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Research to improve the detection and treatment of latent tuberculosis infection: Treatment

Submission date
18/05/2022

Recruitment status
No longer recruiting

Registration date
24/05/2022

Overall study status
Ongoing

Last Edited
09/04/2025

Condition category
Infections and Infestations

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims

The RID-TB program aims to contribute to a substantial reduction in the incidence of tuberculosis (TB) in England by evaluating complementary interventions targeted at different stages in the diagnosis, treatment and prevention of latent TB infection (LTBI), where you have a TB infection, but do not have symptoms of an active infection. The interventions are designed to improve access to diagnosis, increase uptake of testing and enhance treatment completion in individuals with or at risk of LTBI. The researchers in this study think that this approach will enable the NHS to more effectively address the burden of LTBI and decrease the rate of active TB in the UK. Improving how well patients take their LTBI medications correctly (adherence) is critical to achieving the goals of the national TB strategy. Research to understand barriers and enablers of adherence as well as the evaluation of promising technology and treatment plans in the NHS, may provide the tools to reduce TB rates.

Specific promising interventions in active TB adherence studies include the use of mobile/digital technology (mHealth) and evaluation of shorter treatment plans. Data are limited on mHealth interventions for treatment of active TB. A recent study in China found electronic reminders using specially designed medication monitors improved adherence in active TB patients, but text messaging reminders did not. Most of the evidence available is on active TB with little research on mHealth interventions to improve LTBI treatment adherence. Motivation to complete treatment may differ between patients with active disease and LTBI due to different severity and outcome of the two conditions. In addition, decreasing the complexity of current treatment plans may promote better adherence. A treatment plan that is shorter or administered only weekly may result in better treatment completion than the current daily 3-month treatment plan. Additionally, in the COVID-19 epidemic, shorter treatment plans can reduce the number of clinic visits, and hence reduce risk of infection and pressure on the health care. Therefore, a 1-month treatment plan that is now newly recommended by the World Health Organization (WHO) has a great potential to help continue LTBI care at this challenging moment due to COVID-19.

We aim to conduct a study to assess the effect of novel short-course rifapentine-based treatment plans for TB prevention and additional adherence support on LTBI treatment completion against standard-of-care (SOC).

Who can participate?
Patients aged 16-65 years attending a RID-TB clinic who are eligible for latent TB infection treatment according to UK guidance

What does the study involve?
Patients will be randomly allocated to the following groups:
Group 1. Daily isoniazid + rifampicin for three months (3HR), routine adherence support (control)
Group 2. Daily 3HR, additional adherence support
Group 3. Weekly isoniazid + rifapentine for three months (3HP), routine adherence support
Group 4. Weekly 3HP, additional adherence support
Group 5. Daily isoniazid + rifapentine for one month (1HP), routine adherence support
Additional adherence support: Behavioural interventions target perceptual and practical barriers to adherence, which will be administered through adherence support material (e.g. video) and Wisepill EvriMed – electronic pill box and monitor with reminders switched.

Investigations:
Following informed consent procedures, participants will be screened for eligibility. A TB symptom screen and urine pregnancy test will be carried out, and data on the participant's TB risk group category will be collected.
Demographic and medical history information will be collected. Eligibility for TB preventive treatment as per NICE guidance will be confirmed. We will check results of clinical, laboratory, and radiological assessments performed under routine care before entry to the trial to confirm eligibility. Clinical, laboratory, and radiological results conducted within 3 months prior to enrolment are considered valid.

A TB symptom screen and urine pregnancy test will be repeated (unless the screening and randomization visits occur on the same day). Pregnancy tests need to be performed within 7 days of initiation treatment. Eligible participants will be randomized to one of the study arms. Participants will be required to visit the clinic or receive a remote consultation as per the local policy every month. Additionally, blood test needs to be done at week 2 to check side effects, including signs of active TB and side effects. Blood tests may be performed if a doctor finds it necessary to check liver problems or other side effects. Urine pregnancy tests will be done at every visit for participants with childbearing potential. Participants will be requested to bring a pill box to check the remaining tablets. If the participant agrees to take part in optional behavioural and economics sub-studies, additional questionnaires will be required to be completed at every visit or remotely.

What are the possible benefits and risks of participating?
There is no direct benefit to research to the participants enrolled in the study; patients are already eligible for LTBI treatment as part of their usual care. The results will help improve care for other people who may be at risk from latent TB. New drug combinations may cause side effects (e.g. liver toxicity and hypersensitivity reactions). The frequency of side effects is considered similar to the current standard treatment plan. The study doctors/nurses will discuss the side effects and any medication to alleviate symptoms with the participants. Participants will be given the contact details of the study team in case they have any concerns/symptoms are worse than anticipated. Study visits will take longer than usual visits while data is collected for

CRF completion. In addition, the behavioural and health economic sub-study questionnaires will further increase visit length. However, these sub-studies are optional so participants who are not able to spend additional time at clinical can still enrol in the study.

Where is the study run from?
University College London (UK)

When is the study starting and how long is it expected to run for?
October 2018 until September 2023

Who is funding the study?
National Institute for Health and Care Research (UK)

Who is the main contact?
RID-TB Trial Manager
mrcctu.rid-tb@ucl.ac.uk

Study website
https://www.ctu.mrc.ac.uk/

Contact information

Type(s)
Scientific

Contact name
Dr RID-TB Trial Manager

Contact details
MRC Clinical Trials Unit at UCL
Institute of Clinical Trials & Methodology
90 High Holborn
2nd Floor
London
United Kingdom
WC1V 6LJ
+44 7906 752 079
mrcctu.rid-tb@ucl.ac.uk

Additional identifiers

EudraCT/CTIS number
2020-004444-29

IRAS number
282304

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 47005; IRAS 282304

Study information

Scientific Title
An open-label, multi-centre, randomised controlled trial evaluating the effects of short-course rifapentine-based regimens and additional adherence support on LTBI treatment adherence and completion among adults in the UK

Acronym
RID-TB:Treat

Study objectives
The main hypotheses are that the novel regimens will improve treatment adherence compared to 3-month daily rifampicin plus isoniazid (3HR), and additional support will improve adherence to each regimen compared to routine support.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 25/11/2020, London-Riverside REC (Temple Quay House, Ground Floor, 2 The Square, Bristol, BS1 6PN; +44 (0)207 104 8340; riverside.rec@hra.nhs.uk), Ref: 20/LO/1097

Study design
Randomized; Interventional; Design type: Treatment, Drug, Psychological & Behavioural

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 the contact details below to request a patient information sheet

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

Interventions
Study design: 920 participants will be randomized with allocation ratio 5:5:6:6:6:6 to one of the following arms:

ARM 1- Daily isoniazid plus rifampicin (<50 kg = 150/100 mg fixed dose oral tablet, ≥50 kg = 300 /150 mg fixed dose oral tablet) for 3 months (3HR), routine adherence support (control)
ARM 2- Daily 3HR, additional adherence support
ARM 3- Weekly rifapentine (30 to <32 kg = 600 mg, 32 to <50 kg = 750 mg, and ≥50 kg = 900 mg) plus isoniazid (15 mg/kg) for 3 months (3HP), routine adherence support
ARM 4- Weekly 3HP, additional adherence support
ARM 5- Daily rifapentine (30 to <35 kg = 300 mg, 32 to <45 kg = 450 mg, and ≥45 kg = 600 mg) plus isoniazid (300 mg) for 1 month (1HP), routine adherence support
ARM 6- Daily 1HP, additional adherence support
Additional adherence support: Behavioural interventions target perceptual and practical barriers to adherence, which will be administered through adherence support material (e.g. video) and Wisepill EvriMed – electronic pill box and monitor with reminders switched.

Investigations:
Screening: Following informed consent procedures, participants will be screened for eligibility. A TB symptom screen and urine pregnancy test will be carried out, and data on the participant's TB risk group category will be collected.
Demographic and medical history information will be collected. Eligibility for TB preventive treatment as per NICE guidance will be confirmed. We will check the results of clinical, laboratory, and radiological assessments performed under routine care before entry into the trial to confirm eligibility. Clinical, laboratory and radiological results conducted within 3 months prior to enrolment are considered valid.

Randomization & Baseline: A TB symptom screen and urine pregnancy test will be repeated (unless the screening and randomization visits occur on the same day). Pregnancy tests need to be performed within 7 days of initiation of treatment. Eligible participants will be randomized to one of the study arms.

Follow-up: Participants will be required to visit the clinic or receive a remote consultation as per the local policy every month. Additionally, blood test needs to be done at week 2 to check side effects, including signs of active TB and side effects. Blood tests may be performed if the doctor finds it necessary to check for liver problems or other side effects. Urine pregnancy tests will be done at every visit for women with childbearing potential. Participants will be requested to bring the pill box to check the remaining tablets. If participants agree to take part in optional behavioural and economics sub-studies, completion of an additional questionnaire will be required at every visit or remotely.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Rifapentine, isoniazid, rifampicin

Primary outcome measure
Adequate treatment adherence is defined as taking ≥90% of allotted doses within the allowable time frame specified by the treatment plan. Time-frames differ depending on the treatment arm

that a participant is randomized to. 3HR and 3HP arms (i.e. arms 1, 2, 3, 4) have 16 weeks to complete, and the 1HP arm (i.e. arm 5) has 8 weeks to complete. Adherence data is checked at all follow-up visits.

Secondary outcome measures
1. Proportion of doses missed over the treatment period measured using a dose count, self-reporting, and Wisepill monitoring box at weeks 2, 4, 8, 12, 16, and 20.
2. Proportion of pills missed over the treatment period measured using a pill count, self-reporting, and Wisepill monitoring box at weeks 2, 4, 8, 12, 16, and 20.
3. Taking at least 90% of doses and pills over the treatment period measured using a dose and a pill count, self-reporting, and Wisepill monitoring box at weeks 2, 4, 8, 12, 16, and 20.
4. Early study treatment discontinuation for any reason measured using participant status data collection at weeks 2, 4, 8, 12, 16, and 20.
5. Permanently stopping study treatment due to drug-related adverse events, measured using adverse event data collection at weeks 2, 4, 8, 12, 16, and 20.
6. Grade ≥3 adverse events, measured using adverse event data collection at weeks 2, 4, 8, 12, 16, and 20.
7. Adverse events at least possibly associated with study treatment, measured using adverse event data collection at weeks 2, 4, 8, 12, 16, and 20.
8. Development of active TB within 12 months of starting treatment, measured by assessing TB symptoms at weeks 2, 4, 8, 12, 16, and 20 and using records held by NHS Digital, Public Health England, and/or the National TB register at week 52.

Overall study start date
01/10/2018

Completion date
31/12/2025

Eligibility

Key inclusion criteria
1. Aged > = 16 years to < = 65 at screening
2. LTBI diagnosis is defined on the basis of all of the following:
2.1. A positive result on an Interferon Gamma Release Assay (IGRA), Tuberculin Skin Test (TST) or C-Tb skin test and
2.2. Negative TB symptoms at screening and
2.3. No signs of active TB on a Chest X-ray
3. Eligible for LTBI treatment at TB clinics and national LTBI screening services based on NICE guidelines, which means having one or more of the following :
3.1. Recent infection (contact tracing);
3.2. New entrants at risk (i.e., those that immigrated < 5 years from countries with a high incidence of TB, which is defined as > = 40 cases/100,000 population); or
3.3. Individuals who are assessed in the TB clinic for latent TB testing, or have been referred for treatment following testing by specialities or departments within primary or secondary care settings
4. Agree to LTBI treatment
5. Willing and able to provide written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
16 Years

Upper age limit
65 Years

Sex
Both

Target number of participants
Planned Sample Size: 730; UK Sample Size: 920

Key exclusion criteria
1. Patients weighing < 30 kg.
2. Need for medications that cannot be safely taken together with study drugs
3. Any medical condition deserving priority of treatment (such as: porphyria, malabsorption syndromes, Clostridium difficile-associated diarrhoea and other conditions)
4. History of sensitivity/intolerance to isoniazid or rifamycins
5. Individuals with documented liver disease, defined as:
5.1. LFT (ALT/AST/bilirubin) over three times upper limit of normal (ULN) at baseline. This reflects normal clinical practice. For patient participant safety, liver function tests are carried on a regular basis. One abnormal value prevents the patient from participating on the study.
5.2. Clinical diagnosis of cirrhosis (jaundice, hematemesis, ascites or previous episodes of liver encephalopathy),
5.3. HbsAg positive or HCV antibody positive and deemed ineligible for LTBI treatment by the clinician
6. Intending to move outside of the treatment locality within 20 weeks of starting treatment
7. Individuals who would usually be offered LTBI treatment under Directly Observed Therapy (DOT) as part of enhanced case management in complex cases such as those from under-served groups (such as people who are homeless, misuse substances, have been in prison or who are vulnerable migrants).
8. Use of another experimental investigational medicinal product that is likely to interfere with the study medication within 3 months of study enrolment.
9. Women who are breastfeeding, pregnant, or of childbearing potential* who do not agree to use an effective method of contraception from the time consent is signed until 4 weeks after treatment discontinuation or completion.
10. Women of childbearing potential without a negative urine pregnancy test within 7 days prior to being registered for trial treatment.

Date of first enrolment
15/07/2022

Date of final enrolment
30/09/2023

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
St Marys Hospital
Praed Street
London
United Kingdom
W2 1NY

Study participating centre
Whittington Hospital
Magdala Avenue
London
United Kingdom
N19 5NF

Study participating centre
Northwick Park Hospital
Watford Road
Harrow
United Kingdom
HA1 3UJ

Study participating centre
Ealing Hospital
Uxbridge Road
Southall
United Kingdom
UB1 3HW

Study participating centre
Central Middlesex Hospital
Acton Lane
London
United Kingdom
NW10 7NS

Study participating centre
The Shrewsbury Centre
Shrewsbury Road
Forest Gate
London
United Kingdom
E7 8QP

Study participating centre
Whipps Cross University Hospital
Whipps Cross Road
Leytonstone
London
United Kingdom
E11 1NR

Study participating centre
Mile End Hospital
275 Bancroft Road
London
United Kingdom
E1 4DG

Study participating centre
Royal Free Hospital
Pond Street
London
United Kingdom
NW3 2QG

Sponsor information

Organisation
University College London

Sponsor details
Gower Street
London
England
United Kingdom
WC1E 6BT

+44 (0)207 6704811
m.parmar@ucl.ac.uk

Sponsor type
University/education

Website
http://www.ucl.ac.uk/

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Government

Funder Name
NIHR Central Commissioning Facility (CCF); Grant Codes: RP-PG-0217-20009

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal.

Intention to publish date
30/04/2024

Individual participant data (IPD) sharing plan
The trial data are held at the MRC Clinical Trials Unit at UCL which encourages optimal use of data by employing a controlled access approach to data sharing. Requests for data can be made via application to the Programme Steering Committee. Further information on both the approach and the application process can be found here: http://www.ctu.mrc.ac.uk/our_research/datasharing/

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			26/07/2023	No	No