ASLM

TB LAM technology development pipeline

Morten Ruhwald, MD, PhD
Director of TB, FIND
CURRENT AND 2ND GENERATION LAM TEST
ALERE LAM, AND Fujifilm SILVAMP TB LAM

PLHIV (5 cohorts, n=1595)

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity [95% CI]</th>
<th>Specificity [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>AlereLAM</td>
<td>34.9 [19.5 – 50.9]</td>
<td>95.3 [92.2 – 97.7]</td>
</tr>
<tr>
<td>FujiLam</td>
<td>70.7 [59.0 – 80.8]</td>
<td>90.9 [87.2 – 93.7]</td>
</tr>
</tbody>
</table>

WHO policy review cancelled
• Manufacturing issue has been resolved, test re-designed
• Relaunch expected in 2023
CHALLENGES FOR DEVELOPING LF-LAM TEST

- LAM Structure
- Sample Matrix
- LAM concentration
- Assay Design

LAM structural Integrity and stability varies greatly across samples matrix

Lack of pre-analytical improved reagents
- Antibodies (full coverage)
- Antigen (Cultured LAM varies from Urinary LAM)

LAM Fragmentation in urine
<table>
<thead>
<tr>
<th>Sample Matrixes</th>
<th>Urine</th>
<th>Blood</th>
<th>Stool</th>
<th>CSF</th>
<th>Tongue Swab</th>
<th>Exhale Breath Condensate</th>
<th>Sputum</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAM Concentration</td>
<td>1 – 2000 pg/ml</td>
<td>1 – 2000 pg/ml</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
<td>100 pg-100 µg/ml</td>
<td>100 pg-100 µg/ml</td>
</tr>
<tr>
<td>LAM Structure</td>
<td>Delipidated</td>
<td>Fragmentation</td>
<td>Stability unknown</td>
<td>Unknown</td>
<td>Less explored</td>
<td>Less explored</td>
<td>Less explored</td>
</tr>
<tr>
<td>Advantages</td>
<td>Easy to collect</td>
<td>Potential in EPTB and pediatric TB</td>
<td>Homogenous Potential in EPTB and pediatric TB</td>
<td>Treatment monitoring</td>
<td>Less explored</td>
<td>Potential in EPTB mainly TB Meningitis</td>
<td>Easy to collect sample</td>
</tr>
<tr>
<td>Disadvantages</td>
<td>Matrix Effect</td>
<td>Structure stability and integrity varies greatly</td>
<td>Form Complex with HDL</td>
<td>Less explored</td>
<td>Concentration unknown</td>
<td>Only applicable for Pulmonary TB</td>
<td>Only applicable for Pulmonary TB</td>
</tr>
</tbody>
</table>
3rd Gen LAM Assays

1. Direct Visualization
   - GOLD particle based Lateral Flow test
   - Simple
   - Robust

2. Need sample preparation
   - Extraction and concentration of LAM increasing test sensitivity
   - Multiples steps
   - High cost

3. Need RDT Reader
   - Ultra-sensitive Fluorescence based tests
   - Simple and Robust
   - Less field friendly
THE LAM ASSAY PIPELINE

Alere LAM
- Narrow use case but saves lives

Fujifilm
- Clinical evidence showing better accuracy than Alere TB determine
- Issue with Lot variability
- High cost

SD Biosensors
- Fluorescence based test
- Under development

Boditech
- Fluorescence based test
- Under development

Abbott
- LAM concentration device
- Under development
- Visual readout

Salus
- Integrated sample preparation device
- Under development
- Visual readout

Abbott
Thanks to manufacturers sharing information on prototypes and strategies. We also thank the many partners and other donors who make the work of FIND possible.

Contact: morten.ruhwald@finddx.org