LANDSCAPE OF UPCOMING LAM ASSAYS

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FIND
FUJILAM TEST PRINCIPLE

TB Test Procedure

1. Add urine to the tube
2. Incubate for 40 minutes
3. Add two drops at position "A" and press "2"
4. On orange press "3"
5. Interpret result

60 minutes from sample collection to result

TB Test Principle

Gold conjugated primary antibody captures MTX-LAM in patient urine

Formation of the "sandwich" immune-complex through binding to the immobilized secondary antibody

Silver formation around the gold particles amplifies band intensity
COMPARATIVE PERFORMANCE OF FUJILAM ANDALERELAM IN PLHIV
META ANALYSIS OF 1595 PATIENT SAMPLES FROM 5 COHORTS SSA & VIETNAM

<table>
<thead>
<tr>
<th>All HIV+</th>
<th>N</th>
<th>Sn</th>
<th>[95% CI]</th>
<th>Sp</th>
<th>[95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>FujiLAM</td>
<td>1595</td>
<td>70.7</td>
<td>[59.0 - 80.8]</td>
<td>90.9</td>
<td>[87.2 - 93.7]</td>
</tr>
<tr>
<td>AlereLAM</td>
<td>1595</td>
<td>34.9</td>
<td>[19.5 - 50.9]</td>
<td>95.3</td>
<td>[92.2 - 97.7]</td>
</tr>
<tr>
<td>Diff Sn and Diff Sp</td>
<td>35.8</td>
<td>-4.4</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Stratified by CD4 cell count

<table>
<thead>
<tr>
<th>CD4 group</th>
<th>N</th>
<th>Sn</th>
<th>[95% CI]</th>
<th>Sp</th>
<th>[95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>FujiLAM</td>
<td>CD4 gr0-100</td>
<td>677</td>
<td>87.1</td>
<td>[79.3 - 93.6]</td>
<td>80.5</td>
</tr>
<tr>
<td></td>
<td>CD4 gr0-200</td>
<td>319</td>
<td>62.7</td>
<td>[52.4 - 71.9]</td>
<td>95.0</td>
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<tr>
<td></td>
<td>CD4 gr &gt;200</td>
<td>581</td>
<td>43.9</td>
<td>[34.3 - 53.9]</td>
<td>97.0</td>
</tr>
<tr>
<td>AlereLAM</td>
<td>CD4 gr0-100</td>
<td>677</td>
<td>56.0</td>
<td>[43.9 - 64.9]</td>
<td>93.6</td>
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<td>CD4 gr0-200</td>
<td>319</td>
<td>25.3</td>
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<td>96.7</td>
</tr>
<tr>
<td></td>
<td>CD4 gr &gt;200</td>
<td>581</td>
<td>10.9</td>
<td>[5.2 - 18.4]</td>
<td>97.6</td>
</tr>
</tbody>
</table>

>15 FujiLAM studies ongoing/planned
FIND expects results from a large evaluation in Q1 2022
WHO policy review is likely in 2022

Broger et al, PlosMed 2020
Broger et al, JCI 2020
Muyoyeta et al ERJ 2021
CHALLENGE 1 – LAM IS PROBABLY FOUND IN ALL TB PATIENTS, BUT LEVELS ARE LOW

- FujiLAM Sens ~ 70%
  - 50 pg/mL
- AlereLAM Sens ~ 50%
  - 500 pg/mL

3rd gen LAM Sens > 65% in all

Sigal et al, 2018
CHALLENGE 2, URINE LAM IS PROBABLY MANY THINGS

LAM from mycobacterial culture

LAM in urine
CHALLENGE 3 - LAM IS SMALL, AND GLYCANS ARE EVEN SMALLER

Ara4/6-MTX glycans

Adapted from Sigal et al., 2018 and Broger et al. 2020
A SENSE OF PROPORTIONS

IgG (160 kDa)

LAM (17 kDa)
PATHWAYS TO 3\textsuperscript{rd} GENERATION LAM TESTS

3\textsuperscript{rd} Generation LAM assay
Ultra sensitive (<10 pg/mL) to detect LAM in all TB patients

- Improved reagents (antibodies, antigens)
- Pre-analytical Sample Preparation
- Innovative Assay Design
TAKE HOME MESSAGES

- Despite modest sensitivity, Alere LAM assay has a unique role in the diagnostic landscape providing rapid and accessible diagnosis to the sickest patients with the worst prognosis.

- FujiLAM is a 2nd generation LAM assay in development with improved performance.

- 3rd generation LAM tests with higher sensitivity are pursued by multiple manufacturers, these tests require concentration or readers to deliver urine-based TB detection for all irrespective of HIV status.
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