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Comparing a new test for tuberculosis with conventional tests

Submission date
25/01/2021

Recruitment status
No longer recruiting

Registration date
16/02/2021

Overall study status
Completed

Last Edited
23/01/2025

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Tuberculosis (TB) is an infection caused by a bacterium called Mycobacterium tuberculosis. It can be diagnosed with procedures such as bronchoalveolar lavage (BAL) and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA). BAL is a procedure where sterile water is injected into a segment of the lung and then suctioned back and sent for tests. EBUS-TBNA uses ultrasound to allow doctors to take samples of tissue just outside the lungs. This study will evaluate the Xpert MTB/RIF Ultra test for the detection of Mycobacterium tuberculosis in BAL samples for pulmonary TB and EBUS-TBNA samples for mediastinal TB and will compare the diagnostic performance against conventional tests (smear, culture, cytology), as well as to a clinical composite diagnosis, using a clinical expert panel reviewing the data blindly.

Who can participate?
Patients aged 18 and over suspected of having pulmonary TB or mediastinal TB undergoing a routine clinical bronchoscopy or EBUS-TBNA

What does the study involve?
Participants will follow the routine clinical pathway to investigate the diagnosis of possible TB and will have a BAL and/or EBUS-TBNA sample taken. The researchers will review their medical notes for clinical information and results related to your TB investigations such as blood tests, X-rays, BAL and/or EBUS-TBNA results. Participants will have follow-up arrangements in line with the local trust guidelines and the researchers will review any routine follow up data for a minimum of 3 months after the procedure if available. There will be no additional procedures, sampling or visits as the researchers will only use routinely available clinical and follow up information if available.

What are the possible benefits and risks of participating?
There will be no direct benefit to participants as their team are already using this test but they may be helping by showing that this test can be useful in testing lung samples taken through the bronchoscope for units that do have access to this routinely. As participants will be following the

routine clinical pathway, there will be no additional risks or side effects of the study. Participation in this study will not alter the clinical management or the care participants receive as their clinical team are already using this test routinely.

Where is the study run from?
Imperial College Healthcare NHS Trust and Imperial Clinical Respiratory Research Unit (UK)

When is the study starting and how long is it expected to run for?
October 2020 to October 2021

Who is funding the study?
National Institute for Health and Research (NIHR) Imperial Biomedical Research Centre (BRC) (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
266798

ClinicalTrials.gov (NCT)
NCT04909385

Protocol serial number
CPMS 46846, IRAS 266798

Study information

Scientific Title
Xpert MTB/RIF Ultra assay for the detection of Mycobacterium tuberculosis (MTB) in bronchoalveolar lavage (BAL) for pulmonary TB and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) samples for mediastinal TB

Acronym
TRiBE

Study objectives
1. Xpert Ultra will have a higher diagnostic sensitivity compared to smear microscopy in clinically defined and treated TB cases using a composite diagnosis (category 1 and 2) in BAL and EBUS-TBNA samples for pulmonary and mediastinal TB.
2. Xpert Ultra will have a higher diagnostic sensitivity compared to smear microscopy in culture-positive TB cases (category 1) in BAL and EBUS-TBNA samples for pulmonary and mediastinal TB.
3. Xpert Ultra will have a higher diagnostic sensitivity compared to smear microscopy in culture-negative clinically defined TB cases (category 2) in BAL and EBUS-TBNA samples for pulmonary and mediastinal TB.
4. Xpert Ultra will have a higher diagnostic sensitivity compared to culture in clinically defined and treated TB cases (category 1 and 2) in BAL and EBUS-TBNA samples for pulmonary and mediastinal TB.
5. Xpert Ultra will provide more rapid TB diagnostics compared to the current gold standard of culture in BAL and EBUS-TBNA samples for pulmonary and mediastinal TB.
6. 'Trace' reading from Xpert Ultra will correlate with a true positive result in patients who have not had previous TB or previously had treatment for active or latent TB in BAL and EBUS-TBNA samples for pulmonary and mediastinal TB.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 07/10/2020, South East Scotland Research Ethics Committee 01 (Waverley Gate, 2-4 Waterloo Place, Edinburgh, EH1 3EG, UK; +44 (0)131 465 5473; Sandra.Wyllie@nhslothian.scot.nhs.uk), REC ref: 20/SS/0089

Study design
Non-randomized; Both; Design type: Diagnosis, Device, Cohort study

Primary study design
Interventional

Study type(s)
Diagnostic

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

Interventions

This is a prospective multi-centre study across the UK including London, Birmingham, Leicester and Manchester which account for the highest proportion of TB cases in the UK. These are centres routinely investigate patients with suspected TB and routinely use Xpert Ultra in their practice.

Any patient who is suspected of having pulmonary or mediastinal TB who is routinely undergoing a bronchoscopy or EBUS-TBNA for clinical purposes will be recruited. These patients will be identified mainly by the TB services but also via Accident and Emergency, wards and clinics. Inclusion criteria include any consenting adult ≥18 years of age suspected of having pulmonary or mediastinal TB who is undergoing a routine clinical bronchoscopy for BAL or EBUS-TBNA.

Any patient identified who need a bronchoscopy or EBUS-TBNA for suspected TB will have this done in the local hospital. Patients will follow the routine follow up arrangements in line with the local trust guidelines but the researchers will review any routine follow up data up to 3 month post-procedure if available. There will be no additional procedures or visits as the researchers will merely use routinely available clinical data and follow up data if available.

The study aims to recruit a minimum of 323 participants undergoing a BAL, and 323 participants undergoing an EBUS-TBNA for a minimum of 6 months or until the recruitment targets are reached. The researchers will review any routine follow up data for a minimum of 3 months post-procedure. There will be no additional study follow up visits.

The study outcome is the diagnostic performance of Xpert Ultra in BAL and EBUS-TBNA samples in patients with suspected TB against conventional modalities available (smear microscopy, culture, cytology) using a subgroup analysis of the different clinical categories attributing to the likely TB diagnosis incorporating follow-up data and the clinician's decision to treat. A clinical expert panel will review the culture-negative cases blindly to categorise each case into a clinical diagnosis category.

Category Criteria:
1. Culture confirmed TB: Microbiological culture of MTB, and clinical and radiological findings suggestive of TB.
2. Highly probable TB: Clinical and radiological features highly suggestive of TB and unlikely to be caused by other diseases, a decision to treat made by a clinician, appropriate response to therapy, and histological evidence if available.
3. Clinically indeterminate diagnosis: Final diagnosis of TB neither highly probable nor reliably excluded.
4. Highly unlikely or TB excluded: Other diagnosis made other than TB (e.g. sarcoidosis, cancer or lymphoma).

Prospective data will be collected from Imperial College Healthcare NHS Trust, London North West University Health Care NHS Trust, Chelsea and Westminster Hospital NHS Foundation Trust, Royal Free London NHS Trust, The Hillingdon Hospitals NHS Trust, Barts Health NHS Trust, University Hospitals of Birmingham NHS Foundation Trust, University Hospitals of Leicester NHS Trust, Manchester University NHS Foundation Trust which together serve a diverse cultural population with a high prevalence of TB in the UK and offer EBUS-TBNA services.

Clinical (patient demographics, medical history, TB symptoms, previous TB, history of exposure to TB, medications, HIV status and immunosuppression), microbiological, cytological data,

radiology and biomarkers of infection will be collected throughout the study and documented on the following case report forms (CRFs). A paper or electronic CRF will be used as a clinical data collection tool which will comply with GCP, FDA CFR-21 Part-11, and HIPAA.

This data will be collected by the local clinical team, a clinical research fellow or research nurses using participant hospital records or from the participant directly. Personal data will be kept in pseudo-anonymised form with a link code which can be used to refer to the participant's information. This link code will only be available to the clinical or clinical research team. There will be an audit trail of the staff entering the data.

Statistical analysis software will also be used such as R, GraphPad Prism, SPSS to calculate sensitivity, specificity, positive predictive value and negative predictive value. There will also be an analysis of the differences in time to results being available in the different modalities using paired analysis.

Measures such as the mean and standard deviation will be used to summarise continuous variables. Tables reporting the numbers and percentages will be used for categorical variables such as TB. The Kappa statistic will be used to compare results from different tests. Chi-square or Fisher's exact test will be used to compare categorical variables such as TB and ethnicity. The t-test will be used to compare the average number of years in two groups. One-way ANOVA with Bonferroni correction will be used to compare the average number of years in different clinical categories. Logistic regression will be used to look at factors associated with TB. Factors include HIV, diabetes, ethnicity, sex, and years in UK, having previous TB and other social risk factors such as smoking status.

Intervention Type
Other

Primary outcome(s)
The diagnostic performance of Xpert Ultra in BAL and EBUS-TBNA samples in patients with suspected TB against conventional modalities available (smear microscopy, culture, cytology) using a subgroup analysis of the different clinical categories attributing to the likely TB diagnosis, measured at a single timepoint

Key secondary outcome(s))
1. Turn-around time for Xpert Ultra against standard smear, culture, cytology results and its effects on treatment decisions, measured using clinical, microbiological, cytological data, radiology and biomarkers of infection collected throughout the study
2. The operating characteristics of this platform in varying clinical phenotypes, evaluated by stratifying patients based on risk factors, clinical presentations, radiological appearances and histological results and comparing this with Xpert Ultra results (including 'trace') at a single timepoint

Completion date
29/02/2024

Eligibility

Key inclusion criteria
Any consenting adult ≥18 years of age suspected of having pulmonary TB or mediastinal TB who is undergoing a routine clinical bronchoscopy or EBUS-TBNA

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
394

Key exclusion criteria
Any patient who has had a BAL or EBUS-TBNA but has not had Xpert Ultra testing as part of routine diagnostics for possible TB

Date of first enrolment
17/08/2020

Date of final enrolment
29/02/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
St Mary's Hospital (lead site)
Imperial College Healthcare NHS Trust
Praed Street
London
United Kingdom
W2 1NY

Study participating centre
Chelsea & Westminster Hospital
Chelsea and Westminster Hospital NHS Foundation Trust

369 Fulham Road
London
United Kingdom
SW10 9NH

Study participating centre
Hillingdon Hospital
The Hillingdon Hospitals NHS Foundation Trust
Pield Heath Road
Uxbridge
United Kingdom
UB8 3NN

Study participating centre
The Royal London Hospital
Barts Health NHS Trust
Whitechapel
London
United Kingdom
E1 1BB

Study participating centre
University Hospitals of Birmingham NHS Foundation Trust
Trust HQ
PO Box 955
Queen Elizabeth Medical Centre
Edgbaston
Birmingham
United Kingdom
B15 2TH

Study participating centre
Leicester Royal Infirmary
University Hospitals of Leicester NHS Trust
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre

Manchester University NHS Foundation Trust
Cobbett House
Oxford Road
Manchester
United Kingdom
M13 9WL

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

Study participating centre
Northwick Park Hospital
London North West University Health Care NHS Trust
Watford Road
Harrow
United Kingdom
HA1 3UJ

Sponsor information

Organisation
Imperial College Healthcare NHS Trust

ROR
https://ror.org/056ffv270

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Research (NIHR) Imperial Biomedical Research Centre (BRC)

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No