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Tuberculosis child and adolescent multidrug-resistant preventive therapy: TB CHAMP trial

Submission date
31/03/2016

Recruitment status
No longer recruiting

Registration date
28/04/2016

Overall study status
Completed

Last Edited
18/03/2025

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
The World Health Organisation (WHO) estimates that there were half a million multidrug-resistant tuberculosis (MDR-TB)cases in the world in 2013. Conservative assessments suggest that in areas with a high number of TB cases, there are at least two children in direct household contact with an adult with TB, putting them at high risk of developing the disease. The treatment of MDR-TB in children is complex, expensive, long, associated with frequent and significant side effects, and frequently requires long stays in hospital. Prevention of MDR-TB in children is therefore very important. Although the need for a research study to assess potential preventive therapies (treatments) for children in contact with MDR-TB patients was identified in 1992, there haven't been any done yet. Therefore the WHO cannot recommend any specific drug treatments for people who are in contact with others in the same household that have infectious MDR-TB. While infection with normal (non-drug resistant) TB bacteria can be prevented by using a drug called isoniazid taken daily for six months, MDR-TB bacteria are resistant to isoniazid. However, there is the possibility that these MDR-TB bacteria can potentially be treated with another drug called levofloxacin, which is also taken daily for six months. Levofloxacin is approved by the United States Food and Drug Administration (FDA) and the South African Medicines Control Council (MCC) for treating MDR-TB in adults. It is also routinely used for the treatment of MDR-TB in young children. Levofloxacin is not approved for the prevention of MDR-TB. No rigorous research has yet been done to specifically study this in children, hence the need for this study. TB-CHAMP is a study being carried out in South Africa, involving children who live with someone who has, or who has recently had, MDR-TB. It will seek to answer the following important questions:
1. Will treating children living with an adult who had or has MDR-TB with levofloxacin tablets reduce their risk of developing TB compared to treatment with a placebo (inactive "dummy" tablets)?
2. Is it safe to treat children living with an adult who had or has MDR-TB with levofloxacin?

Who can participate?
Children aged five and under who live with adults who have been diagnosed with MDR-TB.

What does the study involve?
Participants are randomly allocated to one of two groups, with all children living in the same

household being in the same group. Those in group 1 are given levofloxacin every day for 24 weeks. Those in group 2 are given a placebo (dummy pill) every day for 24 weeks. This is a "double blind" study, which means that neither the children (or their family) or the researchers know whether the tablets each child is taking are levofloxacin or placebo. All participants attend about ten study visits over the 2 year period. At each visit, details of the child's health, height and weight are recorded, as well as information about how well they take their medicines and if there are any particular problems taking them. The study tests done on the children (investigation for TB, blood tests, etc.) are part of routine recommended clinical care in children exposed to MDR-TB. At some visits some additional blood and urine samples are collected for storage and future testing.

What are the possible benefits and risks of participating?
There may be a direct benefit to children who participate in this study, but no guarantee can be made. It is also possible that the children may receive no benefit from being in this study. Information learned from this study may help others who risk the possibility of having TB.

Where is the study run from?
This research study is led by Stellenbosch University and will be conducted in four clinical sites in South Africa:
1. Desmond Tutu TB Centre, Stellenbosch University (SU), Cape Town (DTTC)
2. Perinatal HIV Research Unit, Klerksdorp, Wits Health Consortium (PHRU)
3. Wits Reproductive Health and HIV Institute Shandukani Research Centre (WRHI)
4. Tuberculosis & HIV Investigative Network, Pietermaritzburg, KwaZulu Natal (THINK)

The trial management will be coordinated from MRC Clinical Trials Unit at UCL, London, UK.

When is the study starting and how long is it expected to run for?
January 2016 to February 2023

Who is funding the study?
1. Joint Global Health Trials Scheme of the Department for International Development in the United Kingdom
2. The Wellcome Trust
3. Medical Research Council
4. South African Medical Research Council

Who is the main contact?
TB-CHAMP Trial Management Team
Email: TBCHAMP.MRCCTU@ucl.ac.uk

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
MR/M007340/1

Study information

Scientific Title
A phase III cluster randomised placebo-controlled trial to assess the efficacy of preventive therapy in child and adolescent contacts of multidrug-resistant (MDR) tuberculosis (TB)

Acronym
TB-CHAMP

Study objectives
24 weeks daily dosing of levofloxacin will protect children exposed to MDR-TB from developing TB disease

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Stellenbosch University HREC, 13/05/2016, ref: M16/02/009
2. Medicines Control Council of South Africa (MCC), 08/12/2016, ref: 20160128

Study design
Parallel group two-arm cluster randomized double-blind placebo-controlled trial

Primary study design
Interventional

Secondary study design
Cluster randomised trial

Study setting(s)
Home

Study type(s)
Prevention

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

Health condition(s) or problem(s) studied
Multi drug resistant tuberculosis (MDR-TB)

Interventions
TB-CHAMP will compare 24 weeks of daily levofloxacin (15-20 mg/kg, maximum 750 mg) against 24 weeks of daily placebo. All eligible children within the household will be treated with the same drug (either all levofloxacin or all placebo). Households will be randomised (allocated by chance) to be in either the levofloxacin or placebo group. This allocation is carried out by a computer, and the households have an equal chance of being in either group.

This is a “double blind” study, which means that neither the children (or their family) or the researchers will know whether the tablets each child is taking are levofloxacin or placebo.

Children who participate in the study will undergo approximately ten study visits over two years. Enough tablets will be prescribed for the child to take daily until they are seen at their next clinic visit. Visits will be monthly whilst taking the study drugs, and then every three months. At each visit details of the child’s health, height and weight will be recorded, as well as information about how well they take their medicines and if there are any particular problems taking them. The study tests to be done on the children (investigation for TB, blood tests, etc.) are part of routine recommended clinical care in children exposed to MDR-TB. At some visits some additional blood and urine samples will be collected for storage and future testing.

Intervention Type
Drug

Phase
Phase III

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

Primary outcome measure
Incident TB disease (probable or confirmed) including TB death, by 48 weeks post-randomisation

Secondary outcome measures
1. Mortality (all cause, non-traumatic, and TB related)
2. Adverse events ≥ grade 3 (at least possibly associated) during 24 weeks of treatment
3. Percentage of levofloxacin or levofloxacin-placebo doses ingested and retained over 24 weeks
4. TB disease over 96 weeks
5. Incidence of levofloxacin resistant TB disease

Overall study start date
01/01/2016

Completion date
28/02/2023

Eligibility

Key inclusion criteria
Current inclusion criteria as of 17/08/2022:
1. Child or adolescent aged <18 years who is a household contact of an adult MDR-TB index case (as stated under adult MDR-TB eligibility criteria). The eligibility criteria would be including diagnosis in the previous 6 months. If ≥5 years and <18 years of age, the child/adolescent must have a positive IGRA test before enrolment unless HIV positive.
2. Primary residence in the household of the adult MDR-TB index case
3. Consent from the parent or legal guardian for the child for HIV testing (HIV-infected and uninfected children will be included)
4. Consent obtained from the parent or legal guardian for the child to be enrolled

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Previous inclusion criteria:
1. Child <5 years who is a household contact of an enrolled adult MDR-TB index case diagnosed during the previous 6 months
2. Primary residence in the household of the adult MDR-TB index case
3. Consent from the parent or legal guardian for the child for HIV testing (HIV-infected and uninfected children will be included)
4. Consent obtained from the parent or legal guardian for the child to be enrolled

Participant type(s)
Mixed

Age group
Child

Upper age limit
18 Years

Sex
Both

Target number of participants
778 households (1556 children) of adult MDR-TB index case (with on average 2 children aged 0-5 years per household)

Total final enrolment
922

Key exclusion criteria
1. TB disease at enrolment
2. Currently on INH or a FQN (e.g. LFX, MFX, ofloxacin or ciprofloxacin) for ≥14 days
3. Treated for TB in the previous 12 months
4. Known concurrent exposure to an INH-susceptible (including RIF-monoresistant) index case
5. Children with myasthenia gravis or Guillain-Barré syndrome

Date of first enrolment
01/10/2016

Date of final enrolment
31/03/2018

Locations

Countries of recruitment
South Africa

Study participating centre
Desmond Tutu TB Centre (DTTC)
Department of Paediatrics and Child Health
Faculty of Medicine and Health Sciences
Stellenbosch University
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South Africa
8000

Study participating centre
Perinatal HIV Research Unit (PHRU)
P.O Box 114 Diepkloof
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Johannesburg
South Africa
1864

Study participating centre
Clinical Trial Unit – Doris Goodwin TB Hospital
THINK: Tuberculosis & HIV Investigative Network
Edendale Main Road, Plessislaer
KwaZulu Natal
Pietermaritzburg
South Africa
3216

Study participating centre
Wits Reproductive Health and HIV Institute (Wits RHI)
Hillbrow Health Precinct
Corner Esselen Street & Klein Street, Hillbrow
Johannesburg
South Africa
20012

Sponsor information

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Stellenbosch University

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Sponsor type
University/education

ROR
https://ror.org/05bk57929

Funder(s)

Funder type
Government

Funder Name
Joint Global Health Trials Scheme of the Department for International Development (UK)

Funder Name
Wellcome Trust

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
United Kingdom

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
South African Medical Research Council

Alternative Name(s)
SAMRC

Funding Body Type
Government organisation

Funding Body Subtype
Other non-profit organizations

Location
South Africa

Results and Publications

Publication and dissemination plan
The main messages from TB CHAMP will be whether giving levofloxacin (LFX) will prevent tuberculosis (TB) in children from the same household as an adult who has infectious multidrug-resistant (MDR)-TB. There will also be a health economic evaluation and evaluation of acceptability to caregivers, children and TB control programmes.

We will work closely with key beneficiaries, particularly national and international policy makers e.g. WHO, the International Union against Tuberculosis and Lung Diseases (The Union), Unicef and TB Alliance. We will conduct face-to-face meetings with the South African Department of Health (DOH) and the South African national TB Programme (NTP) to promote their engagement with the research. We will also produce policy briefs of trial results, and place them in context for the DOH and NTP.

Once the trial has been completed, we intend publishing our results in high-profile open-access journals. It is estimated that the results would be published around 6 months after trial end.

Recommendations from the trial will be communicated to health workers via a video of the trial results and implications. We will also communicate our trial results to academic, policy and health worker audiences through presentations at national and international conferences and working groups, including WHO and The Union.

We will communicate the trial results to study participants through meetings where they can ask questions and give their response to the results. We will also produce lay summaries in printed form, where appropriate. We will engage with the broader population of children with MDR-TB and local communities via the local and national media. A lay summary of the aims of the trial, and, when available, the results, will be made available via the websites of the trial partners.

Formal academic publications are planned throughout the study, including a trial methods paper, social science formative work, and primary as well as other end point analyses (including interim analyses as appropriate).

In-country communication will be led by the PIs, who are experienced in working with the South African DOH and NTP. A dedicated communications officer at the DTTC, Stellenbosch University will support our communication strategy. The video will be produced by an experienced South African film-maker, with a track record of producing films and training materials related to clinical trials. We will also liaise closely with our local press including web media, newspapers and radio. Our communications officer will establish regular Twitter and Facebook feeds.

Intention to publish date
31/01/2025

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	20/12/2018		Yes	No
Results article		19/12/2024	19/12/2024	Yes	No
Other publications	Acceptability	12/03/2025	18/03/2025	Yes	No