Update on New HIV Platform Ancillary Study

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Lab Breakout Session
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Update HIV Testing Algorithms

• 31 acute infections in VOICE were missed by current rapid tests (22 @ enrollment; 9 @ PUEV)

• High rate of resistance (8/28; 29%) in subjects acutely infected at enrollment assigned to product arms (iPrEx, Partners, TDF2, VOICE)

• Updated algorithm using Ag/Ab rapids and Multispot confirmation could:
  – Allow detection and confirmation same day
  – Eliminate ambiguity from WB
  – Allow detection 1-2 weeks earlier than current tests
# New Diagnostic Tests

<table>
<thead>
<tr>
<th>Kit Name</th>
<th>Advantages</th>
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</table>
| **Determine® HIV-1/2 Ag/Ab Combo Rapid Test** | • Detects p24 antigen  
• Mixed results on ability to detect infection earlier |
| **Bio-Rad Multispot HIV-1/2 Rapid Test**      | • Can be performed as a point-of-care confirmatory test                      |
| **Bio-Rad EIA HIV-1/2+O Ag/Ab Combo**         | • Improved diagnostic window up to 20 days but not point-of-care  
(Jentson, J Clin Virol 2011) |
| **INSTI™ HIV-1 Rapid Test**                   | • 3rd generation antibody only test  
• Could improve visit flow with “instant” results; test does not require incubation |
Determine Combo Rapid HIV 1/2 Ag/Ab Test

- CLIA moderate complexity
- Distinguishes Ag from Ab
- Whole blood, serum plasma
- FDA-approved August 2013
Bio-Rad EIA HIV-1/2+O Ag/Ab Combo

- Microwell plate assay
- Automated version available (EVOLIS™)
- FDA-Approved
Evaluation Plan

Multispot Validation

Test up to 245 samples from VOICE that have WB results

Determine Ag/Ab and BioRad Ag/AB EIA Evaluation

Test pre-seroconversion RNA positive samples by Determine Ag/AB, Multispot, and Bio-Rad 4th Gen EIA

• Ancillary Study approved by EC
• Calculate sensitivity/specificity and compare with results from currently used tests
Evaluation Plan

INSTI Validation

Standard test of 100 HIV positive and 100 HIV negative samples (stored plasma)

- Calculate sensitivity/specificity and compare with results from currently used tests
Preliminary Results

Using pooled RNA testing would have detected infection earlier in 40% of seroconverters (up to 82 days)

<table>
<thead>
<tr>
<th>Archive Category (prior to seroconversion)</th>
<th>N</th>
<th># with Detectable RNA (%)</th>
<th>HIV RNA copies/ml Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Month 1 (0-31 d)</td>
<td>9</td>
<td>6 (67%)</td>
<td>1,815,235</td>
</tr>
<tr>
<td>Month 2 (33-62 days)</td>
<td>83</td>
<td>42 (51%)</td>
<td>55,120</td>
</tr>
<tr>
<td>Month 3 (63-93 days)</td>
<td>94</td>
<td>12/59 tested (20%)</td>
<td>96,410</td>
</tr>
<tr>
<td>Month 4 (94-124 days)</td>
<td>39</td>
<td>Not yet tested</td>
<td>-</td>
</tr>
<tr>
<td>Month ≥ 5 (125-385 days)</td>
<td>18</td>
<td>Not yet tested</td>
<td>-</td>
</tr>
<tr>
<td>TOTAL</td>
<td>243</td>
<td>60/151 tested (40%)</td>
<td></td>
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Plan for Sites

• Change follow-up algorithm for MTN-025 (HOPE) if new tests are better than current tests

• Site validations will be required
  – Use known HIV+ and HIV- samples
  – Submit ancillary study to use low-priority samples from HPTN 035 and MTN015
  – Have an investigator from each site participate in the ancillary study
Acknowledgements

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