EVALUATION OF THE MEDMIRA REVEAL G4 RAPID HIV ANTIBODY TESTS WITH WHOLE BLOOD AND PLASMA SPECIMENS

Rebecca Rossetti[1], Tara Smith[2], Wei Luo[1], Silvina Masciotra[1]

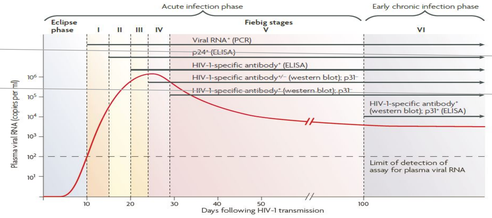
[1]Centers for Disease Control and Prevention, Division of HIV/AIDS Prevention; [2]ORISE

40

BACKGROUND

1.2 million Americans have HIV…**but 1-in-8[1] don't know & they account for 1/3 of HIV transmissions** in the U.S.[2]

- Sensitive and accurate rapid tests performed in point of care (POC) settings can help increase access to testing and awareness of HIV status, thus would help decrease transmission of HIV
- The MedMira Reveal G4 Rapid HIV-1 Antibody Test (G4) (< 2 min run time):
  - FDA-approved for use in laboratory settings for HIV-1 IgG antibody detection with plasma and serum (LAB/SP format) and whole blood (POC format) specimens
  - CE-marked for use in POC and laboratory settings for detection of both HIV-1/HIV-2 antibodies
- IgG is not present early after HIV infection, so the use of antibody-based HIV tests may miss detection of acute infections [3]



1 "CDC Fact Sheet – HIV Testing in the United States." June, 2015. Centers for Disease Control. http://www.cdc.gov/nchhstp/newsroom/docs/factsheets/hiv-testing-us-508.pdf
2 "CDC: More Than 1 in 8 Americans Infected with HIV Don't Know It." June, 2015. Los Angeles Times. http://www.latimes.com/science/sciencenow/la-sci-sn-undiagnosed-hiv-patients-20150624-story.html
3 McMichael AJ, Borrow P, Tomaras GD, Goonetilleke N, Haynes BF. The immune response during acute HIV-1 infection: clues for vaccine development. Nat Rev Immunol. 2009;10(1):11-23.

OBJECTIVE

To evaluate the performance of the G4 POC using simulated whole blood (wb) and LAB/SP using plasma for detecting early and established HIV-1 and established HIV-2 infections

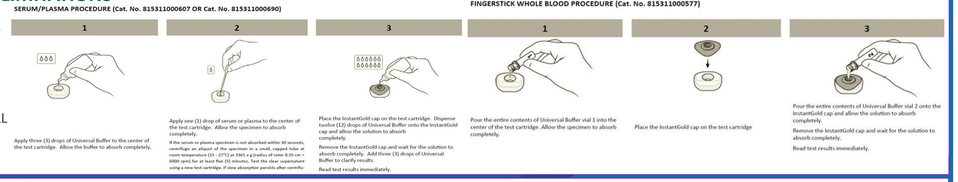
HIV SAMPLES and METHODS

429 previously characterized plasma specimens were used to prepare simulated wb and tested with LAB/SP and POC tests, respectively

- Sensitivity in 104 HIV-1 positive (56 B subtypes and 48 non-B subtypes) and 55 HIV-2 positive samples from established infections
- Specificity in 49 HIV-negative samples
- Early HIV-1 infection reactivity was evaluated in:
  - 38 samples from performance panels characterized by Fiebig staging
  - 18 commercial seroconversion panels (SCP) (n=183)
    - 3 SCP (n=39) that initiated antiretroviral therapy (ART) were tested for viral load to measure viral suppression and 15 SCP (n=144) were ART-naïve
    - Days after first available HIV-1 RNA-positive (NAT+) result was calculated for 13 SCPs (n=129, range of 5-28 samples in each panel followed up for a median of 42 days) for plasma (LAB/SP) and wb (POC) and results compared
- McNemar's paired analysis was done to compare results in plasma and wb

Reveal G4 Rapid HIV: PROTOCOL and LIMITATIONS

- Study was performed in laboratory with no access to fingerstick blood
- Simulated wb might not completely mimic true specimen type
- Plastic pipettes in kit did not work for plasma or wb samples, so based on measurement of the drop 30 µL was used for each specimen type



RESULTS 1- Performance of G4 LAB/SP and POC HIV tests

	G4 LAB/SP-plasma				G4 POC-wb			
	Reactive (R)	Non-Reactive (NR)	% reactivity	95% Confidence interval	Reactive (R)	Non-Reactive (NR)	% reactivity	95% Confidence interval
Established HIV Infections								
HIV-1 +	104	0	100	96.52- 100	104	0	100	96.52- 100
HIV-2 +	54	1*	98.18	90.28- 99.95	54	1*	98.18	90.28- 99.95
HIV-1 Seroconversion Panels								
Before 1st NAT +	0	47	0	-	0	47	0	-
After 1st NAT +	95	41	69.85	61.40- 77.42	86	50	63.24	54.55- 71.33
HIV Negative Samples								
	0	49	0	-	0	49	0	-

*HIV-2 sample previously tested HIV-2 Western blot-positive and Geenius HIV-Antibody negative

Sensitivity
- LAB/SP: 100% for HIV-1 and 98.18% for HIV-2
- POC: 100% for HIV-1 and 98.18% for HIV-2

Specificity
- LAB/SP: 100% [95% CI: 92.75%-100%] for HIV-1 and HIV-2
- POC: 100% [95% CI: 92.75%-100%] for HIV-1 and HIV-2

- McNemar's paired comparison analysis plasma vs wb was statistically significant *p=0.0077*

RESULTS 2- Reactivity of G4 LAB/SP and POC HIV tests in early HIV-1 infections

A- Test Results of Early Infection characterized by Fiebig Stages

- **Reactivity with simulated wb with POC was inferior compared to plasma with LAB/SP**
- G4 showed 54% reactivity of plasma specimens from F-IV in LAB/SP when HIV-1 Western blot is indeterminate (evidence of IgG response)
- Both tests were 100% R with samples Fiebig Stage V when HIV-1 Western blot and Geenius HIV-1/2 Supplemental assay were HIV-1 positive (p31-)

		LAB/SP	POC
Fiebig Stage	n=	Total (%) with positive test	
Neg/Eclipse	5	0 (0)	0 (0)
I	4	0 (0)	0 (0)
II	4	0 (0)	0 (0)
III	6	1 (17)	0 (0)
IV	13	7 (54)	2 (15)
V	6	6 (100)	6 (100)

B- Test Results of Seroconversion Plasma Panels

Of 18 SCP (n=183):
- Ten panels (55.6%, 85 samples) showed no difference in reactivity with LAB/SP-plasma and POC-wb, including 3 panels that initiated early ART
- One panel (5.5%, 8 samples) never became Reactive with POC-wb and LAB/SP-plasma up to 14 days follow-up
- **Seven panels (38.9%, 90 samples) showed discordant reactivity in POC-wb compared to LAB/SP-plasma (nine samples)**
  - One never became Reactive with POC-wb for up to 14 days follow-up when LAB/SP-plasma became Reactive

B-1 Results of other FDA-Approved diagnostic assays from 9 discordant seroconversion samples

SCP #	Days after first sample collected	HIV-1 RNA NAT	Ag/Ab IA	IgG/IgM IA	IgG HIV-1/2 Supplemental IA	IgG Antibody IA	
						G4 LAB/SP plasma	G4 POC wb
4	44	R	R	R	HIV-1 IND	R	NR
7	11	R	R	R	HIV NEG	R	NR
9	10	R	R	R	HIV-1 POS	R	NR
10	35	R	R	R	HIV NEG	R	NR
11	29	R	R	NR	HIV NEG	R	NR
14	57	R	R	R	HIV-1 POS	R	NR
	71	R	R	R	HIV-1 POS	R	NR
15	49	R	R	R	HIV NEG	R	NR
	64	R	R	R	HIV-1 POS	R	NR

B-2 Delayed Reactivity of LAB/SP compared to POC from first available HIV-1 NAT-positive

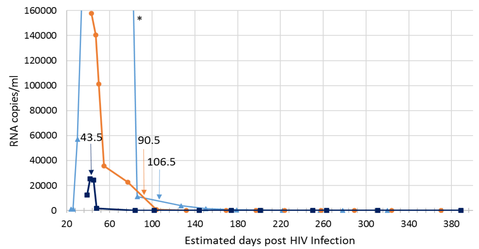
Of 13 SCP (n=129):

- The overall median numbers of days following first NAT+ result was **13 for LAB/SP-plasma** and **14 for POC-wb**
- For the six SCP with delayed reactivity in wb, the median number of days following NAT+ result were 12.5 for LAB/SP-plasma and 16.5 for POC-wb
- Delayed reactivity was seen in wb vs. plasma results at time points ranging from 11-71 days after follow up

- One panel became Non-Reactive after first Reactive tests (plasma and wb) likely due to a secondary negative phase of reactivity

RESULTS 3- Effect of Viral Suppression on Reactivity

Viral Load of 3 SCPs before and after initiation of ART



*Data point not shown on panel 1 at 64 days with 978,249 copies/ml of RNA

- Arrows indicate estimated day of ART treatment initiation in patients
- G4 LAB/SP and POC tests were reactive in all samples before and after ART that were virally suppressed for a median of 238 days

SUMMARY

- Reveal G4 shows reliable performance in different sample sets and various stages of infection for various subtypes of HIV-1 and HIV-2
- Based on the Fiebig stages of infection and the seroconversion results, the test performs well for its ability to detect IgG antibodies
- Viral suppression did not appear to influence the performance of the test
- Overall, there were nine out of 429 invalid results (2%)
  - One sample was Invalid/Invalid for wb, one sample was Invalid/NR for plasma and seven samples were Invalid/R for plasma

CONCLUSIONS

- Reveal G4 reactivity shows good agreement in whole blood and plasma, with overall reactivity in early HIV-1 infections delayed by one day in wb compared to plasma
- If CLIA waived, the G4 POC test using fingerstick wb is a sensitive and fast (< 2 min) testing option when screening for IgG in HIV-1/HIV-2 infections even in presence of long-term viral suppression

CONTACT INFORMATION

Rebecca Rossetti
nvp4@cdc.gov
(404) 718-7558

Silvina Masciotra
svm6@cdc.gov
(404) 639-1004

National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
Division of HIV/AIDS Prevention

Notes

1-2 EmbeddedFile3.xlsx (Attachment)

1-5 As the Geenius HIV antibody test is Negative, in a clinical trial, this would be eliminated so the HIV-2 sensitivity would be 100%. This is minor.

1-7 EmbeddedFile1.xlsx (Attachment)

1-8 2% of invalid results are relatively low and this is mainly due to flow issue as the testings were done with repository specimens.

1-11 EmbeddedFile2.xlsx (Attachment)

1-12 Imagine if CDC would still be in charge of CLIA Waived, based on their evaluation we are approved.