Performance of the Alere Determine™ HIV-1/2 Combo Rapid Test with Specimens from U.S. HIV-1 Seroconverters and HIV-2 Positive Specimens from Ivory Coast

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The view expressed in this presentation are those of the authors and do not necessarily represent those of the Centers for Disease Control and Prevention

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Division of HIV/AIDS Prevention, Lab Branch
**Determine™ HIV-1/2 Ag/Ab Combo rapid test**

- Immunochromatographic lateral flow test for qualitative detection of p24 and antibodies to HIV-1/2
- 4th generation rapid test use outside of U.S. since 2009
- Serum, plasma, whole blood
- 100.0% sensitivity (HIV-1 B and non-B, HIV-1 GO, HIV-2)
- 99.7% Ag and 99.2% Ab specificity
Notice to collaborate from CDC

- **Determine** (original device) from Inverness
  - pre-FDA submission
  - 99.0% sensitivity (n=720 HIV-1 positive)
    - 496/500 B (99.2%), 133/133 non-B (100.0%), 3/3 HIV group O (100%)
    - 82/82 HIV-2 (100%)
  - specificity (n=500 HIV-1 negative)
    - 99.8% Ag and 100.0% Ab
    - Invalids results: absence of control line

- **2011 Determine was reformulated**
Published findings

  - FS testing showed **no benefit** over 3rd gen assays for screening in low prevalence settings and high risk of **false positives** (UK)

- **Chetty, V. et al (JCV 2012)**
  - Did **not detect p24** from plasma in AHI, but antibody response was superior as 3rd gen assays (South Africa)

  - Excellent performance for detecting **established infections**, but poor for AHI in a field evaluation (Malawi)

  - Earlier Ab detection from plasma than other Ab tests used, but < 2% of Ag+ were detected by Determine (Rwanda, Zambia)

  - Determine **failed to detect** AHI
Objective

- To evaluate the performance of the reformulated Alere Determine™ HIV-1/2 Ag/Ab Combo rapid test with plasma specimens from HIV-1 seroconverters and HIV-2 infected individuals
HIV-1 specimens

26 HIV-1 seroconverters from U.S.

- Commercial plasma panels presumably HIV-1 subtype B
  - Zeptometrix and SeraCare Life Sciences

- Previously characterized 230 frozen plasma specimens
  - NAT, 2nd, 3rd, and 4th generation IAs, FDA-approved rapid tests
  - 17 SC followed until positive WB

- Estimation of 50% cumulative frequency of positive tests for
  - Combo Ag/Ab
  - Ab test only
HIV-2 specimens

- **86 HIV-2 plasma specimens**
  - BocaBiolistics
  - 2009 collection from Ivory Coast
  - **Tests**
    - Multispot HIV-1/HIV-2 RT (Bio-Rad)
    - GS HIV-1/HIV-2 Plus O (Bio-Rad)
    - HIV-2 Western blot (MP Diagnostics)
    - HIV-1 Western blot (Bio-Rad)
  - Genotyped in integrase region

The tree was inferred by the Neighbor-Joining method and the numbers on branches are percent posterior probabilities (values of 95% and above are shown). The scale bars indicate 0.05 substitutions per site. HIV-2 subtype A-G references from the Los Alamos HIV/SIV Sequence Database including the outgroup AB553918.
Alere Determine™ Ag/Ab Combo rapid test

- New devices were provided by Alere Medical CO., Ltd
  - Manufactured in Israel

- Protocol was followed as indicated in the package insert

- Plasma specimens were thawed, mixed and spun

- Single testing
Cumulative frequency analysis

17 seroconverters with WB positive used for analysis with different assays
RESULTS
Sensitivity of assay reactivity during early HIV-1 infections relative to number of days before first positive WB

- **NAT**
- **4th gen IA**
- **3rd gen IA**
- **Rapid tests**
- **2nd gen IA**
- **WB POSITIVE**

Days before positive Western blot:
- **Aptima GenProbe (26)**
- **Architect Combo (20)**
- **BioRad combo (18)**
- **Determine Combo Ag+Ab (15.5)**
- **Advia 3rd (14)**
- **Vitros 3rd (13)**
- **BioRad + O (12)**
- **Determine Combo Ab (7)**
- **Insti (9)**
- **Statpak & Complete (7)**
- **Avioq (6)**
- **Multispot (5)**
- **Unigold (2)**
- **Oraquick (0)**
24 observations from 6 SC with quantified p24 (Zeptometrix)

- 3 WB positive and 3 WB indeterminate

p24 reactivity was observed in samples with \([0- >125]\) pg p24/ml (17/24)
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<th>days btw bleedings</th>
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Alere Determine™ in plasma specimens

- Detection of p24 by Determine failed for S/CO = 1.0-7.6
- p24 was detected by Determine but not by p24 assays
- 93.3% of Architect/BioRad Combo positive specimens were positive by Determine Combo Ag+Ab
- 88.2% of BioRad Plus O positive specimens were positive by Determine Combo Ab only
- 100% HIV-2 positive specimens from Ivory Coast were Ab positive and Ag negative with Determine
Conclusions

- Relative sensitivity analysis during early infections for
  - Ag+Ab: between FDA-approved 4th gen and 3rd gen IAs ~15.5 days
  - Ab only: similar to FDA-approved RT that detects Ab ~ 7 days

- Performs well with HIV-2 specimens regardless of the subtype

- Results suggest that Alere Determine™ HIV-1/2 Ag/Ab Combo RT improves detection of early HIV-1 infections in plasma and reliably detects HIV-2 antibodies
However….

- Additional data from whole blood testing are needed

- **Whole blood sensitivity and specificity may be affected**
  - Lower plasma volume in 50 µl of whole blood
  - More non-specific binding
Acknowledgments

HIV Laboratory Branch
HIV Incidence and Diagnostics Team

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