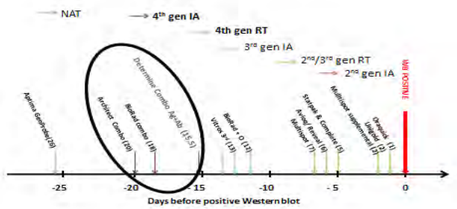
620 Evaluation of Determine™ HIV-1/2 Ag/Ab Combo in the Context of Acute HIV Screening

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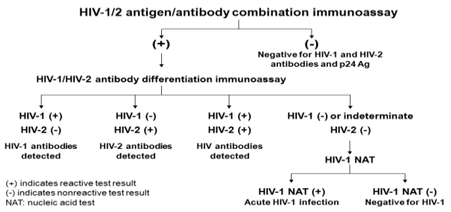
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Background

- Alere Determine™ HIV-1/2 Ag/Ab Combo (DC) is a visually read, rapid qualitative immunoassay for the simultaneous detection of HIV-1 p24 antigen and antibodies to both HIV-1 and HIV-2
- DC received FDA-approval in 2013 for use in human serum, plasma, fingerstick or venipuncture whole blood
- DC in plasma becomes positive 15.5 days before the first positive Western blot (*Masciotra S et al. J Clin Virol 58 Suppl 1, 2013)*



- DC received CLIA waiver in Dec 2014 for fingerstick whole blood
- The performance of DC as screening test in the context of new HIV laboratory diagnostic algorithm has not been evaluated



Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations CDC, June 27, 2014

- Data on the performance of DC on whole blood from individuals in early phases of infection are limited

Objectives

- To evaluate the performance of Determine Combo (DC) as a screening assay in a subset of plasma specimens from an acute HIV screening study in the context of the new HIV laboratory diagnostic algorithm
- To compare the performance of DC with simulated whole blood to plasma samples from HIV-1 seroconverters

Screening Targeted Populations to Interrupt On-going Chains of HIV Transmission with Enhanced Partner Notification (STOP) Study

- Multi-site, prospective study evaluating methods to detect acute HIV infection
- On-site screening in NY and NC was performed with OraSure OraQuick ADVANCE rapid HIV-1/2 antibody test (whole blood)
- 178 plasma samples were classified as acute, established or false-positive after testing with Abbott ARCHITECT HIV Ag/Ab Combo, Bio-Rad Multispot HIV-1/HIV-2 rapid test and Hologic APTIMA HIV-1 RNA Qualitative assay (HIV laboratory algorithm)
- This subset of plasma samples tested with DC represents all the acute and false-positive with remnant volume and a random set of established infections
- McNemar's tests was used for the statistical analysis

Results 1: Determine HIV-1/2 Ag/Ab Combo performance in plasma specimens from the STOP study

Results from previous testing	n	Determine Combo reactive results
Acute HIV-1 infections		
Aptima-pos/ARC-neg	10	0
Aptima-pos/ARC-pos/MS-neg or -ind/OQ-neg	**38**	**20:** 12 Ag+, 8 Ab+ *
Established HIV-1 infections		
ARC-pos/MS-pos/OQ-neg	**15**	**14:** 1 Ag+Ab+, 13 Ab+
ARC-pos/MS-pos/OQ-pos	54	**54:** 1 Ag+Ab+, 53 Ab+
False positive 4th generation specimens		
Aptima-neg/ARC-pos/MS-neg or –ind/OQ-neg	61	**3:** 3 Ab+

ARC: Architect, MS: Multispot, OQ: OraQuick; pos: positive, neg: negative, ind: indeterminate ***p<0.0001*

- **DC detected significantly fewer HIV-1 infections than Architect *(p<0.0001, 107 vs. 88)***
- **DC detected 52.6% of acute HIV-1 infections *(*p<0.0001, 38 vs. 20)***
- **Of 178 specimens analyzed, 3 samples were false reactive on both DC and Architect**
- **53 HIV infections (in bold) missed by OQ-whole blood at screening were identified with ARC in the context of the new algorithm. DC detected 34 (64.2%) of these 53 missed infections and14 (93.3%) of the 15 that were antibody-positive on supplemental testing**
- **Results are limited to samples with remnant volume**

HIV-1 seroconverters

- Whole blood samples were created at 40% hematocrit using sequential plasma samples from 12 seroconverters
- 68 whole blood samples were tested with DC and compared to results from matched plasma samples
- Reactivity of DC in plasma and whole blood was measured in days relative to the first Aptima-positive

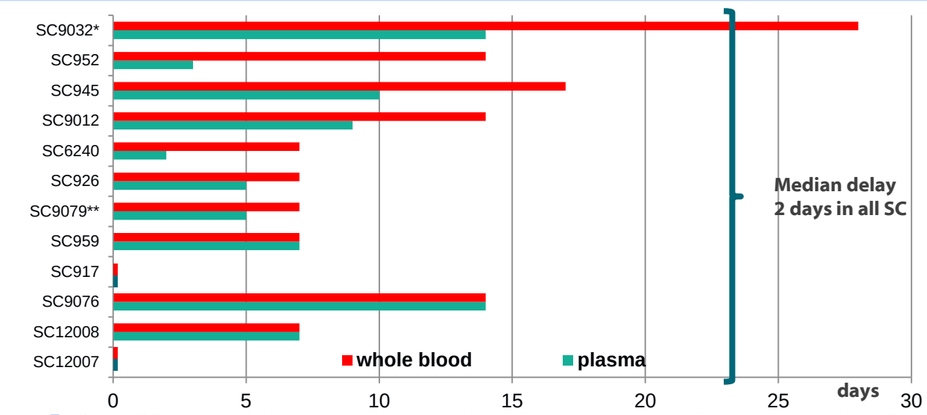
Results 2: Determine HIV-1/2 Ag/Ab Combo performance in HIV-1

		DC plasma				DC whole blood				
Results from previous testing	**n**	Ag-Ab-	Ag+Ab-	Ag+Ab+	Ag-Ab+	Ag-Ab-	Ag+Ab-	Ag+Ab+	Ag-Ab+	inv
Aptima-neg/ARC-neg	5	5				5				
Aptima-pos/ARC-neg	9	9				8				1
Aptima-pos/ARC-pos/MS-neg-ind/OQ-neg	39	2	**22**	**4**	**11**	17	**16**	**2**	**3**	1
Aptima-pos/ARC-pos/MS -ind/OQ-pos	1			**1**					**1**	
ARC-pos/MS-pos/OQ-neg	1				**1**				**1**	
ARC-pos/MS-pos/OQ-pos	13		**1**	**3**	**9**		**1**		**12**	

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- **Of 54 ARC-pos plasma samples, DC detected:**
  - **96.3% with plasma *(p=0.4795, 54 vs. 52)* and 66.6% with whole blood**
  - **Significant difference between plasma and whole blood detection *(p=0.0003. 52 vs. 36)***
- **Of 40 Aptima-pos/ARC-pos/MS-neg or –ind samples, 38 (95%) were DC-pos with plasma and 22 (55%) were DC-pos in whole blood**
- **DC detected 38 (plasma) and 22 (whole blood) more infections than OQ-plasma**
- **Results are limited to simulated whole blood samples**

Results 3: Determine HIV-1/2 Ag/Ab Combo reactivity relative to the first Aptima-positive



SC9032* never become reactive up to 28 days

SC9079** initially Ag+, then become Ag -/Ab- then Ab+

- **Seven SC showed delayed response with whole blood compared to plasma (median delay 5 days)**

Conclusions

- **DC with plasma detected fewer HIV-1 acute infections compared to a instrumented lab-based 4th generation assay**
- **DC with whole blood detected significantly fewer infections than plasma and reactivity to the Ag component was most impacted by sample type**
- **Despite the delays in reactivity observed using whole blood, DC with plasma and whole blood detected more infections than OraQuick using whole blood or plasma in acute and established HIV-1 infections**
- **As a CLIA-waived rapid test, DC may represent an advantage over some other rapid tests in settings where instrumented lab-based testing is not feasible**

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.