniazid placebo and the rifampicin placebo.

Regimen three:
Eight weeks of chemotherapy with ethambutol, moxifloxacin, rifampicin and pyrazinamide plus the isoniazid placebo, followed by nine weeks of moxifloxacin and rifampicin plus the isoniazid placebo, followed by nine weeks of the isoniazid placebo and the rifampicin placebo.

Dosages are dependent on the weight category of the patient, and will be provided as follows (all drugs are taken orally):
1. Moxifloxacin: 400 mg
2. Rifampicin:
a. Less than or equal to 45 kg = 450 mg
b. Greater than 45 kg = 600 mg
3. Isoniazid: 300 mg
4. Pyrazinamide:
a. Less than 40 kg = 25 mg/kg rounded to nearest 500 mg
b. 40 to 55 kg = 1000 mg
c. Greater than 55 kg to 75 kg = 1500 mg
d. Greater than 75 kg = 2000 mg
5. Ethambutol:
a. Less than 40 kg = 15 mg/kg rounded to nearest 100 mg
b. 40 to 55 kg = 800 mg
c. Greater than 55 kg to 75 kg = 1200 mg
d. Greater than 75 kg = 1600 mg

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Moxifloxacin, isoniazid, rifampicin and pyrazinamide, ethambutol

Primary outcome measure
1. Efficacy : Combined failure of bacteriological cure and relapse within one year of completion of therapy
2. Safety : Proportion of patients with grade three or four Adverse Events (AEs) according to the World Health Organisation (WHO) grade

Secondary outcome measures
Efficacy:
1. Proportion of patients who are culture negative at eight weeks
2. Time to first culture negative sputum sample
3. Speed of decline of sputum viable count

Overall study start date
01/06/2007

Completion date
01/01/2011

Eligibility

Key inclusion criteria
1. Signed written consent or witnessed oral consent in the case of illiteracy, before undertaking any trial related activity
2. Two sputum specimens positive for tubercle bacilli on direct smear microscopy at the local laboratory
3. No previous anti-tuberculosis chemotherapy
4. Aged 18 years and over
5. A firm home address that is readily accessible for visiting and willingness to inform the study team of any change of address during the treatment and follow-up period
6. Agreement to participate in the study and to give a sample of blood for Human Immunodeficiency Virus (HIV) testing
7. Laboratory parameters performed up to 14 days before enrolment
8. Serum aspartate aminotransferase (AST) activity less than three times the Upper Limit of Normal (ULN)
9. Serum total bilirubin level less than 2.5 times ULN
10. Creatinine Clearance (CrCl) level greater than 30 mls/min
11. Haemoglobin level of at least 7.0 g/dL
12. Platelet count of at least 50 x 10^9 cells/L
13. Serum potassium greater than 3.5 mmol/L
14. Negative pregnancy test (women of childbearing potential)
15. Pre-menopausal women must be using a barrier form of contraception or be surgically sterilised or have an Intra-Uterine Contraceptive Device (IUCD) in place

Participant type(s)
Patient

Age group
Adult

Lower age limit

18 Years

Sex
Both

Target number of participants
1500

Key exclusion criteria
1. Unable to take oral medication
2. Previously enrolled in this study
3. Received any investigational drug in the past three months
4. Received an antibiotic active against M. tuberculosis in the last 14 days (fluoroquinolones, macrolides, standard anti-tuberculosis drugs)
5. Any condition that may prove fatal during the first two months of the study period
6. TB meningitis or other forms of severe tuberculosis with high risk of a poor outcome
7. Pre-existing non-tuberculosis disease likely to prejudice the response to, or assessment of, treatment e.g. insulin-dependent diabetes, liver or kidney disease, blood disorders, peripheral neuritis, chronic diarrhoeal disease
8. Pregnant or breast feeding
9. Suffering from a condition likely to lead to uncooperative behaviour e.g. psychiatric illness or alcoholism
10. Contraindications to any medications in the study regimens
11. Known to have congenital or sporadic syndromes of QTc prolongation or receiving concomitant medication reported to increase the QTc interval (e.g. amiodarone, sotalol, disopyramide, quinidine, procainamide, terfenadine)
12. End stage liver failure (class Child-Pugh C)
13. Uncorrected hypokalaemia
14. Weight less than 35 kg
15. Known allergy to any fluoroquinolone antibiotic or history of tendinopathy associated with quinolones
16. HIV infection with CD4 count less than 250 x 10^9/lit
17. Patients already receiving anti-retroviral therapy
18. Patients whose initial isolate is shown to be multiple drug resistant

Date of first enrolment
01/06/2007

Date of final enrolment
01/01/2011

Locations

Countries of recruitment
England

Kenya

South Africa

Tanzania

United Kingdom

Zambia

Study participating centre
Royal Free and University College Medical School
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Sponsor information

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University/education

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ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Industry

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

Alternative Name(s)
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, The European &

Developing Countries Clinical Trials Partnership, European and Developing Countries Clinical Trials, EDCTP

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
Netherlands

Funder Name
TB Alliance (USA)

Funder Name
Bayer HealthCare Pharmaceuticals (USA)

Funder Name
Sanofi-Aventis (France)

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?
Basic results				No	No
Results article	results	23/10/2014	10/04/2019	Yes	No
Results article	results	04/02/2016	10/04/2019	Yes	No
Results article	results	01/05/2018	10/04/2019	Yes	No