### Study Design

#### Objective
- To compare the performance of commercially available immunotests with routine CD4 testing to the routine use of the tuberculin skin test (TST), the current standard of care for diagnosing latent tuberculosis infection (LTBI) in South Africa. The investigators hypothesize that QGIT clinics will identify LTBI and initiate isoniazid preventive therapy (IPT) in a higher proportion of patients and in a significantly faster timeframe. The cost-effectiveness of linking QGIT with routine CD4 compared to routine TST will also be evaluated.

#### Intervention
- **Intervention Model:** Parallel Assignment
- **Primary Purpose:** Diagnostic
- **Time Perspective:** Longitudinal
- **Population:** South Africa

#### Endpoint Classification:
- **Primary Endpoint:** Performance of commercially available immunotests
- **Secondary Endpoints:** Diagnosis of tuberculosis

#### Masking:
- **Masking:** Open Label

#### Study Population/Condition:
- **Study Population:** Healthy children ages between 6 and 13 years, enrolled in participating schools not currently TB infected.
- **Condition:** Latent tuberculosis infection (LTBI)

#### Treatment/Intervention:
- **Treatment Group:** Cholecalciferol (vitamin D3) weekly
- **Control Group:** Placebo weekly

#### Study Location:
- **South Africa

#### Sponsor:
- **Sponsor:** Harvard School of Public Health

#### Collaborator:
- **Collaborator:** University of Witwatersrand, South Africa

#### Device:
- **Device:** QGIT

#### Alternate Site(s):
- **Site:** Diego who are prescribed 3HP for TB contacts and refugees in San Diego who are prescribed 3HP for TB treatment by their physician will be randomly assigned to be monitored for adherence via either VDOT or in-person DOT

#### Sample size:
- **Sample size:** 330

#### NCT number:
- **NCT number:** NCT021199320

#### Additional Information:
- **Additional Information:**
  - The investigators also plan to conduct additional studies to investigate the preventive role of vitamin D supplementation in school age children in a high transmission setting. The investigators hypothesize that (1) vitamin D supplementation will reduce rate of acquisition of LTBI, (2) vitamin D supplementation will lead to greater reductions in active TB incidence, and (3) children in contact with adults with TB have positive acute reactants such as IFN-$\gamma$ and other cytokine responses; if these responses discriminate between high and low risk of disease progression and whether these could be incorporated into improved diagnostic approaches.

#### Available Source of Information:
- **Available Source of Information:** NCT021199320

#### Sample size:
- **Sample size:** 330

#### NCT number:
- **NCT number:** NCT021199320
Study to Evaluate the Tolerability and Immunogenicity of Nyaditum Resae® Probiotic Administered to Pediatric Population in Contact With Tuberculosis With or Without Latent Tuberculosis Infection

This is a double-blind, masked, randomized clinical trial in pediatric population in contact with tuberculosis with or without tuberculosis infection. This trial aims to study the effect of the probiotic Nyaditum resae® at the level of specific Treg memory cells eight weeks after the first administration, and the global tolerability of the treatment. Nyaditum resae® is a preparation in the form of capsules containing heat-killed environmental mycobacteria Mycobacterium manresensis. The overall objective of the study is the effect of Nyaditum resae® on immunity, which could reduce the risk of developing active tuberculosis.

Treatment/Intervention

Phase 1
Allocation: Randomized, Endpoint Classification: Safety/Efficacy Study, Intervention Model: Parallel Assignment, Masking: Double Blind (Subject, Caregiver, Investigator), Primary Purpose: Prevention

Oral: Daily dose of Nyaditum resae® 10^8 of heat-killed Mycobacterium manresensis
Other: Placebo

Spain

Sponsor: Manresana de Micobacteriologia, IL

Child between 2 and 17 years, who have had contact with tuberculosis

24

NCT0258579

Effect of Flarial Infection on Immune Responses in Latent Tuberculosis

Researchers want to study people with latent tuberculosis (TB) who may or may not be infected with filariasis. This study will look at the way that people with latent TB fight infection with these worms.

Programme management

Interventional
Randomized controlled trial: Parallel Phase: Phase 4

A 12 dose course of weekly rifampicin (300mg) and rifapentine (500mg) tablets.

Australia

Sponsor: Hospital Melbourne Health

Patients with clinical indication for latent tuberculosis infection (LTBI) treatment.

80

ACTRN126130059774

TB mHealth Study - Use of Cell Phones to Improve Compliance in Patients on LTBI Treatment

This study will examine the impact of use of mobile phones and text messaging on adherence to treatment for patients with latent TB infection. Half (50%) of the 350 anticipated study participants will receive weekly test messages inquiring on their health status in relation to their prescribed treatment, while the other half (50%) will not receive weekly test messages at all. Medical adherence will be assessed by monthly blood-work, clinic visits and by interviewing patients at each of these visits.

The investigators hypothesis is that enhanced communication with a health care provider, via a structured cell phone SMS text messaging based program (WallTel), will result in a 15% improvement in the proportion of patients who successfully complete their LTBI treatment regiments.

Adherence and completion of treatment

Interventional
Phase 0
Allocation: Randomized Intervention Model: Single Group Assignment Masking: Open Label Primary Purpose: Health Services Research

Other: Cell phone test messages Participants in the intervention arm will receive weekly test messages from the TB control clinic asking how they are.

Canada

Sponsor: University of British Columbia

Eligibility: Those who are close contacts of active tuberculosis cases or those who have new entrants to the UK from high incidence countries (>40/100000).

350

NCT01549857
### Evaluating the Safety and Effectiveness of Short-Course Rifapentine/Isoniazid for the Prevention of Active Tuberculosis in HIV-Infected Individuals With Latent Tuberculosis Infection

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>United States, Bolivia, Brazil, Haiti, Kenya, Malawi, Peru, South Africa, Thailand, Zimbabwe</strong></td>
<td><strong>Sponsor:</strong> National Institute of Allergy and Infectious Diseases (NIAID)</td>
<td><strong>Primary Purpose:</strong> Treatment</td>
<td><strong>Masking:</strong> Open Label</td>
<td><strong>Drug:</strong> Isoniazid (INH), Rifapentine (RPT)</td>
</tr>
</tbody>
</table>

**HIV-infected people have an increased risk of developing active tuberculosis (TB).** The standard course of treatment for TB is 6-8 months of isoniazid (INH). A shorter course of treatment may be effective and potentially increase treatment adherence. This study will compare the safety and effectiveness of 4-8-week regimens of rifapentine (RPT) plus INH versus a standard 9-month regimen of INH in HIV-infected people who are at risk of developing active TB.
Once children are exposed and infected they are at very high risk to develop active TB - which can be lethal if not detected and treated promptly. This makes it very important to detect TB infections as soon as possible, and treat this while it is still latent or dormant. Current therapy for latent TB infection is 9 months of isoniazid; this is very effective if taken properly but because treatment is so long many children do not finish this. Four months of Rifampin is a recommended alternative. It is hypothesized that among children at high risk for development of active TB, intolerance/adverse events will not be severe (non-inferiority), among those randomized to 4RIF compared to those randomized to 4INH. In addition completion of latent tuberculosis infection (LTBI) therapy will be significantly greater (superiority), and subsequent rates of active TB will not be significantly higher (non-inferiority) in children taking 4RIF.

Phase 3 Allocation: Randomized intervention Model: Parallel Assignment Masking: Open Label Primary Purpose: Treatment

Drug: Isoniazid versus Rifampin

Australia, Benin, Brazil, Canada, Ghana, Guinea, Indonesia

Sponsor: McGill University

Collaborator: Canadian Institutes of Health Research (CIHR)

Information provided by (Responsible Party): Dr. Dick Montan, McGill University.

822

NCT01710209

Predictive Values of Next Generation Interferon Gamma Release Assays for Latent Tuberculosis Infection

Currently available blood tests for latent tuberculosis infection (LTBI) identify people who have been previously infected with M. tuberculosis. Whilst they are sensitive and specific, they cannot be used to assess the effectiveness of treatment for LTBI. New blood tests (“fourth generation Quantiferon tests”) have not yet been evaluated in clinical practice, so their usefulness in identifying people at highest risk of TB disease and monitoring treatment is unknown.

Performance of commercially available immunoassays

Interventional Single Group Assignment Open Label Primary Purpose: Diagnostic Procedure: blood test, not yet marketed, no trade name blood test using the new TB diagnostic test

UK

Sponsor: Public Health England

Collaborator: University College, London

Adult contacts of smearpositive pulmonary TB patients and patients with active TB. Hajj pilgrims: Individuals arranging travel to Saudi Arabia for the Hajj through participating tour operators.

2000

NCT02512939

Early Detection and Management of Tuberculosis in the EU: A-DETECT TB

Establishing a database of latent and active TB in Europe starting with Italy, Sweden, the Netherlands and the UK to inform epidemiological analysis and future interventions to control TB.

Programme management

Observational Cohort LTBI testing and treatment programmes

Multiple: UK, Netherlands, Switzerland, Italy, Romania and Bulgaria

EU Third Health Programme

Chief investigator: Ibrahim Abu bakar

Contact, Migrants

10,000

NCT0118265

CATAPULT

Treatment of latent TB in primary care compared to secondary care

Programme management

Observational A cluster randomized controlled trial

Treatment of LTBI in primary care

UK

Sponsor: National Health Service

Collaborator: McGill University

Chief investigator: Heinke Kunts

Co-applicant: Ibrahim Abu Bakar

Migrants

780

NCT03088807

Prognostic Study of the interferon gamma release assays for tuberculosis (UK PREDICT TB)

Predictive value of the two commercial IGRAAs compared to TST

Performance of commercially available immunoassays

Observational Cohort Two commercial IGRAAs (T-Spot TB and Quantiferon, TST) Risbank for substudies

UK

Sponsor: University College, London

Collaborator: Public Health England

Chief investigator: Ibrahim Abu Bakar

Contacts, Migrants

10,000

NCT0138265

Optimising approaches for LTBI screening and preventive treatment.

ZonMW TB ENDPoint

Lessons learned from the different pilots will be used to improve intervention within the specific target population, Quantitative results from the pilots on uptake of LTBI screening and PT will be used as input to assess the long term impact in terms of costs and cases averted with different LTBI strategies.

Programme management

Observational Multiple pilots studies Prospective cohort LTBI intervention

The Netherlands

Sponsor: UK

Collaborator: Netherlands Organization for Health Research and Development – Govt institution.

KNCV, RIVM, Municipal Health Services, Universities.

Regular immigrants

Asylum seekers

Sosial and Ethnic minority population


Study is based on a previous evaluation report (2010-2012) with more than 60,000 contacts screened (45,000 for LTBI) and 2,012 LTBI cases identified.

Programme management

Observational Retrospective cohort Evaluation

The Netherlands

KNCV

LTBI cases >60,000 contacts screened ??

To evaluate the predictive value of IGRA results from 2008 - 2011 as a predictive marker for progression to tuberculosis.

Programme management

Observational Performance of commercially available immunoassays

The Netherlands

KNCV

LTBI cases 4000 ??

Enhancing the public health impact of latent tuberculosis (TB) infection diagnosis and treatment (ACT4)

The trial test a complex intervention: a two phase programmatic public health package which includes a standardized public health evaluation and analysis, to identify problems and barriers limiting LTBI diagnosis and treatment among close contacts or active TB cases.

Programme management

Interventional Allocation: Randomized Intervention Model: Parallel Assignment Masking: Open Label Primary Purpose: Prevention LTBI program evaluation & diagnosis

Benin, Brazil, Canada, Ghana, Guinea, Indonesia, Vietnam

Sponsor: McGill University

Collaborator: Canadian Institutes of Health Research (CIHR)

LTBI cases among household contacts of patients with active pulmonary TB

36

NCT02810378
<table>
<thead>
<tr>
<th>Title</th>
<th>Intervention Model</th>
<th>Phase</th>
<th>Sponsor</th>
<th>Investigator</th>
<th>Countries</th>
<th>Sponsorship</th>
</tr>
</thead>
<tbody>
<tr>
<td>Promoting adherence to treatment for latent TB infection through text messaging</td>
<td>Interventional</td>
<td>IV</td>
<td>United States</td>
<td>Marc Lipman</td>
<td>United States</td>
<td>University of Arizona Collaboration: Pima County Health Department, American Lung Association</td>
</tr>
<tr>
<td>Screening latent tuberculosis infection and observing preventive therapy in kidney transplantation</td>
<td>Interventional</td>
<td>IV</td>
<td>Taiwan</td>
<td>National Taiwan University Hospital</td>
<td>Taiwan</td>
<td>Renal transplant patients</td>
</tr>
<tr>
<td>TAF-TB 3HP Study</td>
<td>Interventional</td>
<td>IV</td>
<td>Canada</td>
<td>Ottawa Hospital Research Institute Collaboration: Government of Nunavut, Government of Canada</td>
<td>Canada</td>
<td>LTBI: diagnosed people (2-65 years) with either TST or IGRA</td>
</tr>
<tr>
<td>The correlate of risk targeted intervention study (CORTIS)</td>
<td>Interventional</td>
<td>IV</td>
<td>United States</td>
<td>University Cape Town Collaboration: South African TB Vaccine Initiative, Aurum Institute, Centre for the AIDS Programme fo Research in South Africa, University of Stellenbosch, London School of Hygiene and Tropical Medicine, Fred Hutchinson Cancer Research Center</td>
<td>United States</td>
<td>Aged between 18 and 60, with known COR and HIV status.</td>
</tr>
<tr>
<td>Resource IGRA in immunocompromised individuals (Triberk456)</td>
<td>Observational</td>
<td></td>
<td>Germany, Italy, Republic of Moldova, Norway, Poland, Portugal, Romania, Spain, United Kingdom</td>
<td>National Taiwan University</td>
<td>Germany, Italy, Republic of Moldova, Norway, Poland, Portugal, Romania, Spain, United Kingdom</td>
<td>Tuberculosis Network European Taskgroup</td>
</tr>
<tr>
<td>Testing for Tuberculosis in the United Kingdom HIV infected Population</td>
<td>Observational</td>
<td></td>
<td>United Kingdom</td>
<td>Marc Lipman</td>
<td>United Kingdom</td>
<td>Patients attending an ambulatory clinic for HIV care in London, HIV, latent tuberculosis</td>
</tr>
<tr>
<td>Programme management</td>
<td>Observational</td>
<td></td>
<td>United States</td>
<td>University College, London</td>
<td>United Kingdom</td>
<td>Patients attending an ambulatory clinic for HIV care in London, HIV, latent tuberculosis</td>
</tr>
<tr>
<td>Programme management</td>
<td>Interventional</td>
<td></td>
<td>United States</td>
<td>Marc Lipman</td>
<td>United States</td>
<td>Patients attending an ambulatory clinic for HIV care in London, HIV, latent tuberculosis</td>
</tr>
</tbody>
</table>

**Notes:**
- **Interventional** studies involve direct interaction with patients or communities, such as administering treatments or interventions.
- **Observational** studies observe outcomes or predict effects without direct interaction.
- **Masking:**
  - **Open Label** means both patients and researchers know what treatment they are receiving.
  - **Single Blind** means only patients do not know what treatment they are receiving.
  - **Double Blind** means neither patients nor researchers know what treatment they are receiving.
- **Time Perspective:**
  - **Prospective** studies collect data over time.
  - **Retrospective** studies collect previously existing data.
- **Safety/Efficacy Study** indicates the study is designed to evaluate both the safety and efficacy of an intervention.
- **Pharmacokinetics/Dynamics** studies focus on how the body absorbs, distributes, metabolizes, and excretes a particular drug.
- **Endpoint Classification:**
  - **Primary Purpose:** Prevention indicates the primary purpose of the study is to prevent an event or condition.
Comparing consistency of QuantiFERON-TB gold plus and QuantiFERON-TB gold in latency tuberculosis in dialysis population

In patients receiving long-term dialysis, using new generation of QuantiFERON-TB Gold Plus can have less result variability in inter-experiment and serial follow up in comparing with QuantiFERON-TB gold in tube.

Performance of commercially available immunostats

Observational

Observational Model: Cohort, Time Perspective: Prospective

Examination of LTBI by QuantiFERON TB

Taiwan

Chin-Chung Shyu

Patients on dialysis

200

NCT02378494

Efficacy of weekly rifapentine and isoniazid for tuberculosis prevention.

This is an open-label, randomized, Phase III clinical trial to evaluate the effectiveness and tolerability of the XPT/NIH to prevent tuberculosis compared with those who do not receive preventive treatment among silicotic patients.

Observational

Observational Model: Intervention Model: Parallel Group Assignment: Open Label Primary Purpose: Prevention

Weekly INH/RPT given by DOT

China

Sponsor: Ruishan Hospital

Male adult silicosis

566

NCT02438259

A5027/2003 PHOENIX Study

PHOENIX is a Phase II trial in development by the ACTG and IMPAACT networks to assess the efficacy of 6 months of daily delamanid (novel intervention arm) versus 6 months of isoniazid preventive therapy (control comparison arm) in high-risk household contacts of adult pulmonary MDR TB cases.

Treatment

Interventional

Phase 3 Allocation: Randomized Endpoint Classification: Safety/Efficacy Study Intervention Model: Parallel Assignment Masking: Open Label

Primary Purpose: Prevention

The Role of IGRA in Screening and Programme Management for Latent Tuberculosis Infection (LTBI) among military recruits. The current policy of universal application of the Mantoux tuberculin skin test (MST) is expensive for large populations.

Programme management

Observational

Intervention Model: Single Group Assignment Masking: Double Blind (Subject, Outcomes Assessor) Primary Purpose: Screening

OF: BCG vaccination of age 1-4, pPD test (1 dose) BCG skin test (BST) antigen administered using the Mantoux method. OF: TT (Negative TT: 2 points for each)

USA

Uniformed Services University of the Health Sciences Infectious Diseases Clinical Research Program

Veterans

1781

NCT00840713

TB-Health Study - Use of Cell Phones to Improve Compliance in Patients on LTBI Treatment

This study will examine the impact of use of mobile phones and text messaging on adherence to treatment for patients with latent TB infection. Half (50%) of the 350 anticipated study participants will receive weekly text messages requiring on their health status in relation to their prescribed treatment, while the other half (50%) will not receive weekly text messages.

Treatment adherence

Interventional

Study Type: Interventional Study Design: Randomized Intervention Model: Single Group Assignment Masking: Open Label

Primary Purpose: Screening

All phone users will be asked to assess their symptoms before taking tablets. Study participants will be randomized within a study cohort to receive a single dose of MTBVAC or BCG vaccination administered intradermally on Study Day 0.

MTBVAC Study in Adults with and Without Latent Tuberculosis Infection in South Africa (A-039)

MTBVAC at four dose levels: 5 x 10^5 CFU, 5 x 10^6 CFU, 5 x 10^7 CFU, and 5 x 10^8 CFU. The control arm is BCG (5 x 10^5 CFU). Participants will receive a single dose of MTBVAC or BCG vaccination administered intradermally on Study Day 0.

Vaccination

Interventional

Phase 1a/2a, double-blind, randomized, BCG-controlled, dose-escalation safety and immunogenicity study.

South Africa

Khenseti Biotech, S.A. Universidad de Zaragoza South African Tuberculosis Vaccine Initiative Tuberculosis Vaccine Initiative

Persons of both sexes 18-50 years old, have received a previous BCG vaccination. IGRA positive or negative.

130

NCT00753381

The Role of IGRA in Screening and Monitoring for TB During Anti TNF Therapy for Patients With IMD (IGRA)

This study aims to investigate the role of IGRA in screening for latent TB in IMD patients and control subjects. In part 0 of the study, patients of other immune-mediated inflammatory diseases (IMID) will also be included to investigate the role of serial interferon-gamma release assays (IGRA) for the diagnosis of tuberculous (TB) infection in patients with immune-mediated inflammatory diseases (IMID) treated with biologics.

Programme management

Observational

Observational Model: Case Control, Time Perspective: Prospective

IGRA test performance study

Hong Kong

Chinese University of Hong Kong

Patients aged 18 years or older patients with a diagnosis of Crohn's disease (CD) or ulcerative colitis (UC) for at least 3 months defined by histology or endoscopy.

500

NCT01358389

Performance of IGRA for TB Infection Diagnosis in Elderly (IGRage)

IGRA test performance study.

Elderly people over 65 years old, with a history of tuberculosis, have received one or more doses of isoniazid for tuberculosis or have received preventive treatment among silicotic patients.

Performance of commercially available immunostats

Observational

Observational Model: Case Control, Time Perspective: Prospective

IGRA test performance study

Paris, France

Assistance Publique - Hôpitaux de Paris

Persons aged >70 years, birth before 1935, with suspected TB disease.

100

NCT01855583
**Primary Prophylaxis for Prevention of TB in Prison Populations**

To determine if isoniazid is effective in the prevention of tuberculosis in a prison population, exposed to the high endemicity of the disease.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Interventional</th>
<th>Randomized Intervention Model: Parallel Assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Each subject in the treatment group will receive two oral supervised weekly doses of isoniazid 900 milligrams for 12 weeks.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NCT03026829**

**NCT02653404**

**Interventional**

**Observational**

**Primary Outcome Measures**
- Number of patients with concordance of QFT-GIT test and TST among children exposed to TB (Time Frame: up to 4 years).
- Number of patients with positive QFT-GIT in comparison with TST among children with active tuberculosis disease (Time Frame: up to 4 years).
- Number of patients with a negative QFT-GIT test in comparison of TST among non-infected children (Time Frame: up to 4 years).

| Queen, Italy | University of Siena | Children and young adults between 0 to 17 years.

| Contacts | Evaluation of PET/MRI Using a IGRA and Mantoux Response in Primary Prophylaxis for Prevention of Tuberculosis (TB) in Ethiopia. Clinics are randomized at the HIV clinic randomized at the HIV clinic in Dire Dawa and Harari, Ethiopia. The experimental intervention will be delivered to all patients in HIV clinics assigned to SC, usual care procedures for provision of IPT will be delivered. |

**NCT03026829**

**NCT02653404**

**Diagnosis of Tuberculosis in Adults With Suspected Latent Mtb Infection**

The primary objective is to improve the sensitivity of novel immunodiagnostic tests for detection of TB disease in adults with latent Mtb infection.

<table>
<thead>
<tr>
<th>Development of new tests with improved performance and biomarkers</th>
<th>Observational</th>
<th>Observational Model: Case-Only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Development of new tests with improved performance and biomarkers</td>
<td>Observational</td>
<td>Observational Model: Cohort</td>
</tr>
<tr>
<td>The primary objective is to improve the sensitivity of novel immunodiagnostic tests for detection of TB disease in adults with latent Mtb infection.</td>
<td>Observational</td>
<td>Time Perspective: Prospective</td>
</tr>
</tbody>
</table>

**NCT03026829**

**NCT02653404**

**Evaluation of DOTANOC or PET/MRI Using a somatostatin analog tracer as a diagnostic technique in determining the presence of intracranial tuberculosis**

 הכaste: This study aims to compare the safety and immunogenicity of MVA85A aerosol vs intramuscular placebo for primary prophylaxis in children aged 0 to 17 years.

<table>
<thead>
<tr>
<th>Development of new tests with improved performance and biomarkers</th>
<th>Interventional</th>
<th>Intervention Model: Single Group Assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Development of new tests with improved performance and biomarkers</td>
<td>Interventional</td>
<td>Intervention Model: Single Group Assignment</td>
</tr>
<tr>
<td>The primary objective is to improve the sensitivity of novel immunodiagnostic tests for detection of TB disease in adults with latent Mtb infection.</td>
<td>Observational</td>
<td>Time Perspective: Prospective</td>
</tr>
</tbody>
</table>

**NCT03026829**

**NCT02653404**

**The Correlation of Risk Targeted Intervention Study (CORIS)**

To determine if isoniazid is effective in the prevention of tuberculosis in a prison population, exposed to the high endemicity of the disease.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Interventional</th>
<th>Randomized Intervention Model: Parallel Assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Each subject in the treatment group will receive two oral supervised weekly doses of isoniazid 900 milligrams for 12 weeks.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NCT03026829**

**NCT02653404**

**NIVBDA Aerosol vs Intramuscular Vaccination in Adults With Latent Mycobacterium Tuberculosis (MTB) Infection**

A phase 1 trial to compare the safety and immunogenicity of MVA85A aerosol or intramuscular placebo for primary prophylaxis in children aged 0 to 17 years.

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Interventional</th>
<th>Allocation: Randomized Intervention Model: Parallel Assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>The study is a two-arm cluster randomized trial, randomized at the HIV clinic level, which includes 10 HIV clinics in Drg Dawe and Harari, Ethiopia. Clinics are randomized to deliver the combination intervention package (CIP) or standard of care (SOC), with stratification by facility size (&gt;80 or &gt;80 patients enrolled in HIV care per year)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NCT03026829**

**NCT02653404**

**Enhance Initiation and Retention in Isoniazid Preventive Therapy (IPT) Care for HIV Study (ENRICD Study)**

To evaluate a combination intervention package (CIP) designed to improve implementation of isoniazid Preventive Therapy (IPT) among people living with HIV (PLHIV) in Ethiopia.

<table>
<thead>
<tr>
<th>Programmatic Management</th>
<th>Interventional</th>
<th>Allocation: Randomized Intervention Model: Parallel Assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>The experimental intervention will be delivered to all patients in HIV clinics assigned to SC, usual care procedures for provision of IPT will be delivered.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NCT03026829**

**NCT02653404**
<table>
<thead>
<tr>
<th>Test</th>
<th>Description</th>
<th>Participants</th>
<th>Funder</th>
<th>Sponsor</th>
<th>Principal investigator</th>
</tr>
</thead>
<tbody>
<tr>
<td>IGRA</td>
<td>To assess prevalence of latent TB in hard to reach groups</td>
<td>Unknown</td>
<td>NIHR</td>
<td>Public Health England</td>
<td>Andrew Hayward</td>
</tr>
<tr>
<td>QFT-IT Test</td>
<td>To determine the proportion of Korean Health Care worker using the IGRA</td>
<td>Unknown</td>
<td>MRC</td>
<td>University of Oxford</td>
<td>Ibrahim Abubakar</td>
</tr>
<tr>
<td>MVA85A</td>
<td>To assess adherence and completion of two different LTBI treatment regimens</td>
<td>Unknown</td>
<td>UK Department of Health</td>
<td>Public Health England</td>
<td>Ibrahim Abubakar</td>
</tr>
</tbody>
</table>

**Table:**

<table>
<thead>
<tr>
<th>Test</th>
<th>Description</th>
<th>Participants</th>
<th>Funder</th>
<th>Sponsor</th>
<th>Principal investigator</th>
</tr>
</thead>
<tbody>
<tr>
<td>IGRA</td>
<td>To assess adherence and completion of two different LTBI treatment regimens</td>
<td>Unknown</td>
<td>UK Department of Health</td>
<td>Public Health England</td>
<td>Ibrahim Abubakar</td>
</tr>
<tr>
<td>QFT-IT Test</td>
<td>To determine the proportion of Korean Health Care worker using the IGRA</td>
<td>Unknown</td>
<td>MRC</td>
<td>University of Oxford</td>
<td>Ibrahim Abubakar</td>
</tr>
<tr>
<td>MVA85A</td>
<td>To assess adherence and completion of two different LTBI treatment regimens</td>
<td>Unknown</td>
<td>UK Department of Health</td>
<td>Public Health England</td>
<td>Ibrahim Abubakar</td>
</tr>
<tr>
<td>Study</td>
<td>Title</td>
<td>Programme Management</td>
<td>Study Design</td>
<td>Country(s)</td>
<td>Lead Organization</td>
</tr>
<tr>
<td>-------</td>
<td>----------------------------------------------------------------------</td>
<td>----------------------</td>
<td>-------------</td>
<td>------------</td>
<td>------------------</td>
</tr>
<tr>
<td>1</td>
<td>Assessing the impact of latent TB infection in migrants</td>
<td>Programmatic</td>
<td>Observational Cohort</td>
<td>UK</td>
<td>Chief Investigator: Manish Pareek</td>
</tr>
<tr>
<td>2</td>
<td>Latent Tuberculosis Infection among Migrant Workers from third countries in Cyprus</td>
<td>Programmatic</td>
<td>Observational Prospective cohort</td>
<td>Cyprus</td>
<td>Principal Investigator: Marios Makarios</td>
</tr>
<tr>
<td>3</td>
<td>Assessing the impact of latent TB infection in Norway</td>
<td>Programmatic</td>
<td>Observational Register-based study</td>
<td>Norway</td>
<td>Norwegian Health Association (NHA)</td>
</tr>
<tr>
<td>4</td>
<td>Assessing the outcome of LTBI treatment in Norway</td>
<td>Programmatic</td>
<td>Observational Prospective cohort</td>
<td>Norway</td>
<td>Norwegian Institute of Public Health (NIPH)</td>
</tr>
<tr>
<td>5</td>
<td>Barriers to TB screening among migrants run by an NGO (LHL International) aiming to identify</td>
<td>Programmatic</td>
<td>Observational Qualitative study</td>
<td>Norway</td>
<td>Norwegian Heart and Lung Association (NHL, Intern)</td>
</tr>
<tr>
<td>6</td>
<td>Evaluation of LTBI screening and prevention among at-risk migrant populations</td>
<td>Programmatic</td>
<td>Evaluation Prospective Observational</td>
<td>The Netherlands</td>
<td>KNVC</td>
</tr>
<tr>
<td>7</td>
<td>AS NIH clinical trial NCT027777229</td>
<td>Treatment</td>
<td>Interventional</td>
<td>The Netherlands</td>
<td>KNVC</td>
</tr>
<tr>
<td>8</td>
<td>ViiV Healthcare clinical trial[1] (Phase III-b study)</td>
<td>Treatment</td>
<td>Interventional</td>
<td>The Netherlands</td>
<td>KNVC</td>
</tr>
<tr>
<td>9</td>
<td>Treatment with 3HP in HIV and rifampicin-resistant TB patients</td>
<td>Treatment</td>
<td>Interventional</td>
<td>The Netherlands</td>
<td>KNVC</td>
</tr>
</tbody>
</table>

[1] ClinicalTrials.gov identifier: NCT027777229
<table>
<thead>
<tr>
<th>Funded by</th>
<th>USAID Reproductive Health and HIV/AIDS Program (HRSA)</th>
<th>Treatment</th>
<th>Interventional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health National Institute for Health and Family Planning (INHFP)</td>
<td>Treatment</td>
<td>Interventional</td>
<td></td>
</tr>
<tr>
<td>Support studies planned with this trial likely to generate more evidence of RIF/DTG and RIF/TAF interactions by September 2019</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>French National Institute for Health and Medical Research trial in Cameroon (phase III randomized controlled trial)</td>
<td>Treatment</td>
<td>Interventional</td>
<td></td>
</tr>
<tr>
<td>A sub-study as part of this trial is planned to review the pharmacokinetics of RIF and HIV-100 use in HIV co-infected patients.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improving the Detection of Active Tuberculosis in Accident and Emergency Departments (ACE)</td>
<td>Treatment</td>
<td>Interventional</td>
<td></td>
</tr>
<tr>
<td>This proposal is focused upon early diagnosis, referral and treatment of active tuberculosis, which has two key components: 1) ensuring optimal outcome for individuals; 2) contributing to disease control in public health terms by preventing further spread.</td>
<td>Observational</td>
<td>Prospective cohort</td>
<td></td>
</tr>
<tr>
<td>Individuals at high risk of TB 1000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3HP pharmacokinetics when given with dolutegravir or efavirenz</td>
<td>Treatment</td>
<td>Interventional</td>
<td></td>
</tr>
<tr>
<td>Pharmacokinetics</td>
<td>3HP self-administered therapy, single course or on a yearly basis in high TB burden settings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACTG 5279: Phase II Clinical Trial of Ultra-Short-Course Rifapentine/Isoniazid for the Prevention of Tuberculosis in Persons with HIV</td>
<td>Treatment</td>
<td>Interventional</td>
<td></td>
</tr>
<tr>
<td>To compare two treatments to prevent active TB in persons with HIV and latent tuberculosis</td>
<td>Randomised, controlled phase III</td>
<td>Subjects will take Rifapentine/Isoniazid plus B6 for 4 weeks</td>
<td>JHU</td>
</tr>
<tr>
<td>TBTC Study 37:</td>
<td>Treatment</td>
<td>Interventional</td>
<td></td>
</tr>
<tr>
<td>Shortened RPT regimen for PT</td>
<td>Randomised, controlled</td>
<td>q4 for 6 wks vs. RIF q4 m vs. RPT+INH qwk</td>
<td></td>
</tr>
</tbody>
</table>
The trial is conducted in patients diagnosed with latent tuberculosis infection (LTBI) who are recommended for treatment. The primary objective is to evaluate adherence in a three-month (12-dose) regimen of weekly rifapentine and isoniazid (RHTP/INH) given by directly observed therapy (DOT) compared to self-administered therapy (SAT).

**Operational/treatment adherence**

<table>
<thead>
<tr>
<th>Trial Name</th>
<th>Design</th>
<th>Primary Purpose</th>
<th>Endpoint Classification</th>
<th>Safety/Efficacy Study</th>
<th>Allocation</th>
<th>Intervention Model</th>
<th>Phase 3 Allocation: Randomized</th>
<th>Behavioral: Self-Administered Therapy (SAT)</th>
<th>Sponsor: Centers for Disease Control and Prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>iAdhere</td>
<td>Observational</td>
<td>Retrospective cohort</td>
<td>Evaluation</td>
<td>Research of QFTB-G and T-SPOT.TB tests for diagnosis of LTBI in patients before anti TBF therapy</td>
<td>Randomized</td>
<td>Parallel</td>
<td>Open Label</td>
<td>Primary Purpose: Prevention</td>
<td>Retrospective</td>
</tr>
<tr>
<td>KNCV</td>
<td>Observational</td>
<td>Retrospective cohort</td>
<td>Evaluation</td>
<td>Research of QFTB-G and T-SPOT.TB tests for diagnosis of LTBI in patients before anti TBF therapy</td>
<td>Randomized</td>
<td>Parallel</td>
<td>Open Label</td>
<td>Primary Purpose: Prevention</td>
<td>Retrospective</td>
</tr>
</tbody>
</table>

**Risk to develop TB among persons diagnosed with LTBI in the Netherlands (1993-2013).**

Risk to develop TB among persons diagnosed with LTBI in the Netherlands. This study examines TB incidence among persons identified with LTBI and determines risk factors associated with progression to TB among those treated and untreated.

**Evaluation of LTBI management in the Netherlands (1993-2013).**

Description of LTBI recording and reporting system and the results of 21 years of LTBI monitoring and evaluation, focusing on trends in target groups for LTBI screening and preventive treatment (PT) regimens, including PT initiation, PT completion and PT discontinuation related to the prevention of TB among persons identified with LTBI and determines risk factors associated with progression to TB among those treated and untreated.

**Adherence on on-going developments for tests that better predict progression from latent TB**

Disease progression and risk factors for progression from infection to disease are assessed.

**Target Product Profile (TPP): Test for Progression of Tuberculosis Infection**

Guide test developers as to key requirements for assays to better predict progression from infection to active disease.

**Document to outline trial guideline to evaluate tests that better predict progression from latent TB**

Disease progression and risk factors for progression from infection to disease are assessed.

**Development of Human Nasal Challenge Models With Microbial Constituents and Grass Pollen**

The investigators will carry out nasal challenge with bacterial and viral components and allergens. In this way the nasal upper respiratory tract mucosa is challenged with stimuli of the immune system, causing various types of inflammation. Samples will be taken by blotting the nostril surface and by scraping off tiny surface samples.

**Impact of New Immunological Diagnostic Tests of Latent Tuberculosis Before Anti-TNF Therapy**

The primary endpoint of this study is the evaluation of the therapeutic impact of the use of new tests for diagnosis of LTBI in patients before anti-TNF therapy.

**Adherence on on-going developments for tests that better predict progression from latent TB**

Disease progression and risk factors for progression from infection to disease are assessed.
Evaluation of an Enhanced Tuberculosis Infection Control Intervention in Healthcare Facilities in Vietnam and Thailand (EnTIC)

- Thailand: NCT01685086
- Taiwan: NCT02073240
- Vietnam: NCT01398618
- Vietnam: NCT01571739
- Vietnam: NCT02073669

Programme management

Observational Model: Case Control
Time Perspective: Prospective

T-Spot.TB test
United States
Sponsor: North Shore Long Island Jewish Health System

Adult patients with HIV confirmed by standard methods
53 NCT02073669

Determine Risk in Latent Tuberculosis

Understanding the risk factors that contribute to latent TB developing into active TB, and whether it is possible to test for this risk.

Development of new tests with improved performance and biomarkers
Observational

Observational perspective
Not provided

Korea, Republic of
Sponsor: National Institute of Allergy and Infectious Diseases (NIAID)

Healthy participants not exposed to TB, active TB, latent TB
1200 NCT01571739

Improving Latent Tuberculosis (TB) Diagnosis in The Children

Objective is to assess the sensitivity and specificity of IGRA and TST in screening for latent TB in HIV-infected and HIV-uninfected children in Thailand, to improve the diagnosis and management of latent TB.

Performance of commercially available immunostests
Observational

Observational cohort, prospective
Not provided

Thailand
Sponsor: South East Asia Research Collaboration with Hawaii Collaborators: • Columbia University • New York Blood Center • HIV Netherlands Australia Thailand Research Collaboration • Khun Sirikit National Institute of Child Health

Thai children between the ages of 2 months and 16 years with exposure to active TB adults will be referred to the two study sites for eligibility screening.
158 NCT00497609

Comparing the Efficacy of Two Preventive Regimens for Adult Household Contacts With Latent Tuberculosis Infection

Though still an endemic area, the incidence of tuberculosis (TB) in Taiwan is decreasing in recent years. Further reduction in TB incidence, or even elimination should rely on treatment for LTBI. However, which is the cost-effective screening method or what is the cost-effective regimen in Taiwan is still unclear.

Therefore, the investigators designed this prospective study to follow up adult household contacts with LTBI for 2 years of follow-up to determine the incidence of active TB.

Performance of commercially available immunostests
Observational

Observational cohort, prospective
Not provided

Thailand
Sponsor: National Taiwan University Hospital

Adult household contact of patients newly diagnosed, culture-confirmed pulmonary tuberculosis
300 NCT01398618

Better Identification of Latent Tuberculosis Infection Among Israeli Young Adults by Comparison Skin Tests and Interferon Gamma Relaxing Assays (IGRA)

The aim of this study is to evaluate the prevalence of latent TB in second-generation immigrants from countries with high incidence of tuberculosis (above 20 of 100,000) compared to the control native Israelis without a family member who was born in a country with high incidence of tuberculosis. Using study questionnaire IGRA and tuberculin skin test the investigators expect that the second-generation immigrants group will have more positive IGRA test than the control native group.

Programme management

Non-Randomized, Single Blind (Investigator), Parallel Assignment
Observational

Answering the study Questionnaire and blood sampling for Interferon gamma release assay (IGRA)
Israel
Sponsor: Sheba Medical Center Collaborator: Tel Aviv Lung Association

Second-generation immigrants from countries with high incidence of tuberculosis above 20 of 100,000; Native Israelis without a family member who was born in a country with high incidence of tuberculosis.
200 NCT02073669

Surveillance and Follow-up for Latent Tuberculosis Infection and Observation of the Effect of Prophylactic Latent Tuberculosis Treatment in Patients With Severe Chronic Kidney Disease or Receiving Long-term Dialysis

To follow-up latent tuberculosis infection and evaluate the risk of developing active tuberculosis in patients with severe chronic kidney disease or receiving long-term dialysis.

Programme management

Observational Model: Cohort
Time Perspective: Prospective

Not provided

Taiwan
Sponsor: National Taiwan University Hospital

The patients with severe chronic kidney disease or long-term dialysis
500 NCT01685086

Thur Tuberculosis Skin Testing Effective in Screening for Latent Tuberculosis in Patients With HIV?

TB infection highly increases the risk of progression of latent tuberculosis (TB) to active disease that therapy is recommended for all PPD-positive, HIV-infected patients, regardless of age. Sensitivity of the PPD testing is, however, dependent on a normal T cell function. Therefore, an accurate and reliable method for detection of latent tuberculosis in patients with HIV is urgently needed.

Programme management

Observational

Observational Model: Case Control
Time Perspective: Prospective

T-spot.TB test
United States
Sponsor: National Taiwan University Hospital

Adult patients with HIV confirmed by standard methods
53 NCT02073669
Impact of HIV Infection on Latent TB Among Patients With HIV-TB Co-Infection

HIV-induced altered representation and function of regulatory T cell subsets (NKT and Treg cells) impair the protective T-cell response against M. tuberculosis and disrupts LTBI, thus facilitates faster progression and development of severe forms of clinical TB in HIV-TB co-infection.

Other (immunology, pathogenesis, co-infection)  
Observational  
Prospective  
Not provided  
India  
Sponsor: Ministry of Science and Technology, India  
Collaborator: Indian Council of Medical Research  
HIV+ve+LTBI HIV+ve+clinical TB HIV+ve+clinical TB Normal control  
180  
NCT06028209

Screening for Latent Tuberculosis in Healthcare Workers With QuantiFERON-Gold Assay: A Cost-Effectiveness Analysis

The ministry of health in Israel requires all health-care workers to undergo screening for latent tuberculosis infection (LTBI) prior to starting work. This is based on the Mantoux skin test, which is notoriously unreliable. In recent years, more specific and sensitive tests based on interferon-gamma secretion to TB antigens have come to market, and most current evidence shows that many meritoious positive persons do not have LTBI. Quantiferon-GOLD is one of these assays.

In this prospective study, we will draw blood for the QuantiFERON-GOLD assay in parallel to conventional testing, and perform a cost-effectiveness analysis of the cost of the investigation and treatment of LTBI in health-care workers.

Programme management  
Observational  
Defined Population  
Screening Longitudinal  
Blood test for QuantiFERON-GOLD assay  
Israel  
Sponsor: Assuta Hospital Systems  
Collaborator: Maccabi  
Inclusion Criteria: Individuals at high risk for latent tuberculosis infection or at high risk for progression to tuberculosis

42647  
NCT01622140

Prospective Comparison of the Tuberculin Skin Test and Interferon-Gamma Release Assays in Detecting Latent Mycobacterium Tuberculosis infection and Predicting Progression to Tuberculosis infection

This is a prospective cohort study of persons tested for tuberculosis infection (LTBI) who are candidates of TNF blockers for rheumatic diseases who will be enrolled in a clinical trial for a new TNF inhibitor. This study will enroll patients who receive both QFT-G and TST compared with patients who receive TST alone. The purpose of this study is to evaluate the performance of commercially available immunotests available immunotests and biomarkers with improved performance.

Performance of commercially available immunotests  
Observational  
Cohort  
Prospective  
Not provided  
USA  
Sponsors and Collaborators  
Centers for Disease Control and Prevention  
Individuals at high risk for latent tuberculosis infection or at high risk for progression to tuberculosis

Study of Latent Tuberculosis Infection (LTBI) by High Resolution Scanner

The High Resolution Scanners (HR TC) offer the possibility of detecting any lesion approximately 1 mm in diameter, so the investigators plan to use this technique to screen people already infected by M. tuberculosis (but not ill, following the American Thoracic Society's guidelines).

Development of new tests with improved performance and biomarkers  
Observational  
Case-Only  
Prospective  
Not provided  
Spain  
Sponsor: Germans Trias i Pujol Hospital  
Collaborator: SHORES-CRP-TB program  
Only a single population is going to be studied: the LTBI, thus people with proof to be M. tuberculosis infected but demonstrating not having active disease.  
12  
NCT05994856

The Usefulness of Interferon-gamma Release Assays and Tuberculin Skin Test for Detection of Latent Tuberculosis infection

The purpose of this study is to compare the positivity of tuberculin skin test (TST) and Quantiferon-TB Gold-in-Tube, and T-SPOT.TB) and will examine the rates of positive results among the cohort. This study will also determine the risk and rate of progression to active TB disease, overall and by the results of the three tests.

Performance of commercially available immunotests  
Observational  
Cohort  
Retrospective  
Not provided  
Korea, Republic of  
Sponsor: Hanyang University  
Collaborator: Bristol-Myers Squibb  
Approximately 2,000 patients with rheumatic diseases who examined TST or QFT-G  
Approximately 400 patients with rheumatic diseases who received TST or QFT-G before using anti-TNF agents

2000  
NCT01689095

A Phase II Trial of the Pharmacokinetics, Tolerability, and Safety of Once-Weekly Rifapentine and Isoniazid in HIV-1-Infected and HIV-1-Uninfected Pregnant and Postpartum Women With Latent Tuberculosis Infection

The purpose of this study is to evaluate the pharmacokinetics, tolerability, and safety of once-weekly doses of rifapentine (RPT) and isoniazid (INH) in HIV-1-infected and HIV-1-uninfected pregnant and postpartum women with latent tuberculosis (TB).

Treatment/pharmacokinetics  
Interventional  
Non-Randomized, Pharmacokinetics Study, Parallel Assignment, Open Label  
Drug: Rifapentine (RPT)  
900 mg of RPT  
Drug: Isoniazid (INH)  
300 mg of INH  
Dietary Supplement: Pyridoxine (Vitamin B6)  
Not provided  
Sponsor: National Institute of Allergy and Infectious Diseases (NIAID)  
This study will enroll HIV-1-infected and HIV-1-uninfected pregnant women with latent TB. Cohort 1 participants will be enrolled in their second trimester. Cohort 2 participants will be enrolled in their third trimester

82  
NCT02651259