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Evaluating the performance of blood-based test (Actiphage test) for active tuberculosis

Submission date 07/07/2023	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 11/07/2023	**Overall study status** Completed	
Last Edited 03/01/2024	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims
Tuberculosis (TB) remains a significant global health concern, leading to severe illness and mortality worldwide. The current diagnosis of TB relies on patients producing sputum and culturing bacteria from the sputum, a process that can take several days to weeks, resulting in delayed diagnosis. Moreover, some individuals are unable to produce sputum, necessitating invasive procedures such as bronchoscopy. In order to combat TB effectively, improved diagnostic tests are required to enable rapid detection and treatment.
The objective of this study is to evaluate the performance of a potential novel blood test for TB called the Actiphage test. Developed by PBD Biotech Ltd, the Actiphage test aims to detect the bacteria responsible for causing TB directly from the blood. This study seeks to generate additional data to assess the practical effectiveness of the Actiphage test. To achieve this, two distinct groups of participants will be included: those diagnosed with TB and individuals who are unwell but do not have TB.
A total of 103 participants will be recruited for this observational study, which will be conducted over a period of 12 months at the University Hospitals of Leicester NHS Trust, serving as the sole research center.

Who can participate?
People with suspected or confirmed pneumonia or tuberculosis presenting to University Hospitals of Leicester NHS Trust.

What does the study involve?
This study requires blood to be taken at a single visit. If you agree to take part, we will collect up to 30mls of blood (6 teaspoons) for the research at the time you are having blood taken as part of your clinical investigation. This will avoid the need for you to have additional venepuncture (needle inserted to collect blood). It will take no longer than 10 minutes to collect this additional blood volume. In addition to this, we will collect other clinical and demographic data recorded during your clinical assessment (such as your age, gender, ethnicity, diagnosis and other clinical data collected as part of your normal clinical care.) The visit should not exceed 1 hour.
Your participation in the study will end after one visit. In the unlikely event that a problem arises with the shipment or processing of the blood sample, we may ask you to provide a further 7.5 ml (1.5 teaspoons) blood sample at your next scheduled clinical visit.

What are the possible benefits and risks of participating?
It is unlikely that this study will directly help you but the information we get from this study may help people with TB in the future.
There are minimal risks associated with study procedures. When research blood samples are taken there may be minor discomfort at the site where the needle is inserted. All blood samples will be taken by a doctor or fully trained health professional at the same time as your routine blood samples, to ensure no further venepuncture is required.

Where is the study run from?
University of Leicester (UK)

When is the study starting and how long is it expected to run for?
May 2023 to October 2024

Who is funding the study?
The study is being funded by the company that have developed the test (PBD Biotech Ltd). This study is sponsored by the University of Leicester. It is supported by the NIHR Leicester Biomedical Research Centre - Respiratory & Infection (Glenfield Hospital) (UK).

Who is the main contact?
Dr P Haldar, ph62@leicester.ac.uk

Contact information

Type(s)
Principal investigator

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Additional identifiers

Integrated Research Application System (IRAS)
328778

Central Portfolio Management System (CPMS)
56391

Study information

Scientific Title
Evaluating the diagnostic utility of Actiphage® for active pulmonary TB in a low burden setting

Acronym
PHAGE-TB

Study objectives
Active tuberculosis (TB) disease is an infectious disease caused by Mycobacterium tuberculosis (Mtb) that affects more than 10 million people globally each year. The microbiological diagnosis of pulmonary TB relies on patient producing sputum and culturing bacteria from sputum. For patients who do not produce sputum, invasive sampling with bronchoscopy may be required for microbiological diagnosis. Culturing bacteria takes days to weeks, resulting in delay in diagnosis and treatment. Actiphage is a blood-based assay which can detect viable Mtb in circulation. The assay is potentially advantageous as it is performed on blood which is universally accessible and provides a result within hours.

The study will build on observations reported in a recent, small proof of concept single-centre study (Leicester) that demonstrated Actiphage based detection of Mtb in the blood of treatment naive pulmonary TB patients, with a sensitivity of 73% and specificity of 100%. In that study, sensitivity of the assay associated with radiological and microbiological correlates of increased disease severity. The present study aims to extend these observations to provide supporting evidence for validation in an independent fully characterised cohort at Leicester (UK). This study will gather evidence to determine the utility of the Actiphage assay as a blood-based TB diagnostic.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 03/07/2023, South Central – Hampshire A (Health Research Authority, 2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8388; hampshirea.rec@hra.nhs.uk), ref: 23/SC/0222

Primary study design
Observational

Study design
Single-centre observational cross-sectional cohort study

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Diagnosis of active tuberculosis disease

Interventions
This will be an observational cohort study, recruiting patients who present to hospital with suspected active TB or acute pneumonia (control group). Consenting participants will have blood

collected for research at the time of clinical blood sampling to avoid additional venepuncture. Up to 30mls of blood will be collected for research tests at a single time point and will include: i. two aliquots of blood for Actiphage testing; ii. one aliquot for interferon gamma release assay (IGRA) testing using QuantiFERON-TB Gold Plus (QFT); iii. and one aliquot for Mtb blood culture. The consent and research visit will take place during the hospital stay for hospitalised patients.

Clinical investigations for TB will be in accordance with routine practice and include venous blood sampling (complete blood count, biochemistry, CRP, HIV serology and IGRA); respiratory sample microbiological testing (Xpert MTB/RIF Ultra, routine and mycobacterial culture) for expectorated samples; and chest X-ray. Demographic and clinical data will be systematically recorded on the study case report form.

The outcome of Actiphage testing will not be considered in the diagnosis of active TB. The study will neither interfere with, nor influence the routine clinical management and journey of the patient.

Intervention Type
Other

Primary outcome(s)
Actiphage test for diagnosis of TB at a single time point. Diagnosis of TB is made according to standard clinical criteria based on microbiological, histological, and radiological evidence that is collected by reviewing patient medial notes. Actiphage test will be performed according to the manufacturer’s instructions.

Key secondary outcome(s)
Agreement between Actiphage test results for contemporaneous samples tested at PBD laboratories and Leicester. Actiphage test will be performed according to the manufacturer’s instructions.

Completion date
30/10/2024

Eligibility

Key inclusion criteria
1. Able to give informed consent to participate in the study
2. Aged 16 years or above, presenting with suspected pulmonary TB or acute community acquired pneumonia (CAP) and managed by Adult Services at University Hospitals of Leicester NHS Trust (UHL)
3. Recruitment of CAP patients will be selective and focus on:
3.1. Patients with a CXR that is coded for TB or mentions TB as a possibility in the report; AND / OR
3.2. Demographic matching (age and ethnicity) with recruited pulmonary TB cohort; AND / OR iii. patients with a clinical history of any red flag TB symptoms exceeding 2 weeks (cough, fever, night sweats, weight loss) persisting symptoms after a course of oral antibiotics

Participant type(s)
Patient

Healthy volunteers allowed

No

Age group
Other

Lower age limit
16 Years

Sex
All

Key exclusion criteria
1. Treated with anti-tuberculous medication at any time in previous 12 months
2. Participation in an interventional clinical study in the 3 months prior to Visit 1 or participation in a study using interventional medicinal products in the previous 6 months

Date of first enrolment
17/07/2023

Date of final enrolment
31/07/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University Hospitals of Leicester NHS Trust
Groby Road
Leicester
United Kingdom
LE3 9QP

Sponsor information

Organisation
University of Leicester

ROR
https://ror.org/04h699437

Funder(s)

Funder type
Industry

Funder Name
PBD Biotech Limited

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Dr Pranabashis Haldar (email: ph62@leicester.ac.uk)

IPD sharing plan summary
Available on request