Performance Evaluation of the INSTI HIV-1/2 Antibody Point-of-Care Test in Early and Established Infections

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Why Rapid Tests?

- **Affordable**
- **Easy to use**
- **Accessible testing**
- **Fast results**

- **Increase** awareness of HIV status
- **Provide** opportunities for faster linkage to care and treatment
- **Minimize** transmission

BUT they MUST be accurate!

Low sensitivity of a Rapid Test (RT) during the early stages of HIV infection **increases the risk of misdiagnosing** patients with active viral replication and high risk transmission

INSTI™ HIV-1/2 Antibody Test (INSTI)

- Approved in the U.S. for finger stick (CLIA waived) and venous whole blood and plasma for HIV-1 and HIV-2 antibody testing
- Flow-through HIV-1/HIV-2 Rapid Antibody test
- Test time: 60 seconds

Performance characteristics

Sample Type	Sensitivity	Specificity
Venous Whole Blood	99.9%	100%
Plasma	99.9%	100%
Fingerstick Blood	99.8%	99.5%
CLIA Fingerstick Blood*	100%	99.8%

- Recent study showed that sensitivity of a rapid point of care assay for early HIV antibody detection is enhanced by its affinity for HIV gp41 IgM antibodies**

* Galli RA, Green KF, La Marca A, et al.. J Clin Virol 2013;58 Suppl I:e65-9.

** Moshgabadi N., Galli R., Daly A., Ko S.M.S., Westgard T., Bulpitt A., Shackleton C.R, et al J Clin Virol 2015

INSTI

- Successfully evaluated in several studies outside of the United States
  - Performed well:
    - compared to other POC tests for the detection of early HIV infection using residual serum
    - at detecting HIV exposure in children younger than 18 months and HIV diagnosis in children older than 18 months with whole blood

Darrel Cook, Mark Gilbert, Lillo DiFrancesco, Mel Krajden* Detection of Early Sero-Conversion HIV Infection Using the INSTI™ HIV-1 Antibody Point-of-Care Test. The open AIDS journal, 2010,4, 176-179

Objective

- To evaluate the performance of INSTI in a laboratory using plasma and/or simulated whole blood specimens form early and established HIV infections

Materials and methods

- Plasma from commercial HIV-1 seroconversion panels
  - Estimated relative sensitivity of INSTI and other assays using a 50% cumulative frequency analysis with Western blot positive (n=166)
  - Paired comparison of the performance of INSTI with other FDA-approved RTs using McNemar's statistical test (n=230)

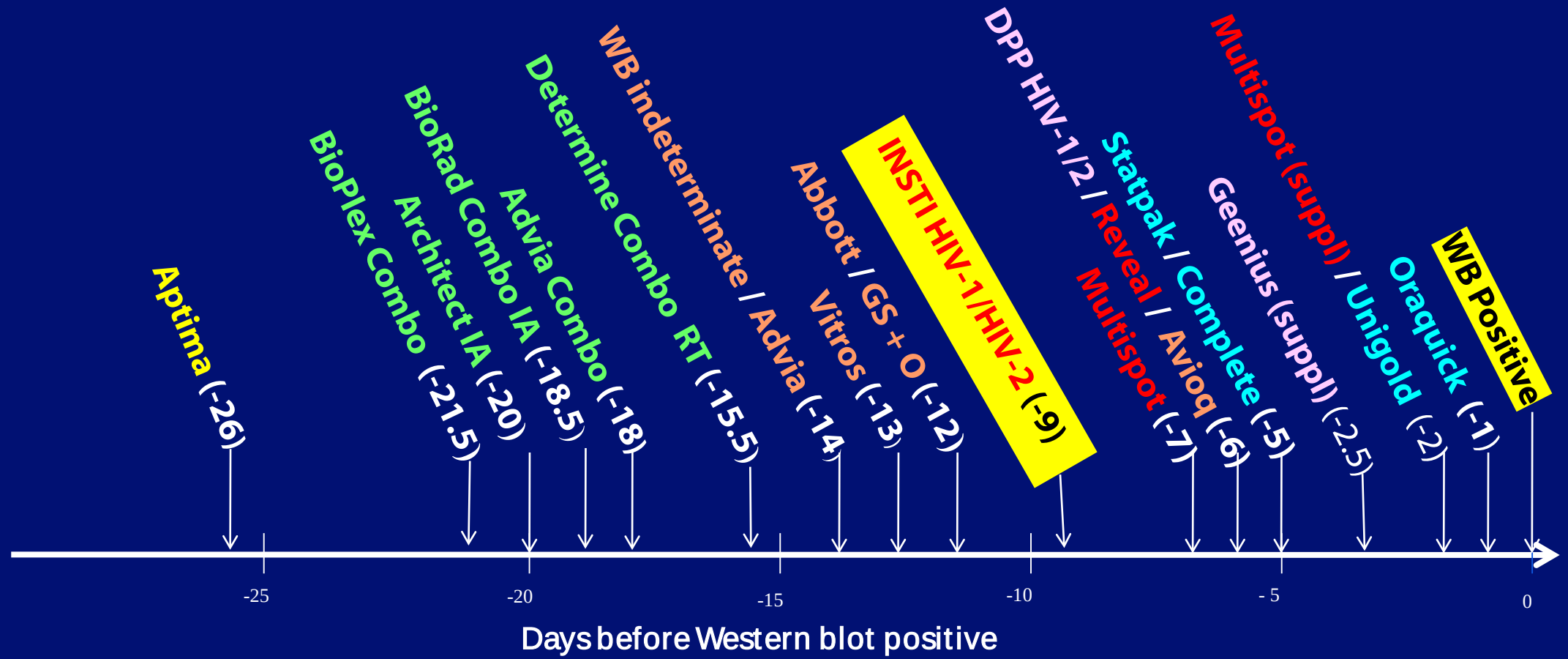
- Eight HIV-1 seroconversion plasma panels (n=40) were used to simulate whole blood
  - INSTI results were compared to results generated with two Ag/Ab Combo tests and one IgG/IgM immunoassay

Methods

- Plasma from HIV-1 positive individuals at different stages of HIV-1 infection
  - Screening Targeted Populations to Interrupt On-going Chains of HIV Transmission with Enhanced Partner Notification (STOP) Study
  - Specimens were tested with INSTI at CDC and compared to Abbott ARCHITECT, Bio-Rad Multispot, Abbott HIV-1 RNA viral load results
- Plasma specimens from
  - Individuals with established HIV-1 and HIV-2 infections (western blot positive) were used to calculate sensitivity
  - HIV-negative individuals were used to calculate specificity
- Plasma specimens from HIV-1 positive individuals who receive antiretroviral therapy (ART)

RESULTS

Assay reactivity during early HIV-1 infections using 50% cumulative frequency analysis



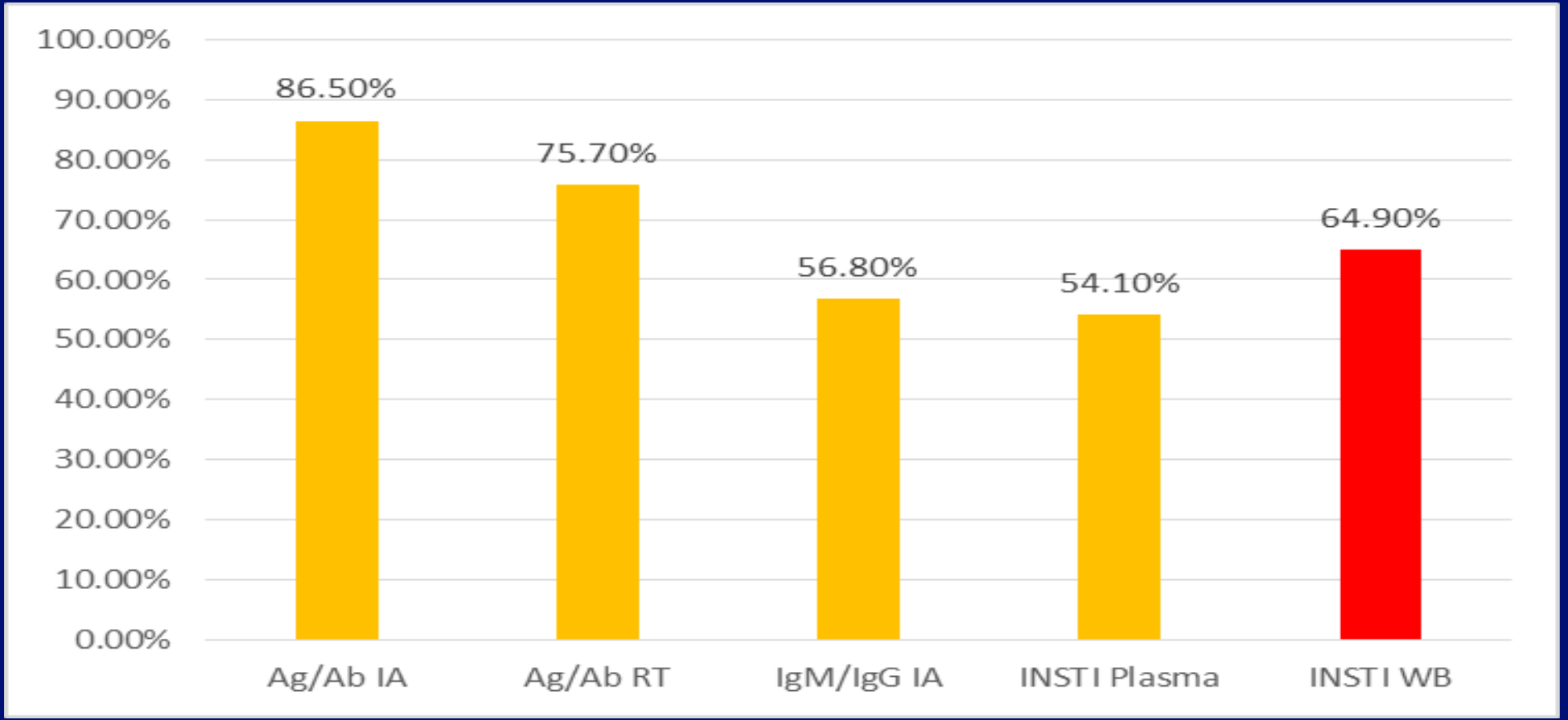
Paired comparison analysis of INSTI and other FDA-approved RTs

	Number of results test 1/results INSTI				
Test 1	NR/NR	NR/R	R/NR	R/R	p value
Determine Ag/Ab	102	2	34	92	<0.0001*
Multispot[a]	133	6	2	88	0.289
Reveal G2/G3[a]	134	14	1	80	0.0019*
DPP HIV-1/2	134	15	2	79	0.0036*
Statpak	134	20	1	74	<0.0001*
Complete	135	22	1	74	<0.0001*
Unigold	136	23	0	70	<0.0001*
Oraquick Advance	134	34	2	60	<0.0001*

[a] 229 total samples available for analysis; R: reactive, NR: not reactive

* statistically significant

Performance with 37 HIV-1 Simulated Whole Blood and Plasma Specimens from 8 Seroconverters



- **INSTI in plasma and simulated whole blood**
  - No delay in early HIV-1 infections
  - 3 samples showed discrepant results

Performance of INSTI with Simulated Whole Blood and Plasma from HIV-1 Seroconverters

- False reactive with whole blood

ID #	Days between bleeds	NAAT	IA Ag/Ab	IA IgG/IgM	RT Ag	RT Ab	INSTI plasma	INSTI whole blood
924-04		nonreactive	-	-	-	-	-	+
924-05	16	reactive	+	-	+	-	-	-
924-06	7	reactive	+	+	+	+	+	+
924-07	2	reactive	+	+	-	+	+	+
924-08	5	reactive	+	+	-	+	+	+

ID #	Days between bleeds	NAAT	IA Ag/Ab	IA IgG/IgM	RT Ag	RT Ab	INSTI plasma	INSTI whole blood
931-05		reactive	+	-	-	-	-	+
931-06	13	reactive	+	+	+	+	+	+
931-07	5	reactive	+	+	-	+	+	+
931-08	2	reactive	+	+	-	+	+	+
931-09	7	reactive	+	+	-	+	+	+
940-01		reactive	+	-	-	-	-	-
940-02	7	reactive	+	-	+	-	-	+
940-03	4	reactive	+	+	+	+	+	+
940-04	4	reactive	+	+	-	+	+	+
940-05	3	reactive	+	+	-	+	+	+
944-01		reactive	-	-	-	-	-	-
944-02	2	reactive	-	-	-	-	-	-
944-03	5	reactive	+	-	+	-	-	+
944-04	2	reactive	+	-	+	-	-	+
944-05	5	nonreactive	+	+	-	+	+	+
944-06	2	reactive	+	+	-	+	+	+

INSTI Reactivity in Early infection

NAT Positive/ ARC Positive			INSTI Results	
Plasma				
Multispot	**StatPak**			
Plasma	Whole blood	**Total**	**Positive**	**Negative**
-	-	51	7	44
-	+	2	0	2
-	NA	21	8	13
ind	-	9	6	3
ind	+	1	1	0
ind	NA	1	1	0

- INSTI with plasma detected more early HIV-1 infections than Statpak with fingerstick whole blood

INSTI Reactivity in Established infection

ARC Positive plasma			INSTI Results	
Multispot plasma	**StatPak** Whole blood	**Total**	**Positive**	**Negative**
+	-	9	9	0
+	+	174	174	0
+	NA	20	20	0

- INSTI detected all established infections including 9 that were StatPak negative with fingerstick whole blood

Sensitivity of INSTI HIV-1/HIV-2 antibody test

		INSTI results				
	Total	Reactive	Non-reactive	Repeatedly Invalid	Sensitivity (%)	95% Confidence Intervals
HIV-1 Group M						
HIV-1 B subtype	501	500	1	0	99.80	98.88- 99.96
HIV-1 non-B subtype	111	110	0	1	100	96.63- 100
HIV-1 Group O	3	3	0	0	100	43.85- 100
HIV-2	80	80	0	0	100	95.42- 100

- Overall sensitivity 99.84% [99.08- 99.97% 95%CI]
- Specificity 99.80% [98.87- 99.96% 95% CI]

Plasma specimens from HIV-1 positive individuals who receive ART

- 35 HIV-1 positive donors with HIV-1 Viral load results (Abbott m2000)
  - 21 Target not detected
  - 5 <40 copies/ml
  - 9 mean of 163 copies/ml (range: 48- 391 copies/ml)
- All of these plasma specimens were reactive with INSTI

Summary

- In HIV-1 early infections, INSTI was positive 9 days before a positive WB
- Flow-through RTs detected significantly more infections than the antibody-based lateral flow FDA-approved RTs
- Using simulated whole blood, INSTI performed similarly to plasma with no delay observed between plasma and whole blood among early HIV-1 infection
- Among cross-sectional plasma samples, INSTI detected 23 (27%) of 85 specimens from early HIV-1 infections and 203 (100%) specimen from established infections
- The sensitivity was 99.84% for HIV-1 and 100% for HIV-2 and the specificity was 99.80% in plasma specimens
- All 35 HIV-1 positive plasma donors who receive ART were reactive with INSTI

Conclusions

- INSTI performed significantly better than antibody-based lateral flow RTs at detecting early HIV-1 infections (IgM detection), and performed slightly better than the other flow through RTs
- Sensitivity and specificity were within the manufacturer's reported ranges
- This study was limited to simulated whole blood. Further evaluation with fingerstick/venipuncture whole blood is needed to evaluate point of care performance
- The ease of use of INSTI and the almost instant result makes the test a good option for point-of-care settings

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Thank you ☺

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