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

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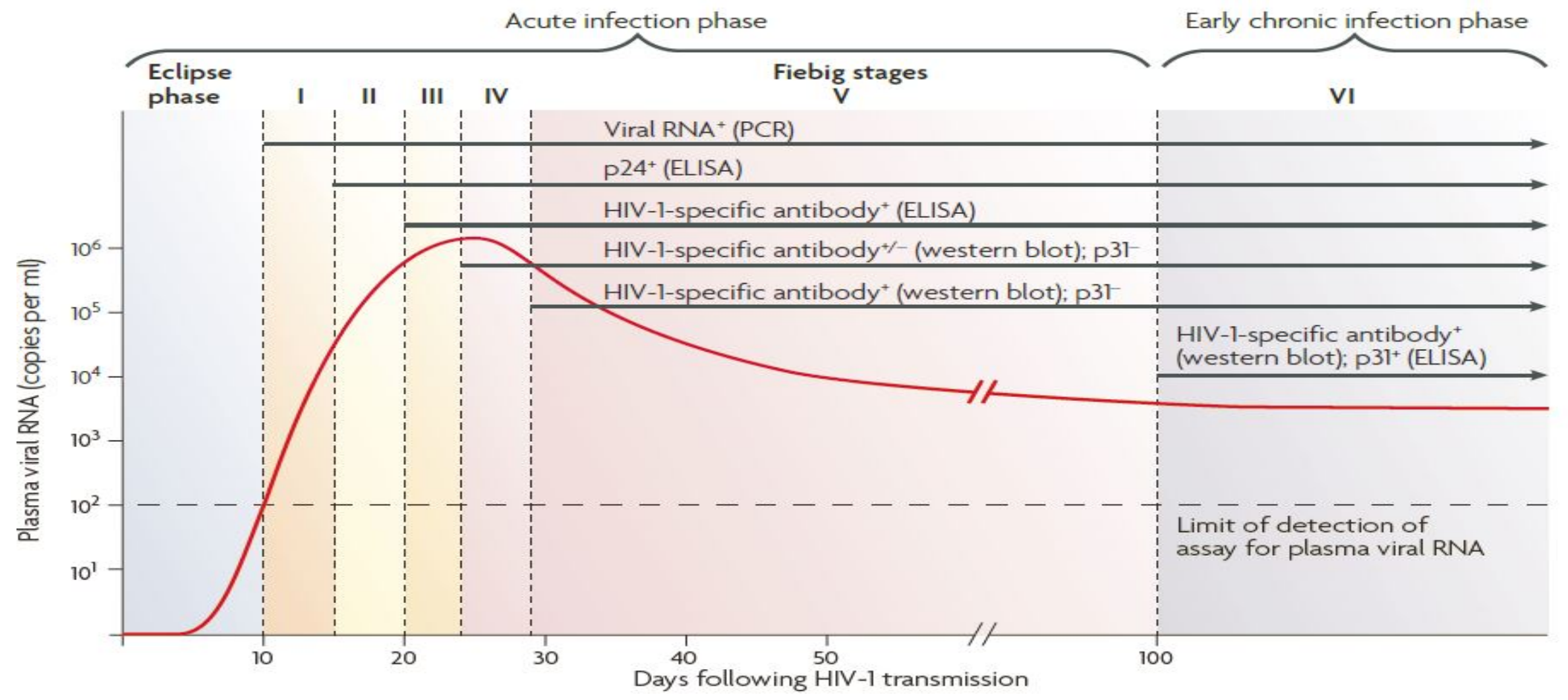
BACKGROUND

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



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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

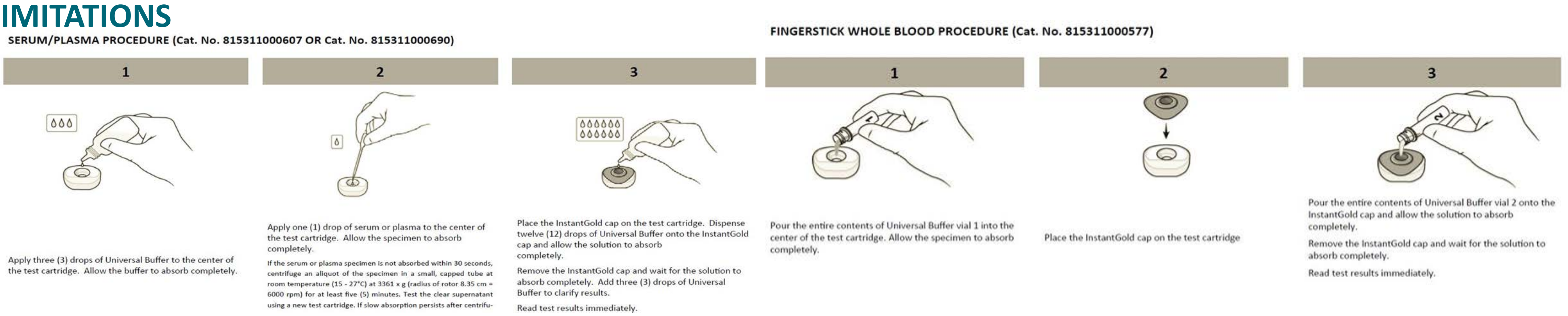
HIV SAMPLES and METHODS

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



SERUM/PLASMA PROCEDURE (Cat. No. 815311000607 OR Cat. No. 815311000690)

1

Apply three (3) drops of Universal Buffer to the center of the test cartridge. Allow the buffer to absorb completely.

2

Apply one (1) drop of serum or plasma to the center of the test cartridge. Allow the specimen to absorb completely.

If the serum or plasma specimen is not absorbed within 30 seconds, centrifuge an aliquot of the specimen in a small, capped tube at room temperature (15 - 27°C) at 3361 x g (radius of rotor 8.35 cm = 6000 rpm) for at least five (5) minutes. Test the clear supernatant using a new test cartridge. If slow absorption persists after centrifu-

3

Place the InstantGold cap on the test cartridge. Dispense twelve (12) drops of Universal Buffer onto the InstantGold cap and allow the solution to absorb completely.

Remove the InstantGold cap and wait for the solution to absorb completely. Add three (3) drops of Universal Buffer to clarify results.

Read test results immediately.

FINGERSTICK WHOLE BLOOD PROCEDURE (Cat. No. 815311000577)

1

Pour the entire contents of Universal Buffer vial 1 into the center of the test cartridge. Allow the specimen to absorb completely.

2

Place the InstantGold cap on the test cartridge

3

Pour the entire contents of Universal Buffer vial 2 onto the InstantGold cap and allow the solution to absorb completely.

Remove the InstantGold cap and wait for the solution to absorb completely.

Read test results immediately.

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

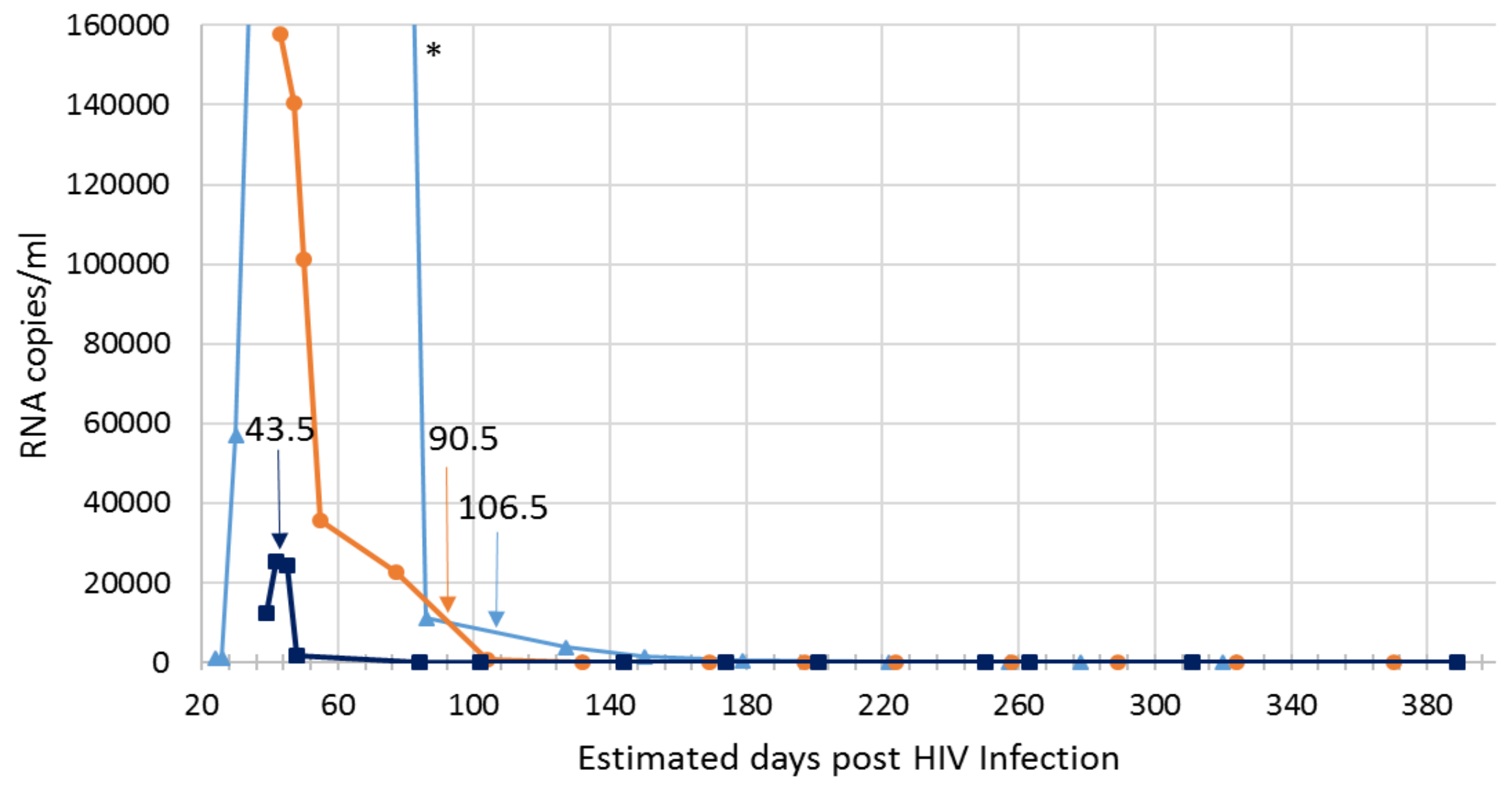
Of 13 SCP (n=129):

- 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

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