

# Comparing a new test for tuberculosis with conventional tests

<b>Submission date</b> 25/01/2021	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 16/02/2021	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 23/01/2025	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> 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?

Prof. Onn Min Kon

Dr Mirae Park, [imperial.respiratory.research@nhs.net](mailto:imperial.respiratory.research@nhs.net)

## Contact information

### Type(s)

Scientific

### Contact name

Dr Mirae Park

### Contact details

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## Additional identifiers

### EudraCT/CTIS number

Nil known

### IRAS number

266798

### ClinicalTrials.gov number

NCT04909385

### Secondary identifying numbers

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

## **Secondary study design**

Non randomised study

## **Study setting(s)**

Hospital

## **Study type(s)**

Diagnostic

## **Participant information sheet**

See additional files

## **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  $\geq 18$  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 measure**

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

## **Secondary outcome measures**

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

## **Overall study start date**

07/10/2020

**Completion date**

29/02/2024

## Eligibility

**Key inclusion criteria**

Any consenting adult  $\geq 18$  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

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

Planned Sample Size: 646; UK Sample Size: 646

**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**

England

United Kingdom

**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

Infirmery 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

**Sponsor details**  
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United Kingdom

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+44 (0)20 7594 9480  
k.boland@imperial.ac.uk

**Sponsor type**

Hospital/treatment centre

**Website**

<http://www3.imperial.ac.uk/>

**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

**Publication and dissemination plan**

Not provided at time of registration

**Intention to publish date**

31/10/2022

**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?
<a href="#">HRA research summary</a>			28/06/2023	No	No