Call for trial partners: Studies to evaluate the performance of Fujifilm SILVAMP TB LAM for the detection of tuberculosis in people living with HIV to inform WHO policy

Background

This Call for trial partners is issued by FIND to solicit applications for trials aimed towards evaluating the performance of Fujifilm SILVAMP TB LAM for the detection of tuberculosis (TB) in people living with HIV (PLHIV).

A novel urine-based assay was co-developed by FIND and Fujifilm; the Fujifilm SILVAMP TB LAM (Fuji LAM). This test detects low concentrations of the LAM-antigen in urine by means of a lateral flow assay. The test result is available in less than one hour. The assay was designed to achieve high analytical sensitivity through the combination of (i) a pair of high affinity monoclonal antibodies with binding to *Mycobacterium tuberculosis*-specific LAM-epitopes and (ii) a silver amplification step that increases the visibility of the test and control lines (Figure 1). This enables the detection of picomolar concentrations of urinary LAM-antigen along with high analytical specificity.

The 5-step test procedure is as follows: (1) Urine is added to the reagent tube up to the indicator line (approximately 200 µl), mixed by tapping the tube and; (2) incubated for 40 minutes at ambient temperature; (3) After mixing again, two drops from the tube are added to the test strip (position "1"). Following this, button "2" is immediately pressed to release a reducing agent for silver amplification; (4) After the "go-next" color indicator mark turns orange (within approximately 3-10 minutes), button "3" is pressed to release a silver ion solution to activate the silver amplification reaction; (5) within less than 10min the result can be read.

Initial results from an evaluation of frozen bio-banked urine samples of almost 1000 PLHIV newly admitted to a hospital found the assay to have a high sensitivity and specificity (non-peer-reviewed manuscript preview). These results suggest that the assay has the potential to transform the rapid diagnosis of TB in hospitalized PLHIV and potentially for PLHIV at large.

Prospective evaluations are now necessary to assess the performance and ease of use of the assay in intended settings of use (i.e. centres of HIV and TB care, inpatient as well as outpatient settings). This will support the evidence generation to inform WHO and national guidance and improve integration of TB/HIV care.

FIND is encouraging researchers to submit their outlines for a prospective trial to evaluate the Fuji LAM test. Trial outlines should meet the following criteria.

Objectives and site eligibility for trials

The objectives of the trials:

- To assess the performance of the Fuji LAM in PLHIV in different settings (e.g. HIV clinics, HIV inpatient care, TB microscopy centres) against a comprehensive microbiological reference standard (incl. culture) and a clinical/composite reference standard
- To assess ease of use and suitability for integration into existing workflows
- Ideally: to perform all rapid diagnostic testing together with Fuji LAM within 24h of admission (i.e. Alere Determine LAM, Xpert Ultra or Xpert MTB/RIF, smear microscopy) in order to assess diagnostic yield in intensive case finding scenarios.

- If feasible: to assess treatment outcomes of patients to evaluate potential impact and resolve misclassifications

Requirements for sites:

- Located in low- or middle-income countries with a high burden of TB and HIV with the site being representative of the regional epidemic;
- On site laboratory or nearby referral laboratory where excellent culture capabilities are available (as relevant for accuracy studies)
- Compliance with good laboratory and clinical practice

Responsibilities of FIND

- Free provision of Fuji LAM test kits and training
- Funding support for some studies will be available (based on funding needs and priority of the study on the basis of pre-defined criteria)
- Protocol guidance to ensure data can be summarized for evidence evaluation and development of policy guidance

Timelines

- Expression of interest and a 2-page summary for the envisioned study is to be submitted by 31st of January 2019. A template for the 2-pager is provided separately (Word doc).
- An initial selection will be performed and in a second round (announced end of March 2019). We will then work with selected applicants on a study protocol that ensures critical components are aligned across partners - to be finalized by end May 2019.
- Decision-making on the final site selection will be done by July 2019 at the latest.

Conditions:

- Priority is given to studies lead by experienced principal investigators who partner with national TB or HIV programs/Ministries of Health
- Priority is given to studies from principal investigators/sites that have demonstrated expertise through previous participation in high quality studies for TB/HIV diagnostics and have access to a sufficient number of patients to accomplish the study objectives within a short period of time.
- Priority will be given to sites with substantial co-funding
- Adult and paediatric trials are within scope. Studies that evaluate the Fuji LAM for treatment monitoring are out of scope.
- Given that the trial should inform evidence-based policy generation, FIND reserves the right to assess the partners and monitor protocol implementation and compliance. FIND will need to have access to all data for analysis by an independent statistician and evidence compilation for WHO – this does not affect individual study publication.
- Selection of studies will be performed by a committee of global stakeholders.

Send submissions before 31st of January 2019 to: Rita Szekely - Rita.Szekely@finddx.org

For questions, contact:

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Figure 1: Fujifilm SILVAMP TB LAM test device, procedure and principle.