ARCHITECT® HIV Ag/Ab Combo: Moving HIV Diagnostics Forward in the U.S.

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Agenda

- ARCHITECT HIV Ag/Ab Combo Assay
  - What is the Combo assay
  - Performance characteristics
- Importance of detecting acute HIV infection
- Early data from US laboratories
ARCHITECT® HIV Ag/Ab Combo

- Chemiluminescent microparticle immunoassay for *in vitro* diagnostic use.
- Simultaneous qualitative detection of HIV p24 antigen and antibodies to HIV-1 group M and group O and/or HIV-2 in human serum and plasma (EDTA and heparin)
- Intended to be used as an aid in the diagnosis of HIV-1/HIV-2 infection, including acute or primary infection
- An ARCHITECT HIV Ag/Ab Combo reactive result does not distinguish between the detection of HIV-1 p24 antigen, HIV-1 antibody, or HIV-2 antibody
- May be used to aid in the diagnosis of HIV-1/HIV-2 infection in pediatric subjects (i.e. children as young as 2 years of age) and in pregnant woman
- Not intended for use in screening blood or plasma donors. However can be used as a blood donor screening assay in urgent situations where traditional licensed blood donor screening assays are unavailable or their use is impractical
ARCHITECT Instrument

- Fully-automated, random-access (no Control brackets)
- Stat capability
- HIV Combo assay:
  - 29 minute time to first result
  - >150 tests per hour on i2000SR
  - >50 tests per hour on i1000SR
ARCHITECT HIV Ag/Ab Combo

- First 4th generation HIV Ag/Ab Combination assay approved in United States; FDA approval on June 18, 2010

- >100,000 data points to evaluate
  - Detection of HIV antibodies to HIV-1 group M (including diverse subtypes), HIV-1 group O, and HIV-2
  - Detection of HIV p24 antigen (diverse virus isolates, seroconversion panels, Ab negative specimens)
  - Specificity and sensitivity in low and high risk populations, pregnant females, and pediatrics

- Overall specificity: 99.77% (95% CI: 99.62-99.88%)
- HIV antibody sensitivity: 100% (95% CI: 99.63-100.00%)
- HIV p24 Ag analytical sensitivity: 18.39 pg/mL (range 17.80-19.68 pg/mL)
What is Acute Phase of HIV Infection?

### Appearance of markers of HIV infection

- Absence of HIV specific antibodies
- Rapid rise in plasma viremia
- Acute viral syndrome: fever, rash, diarrhea, fatigue, headache – opportunity for HIV testing
- Detect AHI by NAT or p24 antigen

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Why is Detection of AHI Important?

AHI makes a significant contribution to the ongoing epidemic
- May account for 15-50% of new infections

During the acute phase, substantially increased risk of transmission
- Estimated 28-fold increase compared to chronic phase
- Period of high viremia
- Virus appears to be more infectious

Individual unaware of infection status
- Often test negative
HIV Combo Acute HIV Infection Studies

Dr. J. Stekler, University of Washington, Seattle
Dr. M. Pandori, San Francisco Department of Public Health
Dr. S. Eshleman, Johns Hopkins University, Baltimore
Dr. P. Patel, CDC, Atlanta
K. Delaney, CDC, Atlanta
Dr. M. Owen, CDC, Atlanta
Dr. L. Wesolowski, CDC, Atlanta
Acute HIV Infection Studies

Basic testing strategy:
- Specimens screened with an HIV antibody test
- All negative specimens tested by HIV NAT

Define acute HIV infection:
- Specimens detected utilizing HIV NAT

Stored specimens blinded and sent to Abbott for Combo testing
- Included HIV antibody positive, Western blot confirmed specimens and HIV negative specimens
- Used ARCHITECT HIV Ag/Ab Combo (CE marked version; 4J27)
Seattle Study

MSM population – high risk, frequent testing
Specimens collected at Public Health-Seattle and King County
2003-2008 specimens screened  N=14,005

- HIV antibody positive       N=328 (2.3%)
- HIV Ab-/RNA+ (acute)        N=36 (0.3%)

NAT algorithm increased yield of HIV infection by 11%
Median time from collection to report of NAT+ result: 16-19 days
Seattle Combo Results

16 of 36 acute HIV specimens available for ARCHITECT HIV Combo testing

HIV Combo detected 15 of 16 (94%)

HIV RNA for Combo negative: 4,946 copies/mL

Median HIV RNA for Combo positive: 4.5 million copies/mL

*RealTime HIV-1 assay performed using residual specimen volume
### Seattle Conclusions

Extrapolation of Combo results to entire study population:

<table>
<thead>
<tr>
<th>Testing Strategy</th>
<th>% HIV Infections Detected</th>
</tr>
</thead>
<tbody>
<tr>
<td>EIA/NAT algorithm</td>
<td>100</td>
</tr>
<tr>
<td>HIV Combo</td>
<td>99.4</td>
</tr>
<tr>
<td>1\textsuperscript{st}/2\textsuperscript{nd} Gen EIA</td>
<td>90</td>
</tr>
<tr>
<td>OraQuick Rapid</td>
<td>80</td>
</tr>
</tbody>
</table>

- The sensitivity of ARCHITECT HIV Combo greatly reduces or eliminates the need for NAT even in a high risk, high prevalence population.

- Combo assay could shorten time to report results. For HIV prevention and partner notification, CDC target for time to report an HIV positive result is <72 hours.
## ARCHITECT HIV Combo Detects Acute HIV Infections

<table>
<thead>
<tr>
<th>Site</th>
<th># AHI Combo tested</th>
<th># AHI Combo detected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seattle (Stekler, CID 2009; 49:444-453)</td>
<td>16</td>
<td>15 (94%)</td>
</tr>
<tr>
<td>San Francisco (Pandori, JCM 2009; 47:2639-2642)</td>
<td>64</td>
<td>57 (89%)</td>
</tr>
<tr>
<td>EXPLORE (Eshleman, JAIDS 2009; 52:121-124)</td>
<td>21</td>
<td>13 (62%)*</td>
</tr>
<tr>
<td>CDC AHI Study (Patel, Arch Int Med 2010; 170:66-74)</td>
<td>38</td>
<td>34 (89%)</td>
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<tr>
<td>CDC Rapid Study (Delaney, CROI 2009, poster 997)</td>
<td>17</td>
<td>13 (76%)*</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>156</strong></td>
<td><strong>132 (85%)</strong></td>
</tr>
</tbody>
</table>

*Site used individual NAT instead of pooled NAT

- Combo assay detected 85% of acute HIV infections
- AHI not detected by HIV Combo: 724 - 21,548 RNA copies/mL
- AHI detected by HIV Combo: 30,734 - >10,000,000 copies/mL
ARCHITECT HIV Combo Seroconversion Sensitivity

- Based on 31 panels, Combo reduced window period a median of 7 days relative to 3rd generation Ab assay; range 0-20 days\(^1\)

Seroconversion Panel HIV 9079 (Vendor data: ZeptoMetrix Corp)

<table>
<thead>
<tr>
<th>Days</th>
<th>Roche Cobas RNA copies/mL</th>
<th>ARCHITECT</th>
<th>BioRad 1/2/O</th>
<th>Unigold</th>
<th>Multispot</th>
<th>Oraquick</th>
<th>BioRad HIV-1 WB</th>
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</thead>
<tbody>
<tr>
<td>0</td>
<td>not detected</td>
<td>0.12</td>
<td>0.648</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>2</td>
<td>not detected</td>
<td>0.07</td>
<td>0.133</td>
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<td>9</td>
<td>not detected</td>
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<td>0.580</td>
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<td>28</td>
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<td>0.222</td>
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<td>33</td>
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<tr>
<td>35</td>
<td>&gt;400</td>
<td>0.15</td>
<td>0.352</td>
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<tr>
<td>42</td>
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<td>23.85</td>
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<tr>
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\(^1\)ARCHITECT HIV Ag/Ab Combo Package Insert
Reduction in Seroconversion Window Period

1st Gen HIV Ab
3rd Gen HIV Ab
4th Gen HIV Ag/Ab

HIV RNA (plasma)
HIV p24 Ag

Day post infection

0 10 20 30 40 50 60 70 80 90 100

17 22 35

1st Gen Ab
3rd Gen Ab
4th Gen Ag/Ab

Fiebig et al, AIDS 2003; 17:1871-1879
Owen et al, J Clin Micro 2008; 46:1588-1595
Kleinman et al, Transfusion 2009; 49:2454-2489
Patel et al, Arch Int Med 2010; 170:66-74
Erie County Medical Center Buffalo, NY: 
Increased HIV Testing and Identification of AHI

- Implementation of NYS law resulted in 5-fold increase in HIV tests performed
- Tested 3601 patients w/ ARCHITECT HIV Combo assay:
  - 31 confirmed HIV infections (0.9%)
    - 6 newly diagnosed chronic HIV infections
    - 1 diagnosed acute HIV infection
  - Specificity: 99.92%
- AHI case:
  - 37 year old with acute viral syndrome came to emergency room
  - Reactive for HIV: ARCHITECT HIV Combo, HIV-1 RNA
  - Nonreactive for HIV: 3rd generation EIA, rapid test, western blot

Myers JB, et al., 27th Clinical Virology Symposium, May 2011, Daytona Beach FL
ARCHITECT HIV Combo: The U.S. Experience

- Avera McKennan Hospital, Sioux Falls, SD
  - 3533 ARCHITECT HIV Combo tests run in 7 months
  - 16 confirmed HIV infections; prevalence 0.45%
  - 4 newly diagnosed HIV infections
    - 3 acute HIV infections
  - 48 minute average turn around time for HIV Combo result (from time of draw)
  - Specificity: 99.86%

- Dallas-Fort Worth, TX
  - Tested 220 specimens from patients being screened for HIV
  - Compare ARCHITECT Combo to comparator tests
  - Combo detected 4 AHI not detected by comparator plus 1 recent infection with indeterminant Western blot

Dr L Serrano, Abbott Workshop, AACC 2011.
ARCHITECT HIV Ag/Ab Combo: Conclusions

- HIV Combo detects HIV infections during the acute, recent, and established phases of infection.
- Substantial improvement over HIV Ab immunoassays
- Sensitive Ag and Ab detection across HIV subtypes/groups
- High specificity (reduced cost associated with false-positives)
- Fully automated, random access, high throughput
- Time to first result: 29 minutes
- Early implementation of ARCHITECT HIV Combo assay has demonstrated benefits of the assay both high and low prevalence settings
Publications on ARCHITECT HIV Combo


