Performance Evaluation of Determine™ HIV-1/2 Ag/Ab Combo in plasma and whole blood from early HIV-1 infections

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Atlanta, March 22, 2016
FDA-approved Ag/Ab HIV-1/2 screening assays

<table>
<thead>
<tr>
<th>Assay</th>
<th>Manufacturer</th>
<th>specimen type</th>
<th>p24 detection</th>
<th>System</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADVIA Centaur HIV Ag/Ab Combo</td>
<td>SIEMENS</td>
<td>serum</td>
<td>with Ab</td>
<td>ADVIA Centaur or Centaur XP</td>
</tr>
<tr>
<td>ARCHITECT HIV Ag/Ab Combo</td>
<td>Abbott</td>
<td>serum/plasma</td>
<td>with Ab</td>
<td>ARCHITECT</td>
</tr>
<tr>
<td>GS HIV Combo Ag/Ab EIA</td>
<td>Bio-Rad</td>
<td>serum/plasma</td>
<td>with Ab</td>
<td>Evolis/automated microplate or manual</td>
</tr>
<tr>
<td>Bio-Plex 2200 HIV Ag-Ab</td>
<td>Bio-Rad</td>
<td>serum/plasma</td>
<td>differentiation</td>
<td>BioPlex 2200</td>
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</tbody>
</table>

- Instrumented or plate-based formats
- from ~30 min to 3 hours
- Not approved for blood or plasma donor screening
Alere Determine HIV-1/2 Ag/Ab Combo (DC)

- Manufacturer: Alere Scarborough, Inc.
- In vitro, visually read, rapid qualitative immunoassay
- Detection of HIV-1 p24 antigen and HIV-1/HIV-2 antibodies
- Point-of-care test to aid in the diagnosis of infection with HIV-1 and HIV-2, including an acute HIV-1 infection
- It may distinguish acute HIV-1 infection from established HIV-1 infection when the specimen is positive for HIV-1 p24 antigen and negative for anti-HIV-1 and anti-HIV-2 antibodies*

*http://www.fda.gov/biologicsbloodvaccines/bloodbloodproducts/approvedproducts/premarketapprovalsmpmas/ucm364651.htm
Alere Determine™ HIV-1/2 Ag/Ab Combo (DC)

- Human serum, plasma, and capillary (fingerstick) or venipuncture (venous) whole blood
- CLIA-waived for fingerstick whole blood
- 20 min using 50 µl of plasma/serum/whole blood
Data on performance of DC as a screening test is limited

- DC detected significantly fewer HIV-1 infections (52.6%) in early stages of seroconversion (38 vs. 20, $p < 0.0001$), but showed no difference with established infections.

- Results from performance of DC on whole blood from individuals during early infections are inconsistent.
Objectives

- To further evaluate the performance of DC as a screening assay in a subset of plasma specimens in the context of the new diagnostic algorithm.

- To compare the performance of DC in simulated whole blood to plasma samples from HIV-1 seroconverters.
STOP sample set

- **329 plasma specimens collected in San Francisco**
  - Screening Targeted Populations to Interrupt On-going Chains of HIV Transmission with Enhanced Partner Notification (STOP)
  - Multi-site, prospective study evaluating methods to detect acute HIV-1 infections
  - Individuals were tested with FS whole blood with StatPak
  - Plasma specimens were tested with:
    - Abbott ARCHITECT, Bio-Rad Multispot and Abbott m2000 HIV-1 RNA viral load in San Francisco
    - DC at CDC and results compared to previous testing (McNemar’s test)
  - Architect-false reactive plasma specimens were tested with Bio-Rad GS HIV Combo Ag/Ab EIA
HIV-1 seroconverters from the US

- 107 selected sequential plasma from 20 commercial seroconverters were used to simulate whole blood samples (40% hematocrit)
  - Whole blood samples were tested with DC and compared to results from plasma samples
  - DC-reactivity was calculated relative to days after the first Aptima-positive for both sample types
Results
DC performance in STOP specimens

- DC detected 54.1% (46/85) of early HIV-1 infections
  - Difference was significantly different $p<0.0001$
- All established HIV-1 infections were detected by DC
- No reactivity was observed among ARC-false reactive
  - All plasma were non-reactive with GS HIV Combo Ag/Ab EIA

### Results from previous testing

<table>
<thead>
<tr>
<th>Results from previous testing</th>
<th>HIV-1 RNA cop/ml</th>
<th>Determine Combo results</th>
<th>DC positivity</th>
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<tbody>
<tr>
<td></td>
<td>total</td>
<td>median</td>
<td>Ag-/Ab-  Ag+/Ab-  Ag+/Ab+  Ag-/Ab+</td>
</tr>
<tr>
<td>ARC-negative/HIV-1 RNA-positive</td>
<td>9</td>
<td>3.49E+03</td>
<td>0 0 0 0</td>
</tr>
<tr>
<td>ARC-positive/MS-negative/HIV-1 RNA-positive</td>
<td>74</td>
<td>1.65E+06</td>
<td>36 25 8 5</td>
</tr>
<tr>
<td>ARC-positive/MS-indeterminate/HIV-1 RNA-positive</td>
<td>11*</td>
<td>2.33E+06</td>
<td>3 1 3 4</td>
</tr>
<tr>
<td>ARC-positive/MS-positive or-undifferentiated</td>
<td>203**</td>
<td>1.47E+05</td>
<td>0 0 6 197</td>
</tr>
<tr>
<td>ARC-positive/HIV-1 RNA-negative</td>
<td>32</td>
<td>target not detected</td>
<td>0 0 0 0</td>
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</table>

* 10 and **30 VL results; ARC: Abbott ARCHITECT HIV Ag/Ab; MS: Bio-Rad Multispot HIV-1/HIV-2
Ag detection among 288 ARC-positive HIV-1 plasma specimens

Among 85 early HIV-1 infections, Ag detection was:
- 33 of 75 (44.0%) of ARC-positive/Multispot-negative
  - Median VL $4.7 \times 10^6$ cop/ml
- 4 of 11 (23.4%) of ARC-positive/Multispot-indeterminate
  - VL $>10 \times 10^7$ cop/ml in 3 samples

*15 of 17 Ag+Ab+ had VL results; $10^7 =$ $>10^7$ cop/ml; 40 = $<40$ cop/ml; 0 = Target not detected
Marked reduction of Ag detection in early HIV-1 infections with whole blood compared to plasma

- Overall DC reactivity in early HIV-1 infections was 91.1% with plasma and 56.4% with whole blood (p<0.0001)

*One whole blood specimen was repeatedly invalid*
Nine of 20 SC showed delayed reactivity in whole blood compared to plasma.

- As with plasma, DC with whole blood did not react in 8 samples collected before HIV-1 RNA was detected or in 14 RNA-positive only samples.
DC performance with whole blood

- Initial invalid results were obtained in 17.8% of whole blood specimens
  - Two specimens that remained invalid after repeat testing were part of a seroconversion panel that never became positive up to 28 days after the first available Aptima positive (no further time points were tested)

- Eight SC showed a median delay between plasma and whole blood of 6 days
  - One SC also exhibited a second negative phase with whole blood for 7 days after being Ag+

- Among 19 SC DC-plasma, the median time of DC reactivity since first Aptima positive
  - Plasma: 6 days
  - Whole blood: 7 days
Conclusions

- DC used with plasma detected fewer specimens with early HIV-1 infection compared to an instrumented lab-based Ag/Ab assay.
- DC with whole blood showed more invalid results than with plasma.
- Results indicate that better sensitivity with plasma may be partially due to Ag detection.
Considerations

- In this study, simulated whole blood was prepared from commercial seroconversion panels. Further studies will address sensitivity and specificity issues with FS whole blood.

- In settings where lab-based testing is not feasible, DC might represent an advantage in detecting HIV-1 infections earlier.

- More results are needed to evaluate the performance in the diagnostic algorithm to detect acute HIV-1 infections.
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<td><strong>CDC HIV lab</strong></td>
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<td><strong>Wei Luo</strong></td>
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<td><strong>Sarah Adams</strong></td>
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Thank you!