Is Xpert MTB/RIF a breakthrough for people living with HIV?
Conflict of interest

- FIND is a non-profit foundation devoted to developing and rolling out diagnostic tools for poverty-related diseases.

- In this role, FIND has development partnerships with industry.

- Xpert MTB/RIF has been developed through a partnership between Cepheid, FIND and UMDNJ with support from BMGF and NIH.

- FIND has no financial beneficial participation in any form.
A multi-disease platform

GeneXpert

Xpert
MTB/RIF

5  20  80  Samples per shift  500-1000
Assay principles and procedure

1. Sputum liquefaction and inactivation with 2:1 sample reagent
2. Transfer of 2 ml material into test cartridge
3. Cartridge inserted into MTB-RIF test platform (end of hands-on work)
4. Sample automatically filtered and washed
5. Ultrasonic lysis of filter-captured organisms to release DNA
6. DNA molecules mixed with dry PCR reagents
7. Seminested real-time amplification and detection in integrated reaction tube
8. Printable test result

Time to result, 1 hour 45 minutes

Assay Name: MTB-RIF
Test Result: MTB DETECTED LOW; RIF Resistance NOT DETECTED
Multi-center implementation studies

- 9 settings of intended use in 6 countries
  - (Sub)-District (3), microscopy centers (3), MDR screening / ER (3)
  - Diverse laboratory conditions (temp up to 40C, space, staff background)
  - 6648 TB or MDR-TB suspected patients screened from diverse populations
  - 1255 known HIV+ (313 C+), 1884 known HIV- (441 C+), 3509 HIV unknown (774 C+)

<table>
<thead>
<tr>
<th>Location</th>
<th>Country</th>
<th>HIV</th>
<th>TB (C+)</th>
<th>MDR TB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lima</td>
<td>Peru</td>
<td>3%</td>
<td>17%</td>
<td>8%</td>
</tr>
<tr>
<td>Kampala</td>
<td>Uganda</td>
<td>80%</td>
<td>42%</td>
<td>2%</td>
</tr>
<tr>
<td>Cape Town</td>
<td>South Africa</td>
<td>77% (K)</td>
<td>26%</td>
<td>4%</td>
</tr>
<tr>
<td>Vellore</td>
<td>India</td>
<td>&lt;1%</td>
<td>10%</td>
<td>7%</td>
</tr>
<tr>
<td>Baku</td>
<td>Azerbaijan</td>
<td>6%</td>
<td>47%</td>
<td>22%</td>
</tr>
<tr>
<td>Manila</td>
<td>Philippines</td>
<td>&lt;1%</td>
<td>20%</td>
<td>54%</td>
</tr>
</tbody>
</table>
Study design

Peru, Uganda, Azerbaijan, India, Philippines

Validation Phase
- 1 Xpert added to routine examinations;
- Culture / DST added as reference standard;
- Patient management on smear/culture;

Implementation Phase
- TB treatment based on Xpert

Continuation Phase
- MDR-TB treatment based on Xpert
- Culture dropped

South Africa

Validation Arm
- Smear microscopy as per routine
- Culture / DST added as reference standard;
- Patient management on smear/culture;

Implementation Arm
- Xpert replacing 1 smear examination

Continuation Phase
- Culture dropped
## Considerations for implementation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Performance / outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preventive maintenance</td>
<td>Annual calibration (logistics and costs).</td>
</tr>
<tr>
<td>Storage, operating temperature</td>
<td>2-28 °C storage; 15-30 °C operation. High lab temperature = no effect on performance. (Error message at &gt;40 °C)</td>
</tr>
<tr>
<td>Electrical supply and back-up power</td>
<td>Uninterruptable power supply with UPS (400 VA) for 20 min. Serial car batteries tested.</td>
</tr>
<tr>
<td>Biosafety requirements</td>
<td>Same as smear microscopy*.</td>
</tr>
<tr>
<td>Waste management</td>
<td>As for sputum containers; additional waste volume compared to smear microscopy.</td>
</tr>
</tbody>
</table>

A breakthrough for people living with HIV?

- Significantly increases pTB or MDR-TB case detection rates compared to current routine practice? Yes
- Robust enough to be implemented near point-of-treatment? Important considerations for implementation
- Ex-pTB? Pediatric TB? Promising preliminary data
- Shortens diagnostic delays, but also time to treatment? Yes
- Decreases drop out rates? Promising preliminary data, but treatment programs need to be strengthened
- Decreases morbidity and mortality? Promising preliminary data Increases cure rates? No data
- Decreases transmission rates (TB or MDR)? No data
- Is a cost-effective intervention? ICER<GDP per capita; resource mobilization critical
- Multi-disease platform? Yes, HIV VL and STD of particular relevance
- Being rolled-out and scaled up? (without weakening other TB control efforts). WHO surveillance program.
Thank you to all partners and patients who participated in this demonstration study.
Glance inside the cartridge

Syringe Barrel

RT-PCR Tube

Sonicator Dome

Rotary Valve