

# Performance of HIV Ag/Ab Assays on Samples from Individuals Initiating Antiretroviral Therapy During Acute HIV Infection

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No Conflict of Interest to Declare

**WRAIR**

Walter Reed Army  
Institute of Research

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The views expressed are those of the presenter and should not be construed to represent the positions of the U.S. Army or Department of Defense



# Background

- **CDC guidelines:** initiation of antiretroviral therapy (ART) as soon as possible after first HIV diagnosis
  - Minimize risk of forward transmission
  - Disrupt establishment of latent reservoirs
  - Better sustained virologic control
  - Enhance overall health outcomes
- **Issue:** ART initiation during Acute HIV Infection (AHI) may
  - Reduce HIV Ag stimulation below threshold for immune response
  - Block/delay emergence HIV serological diagnostic markers

# Acute HIV Infection Studies Leveraged

## RV254/SEARCH010: Bangkok, Thailand

- HIV-1 viremic volunteers initiated ART immediately post diagnosis
- Stage of HIV infection at time of ART initiation
  - Fiebig I (N=23)      HIV RNA+, p24 Ag-, HIV Ab-
  - Fiebig II (N=39)    HIV RNA+, p24 Ag+, HIV Ab-
  - Fiebig III (N=13)   HIV Ab+, WB-
  - Fiebig IV (N=9)     HIV Ab+, WB Indeterminate
- Samples acquired:
  - Initial visit prior to ART:
  - 1, 12, and 24 weeks post ART

SEARCH: South East Asia Research Collaboration with Hawaii

# Acute HIV Infection Studies Leveraged

## RV217 Early Cohort HIV: Kenya, Uganda, Tanzania, and Thailand

- Untreated HIV Infected Controls (N=30)
- Twice weekly testing of at risk populations
  - Infection identified by APTIMA HIV-1 RNA reactivity
- Intensive serial sampling of incident cases
  - ~3 day intervals for first 6 weeks; monthly thereafter

# Study Assays

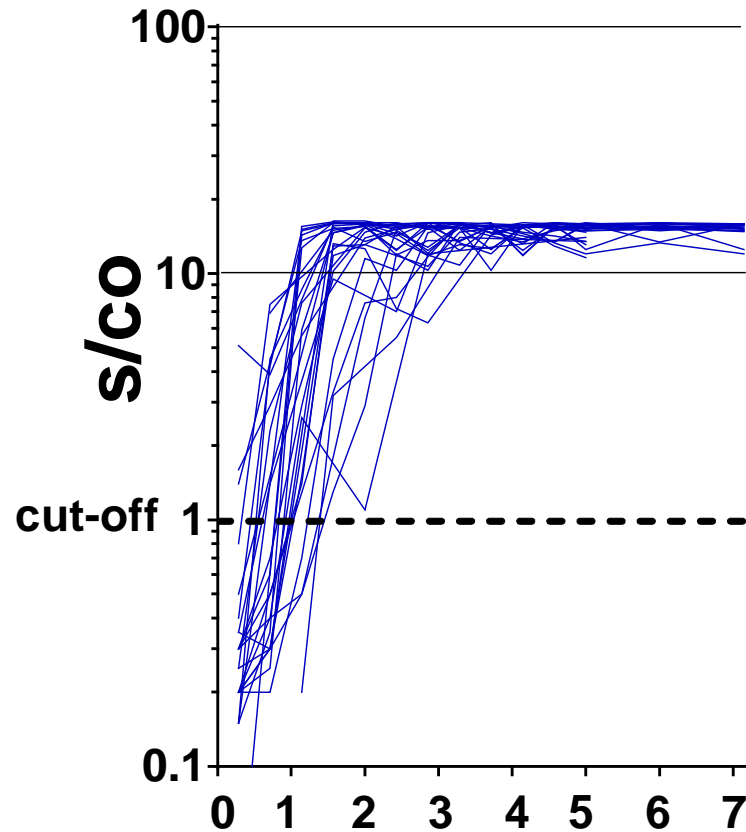
- 4<sup>th</sup> Gen Immunoassays
  - Bio-Rad GS HIV Combo Ag/Ab EIA (BRC)
  - Bio-Rad BioPlex<sup>®</sup> 2200 HIV Ag-Ab Combo (BPX)
  - Abbott Architect HIV Ag/Ab Combo (ARC)
  
- 3<sup>rd</sup> Gen Immunoassay
  - Bio-Rad 3<sup>rd</sup> Gen GS HIV-1/2/ Plus O (1/2/O)
  
- p24 Antigen Assay
  - Bio-Rad Genscreen HIV-1 p24 Ag assay RUO (Ag)
  
- Supplemental, Confirmatory Assays
  - Bio-Rad HIV-1 Western blot (WB)
  - Bio-Rad Geenius<sup>™</sup> HIV-1/2 (Geenius)

# Serological Detection After HIV Infection

## RV 217 - No ART

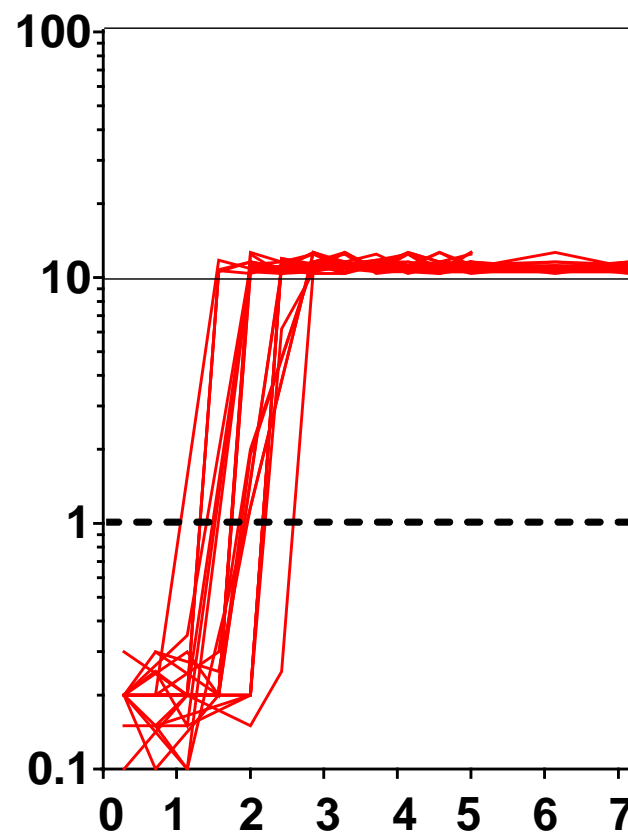
**4<sup>th</sup> Gen Bio-Rad Ab/Ag Combo**

Ave. 6.5 +/- 2.8 days



**3rd Gen Bio-Rad 1/20 (Ab Only)**

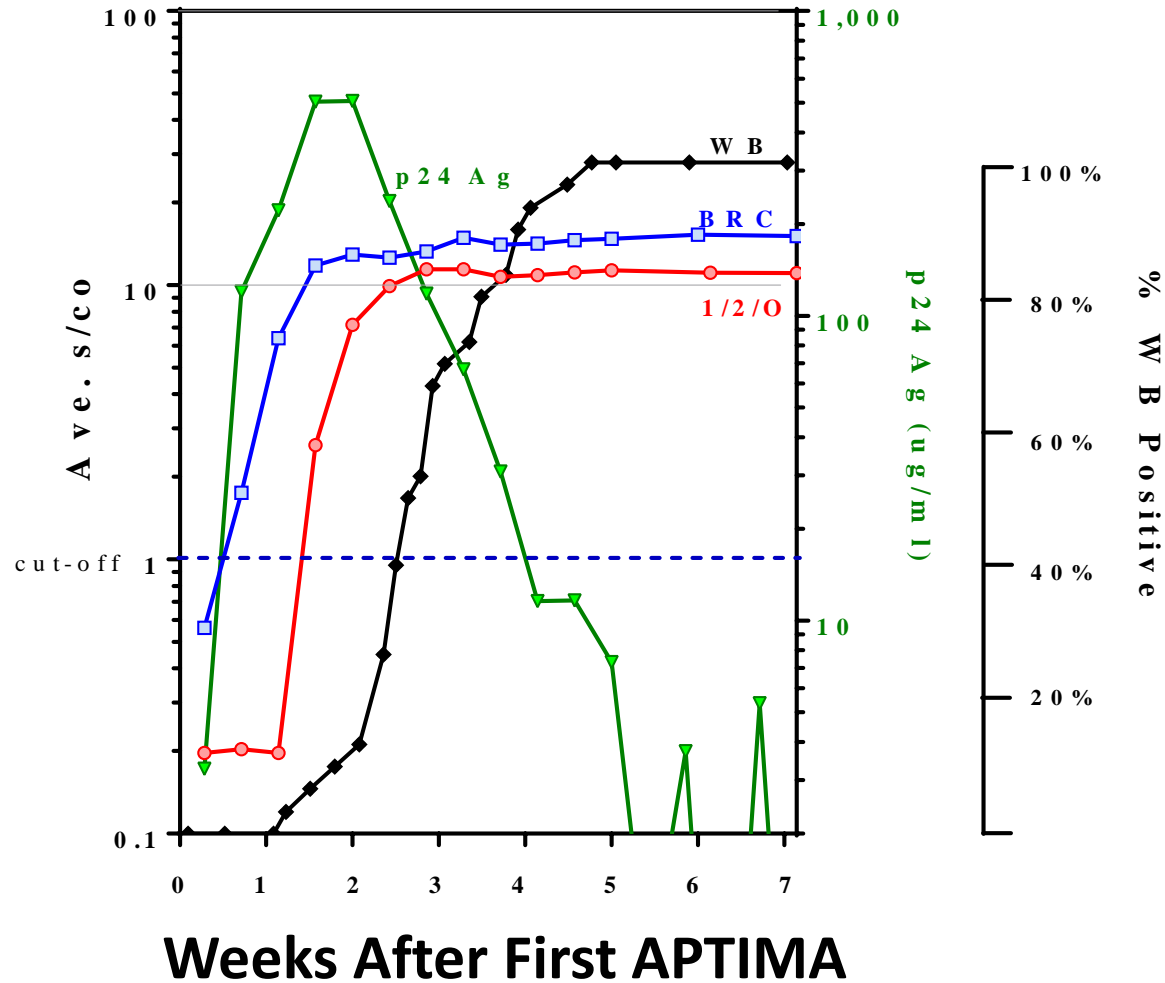
Ave. 15.0 +/- 4.8 days



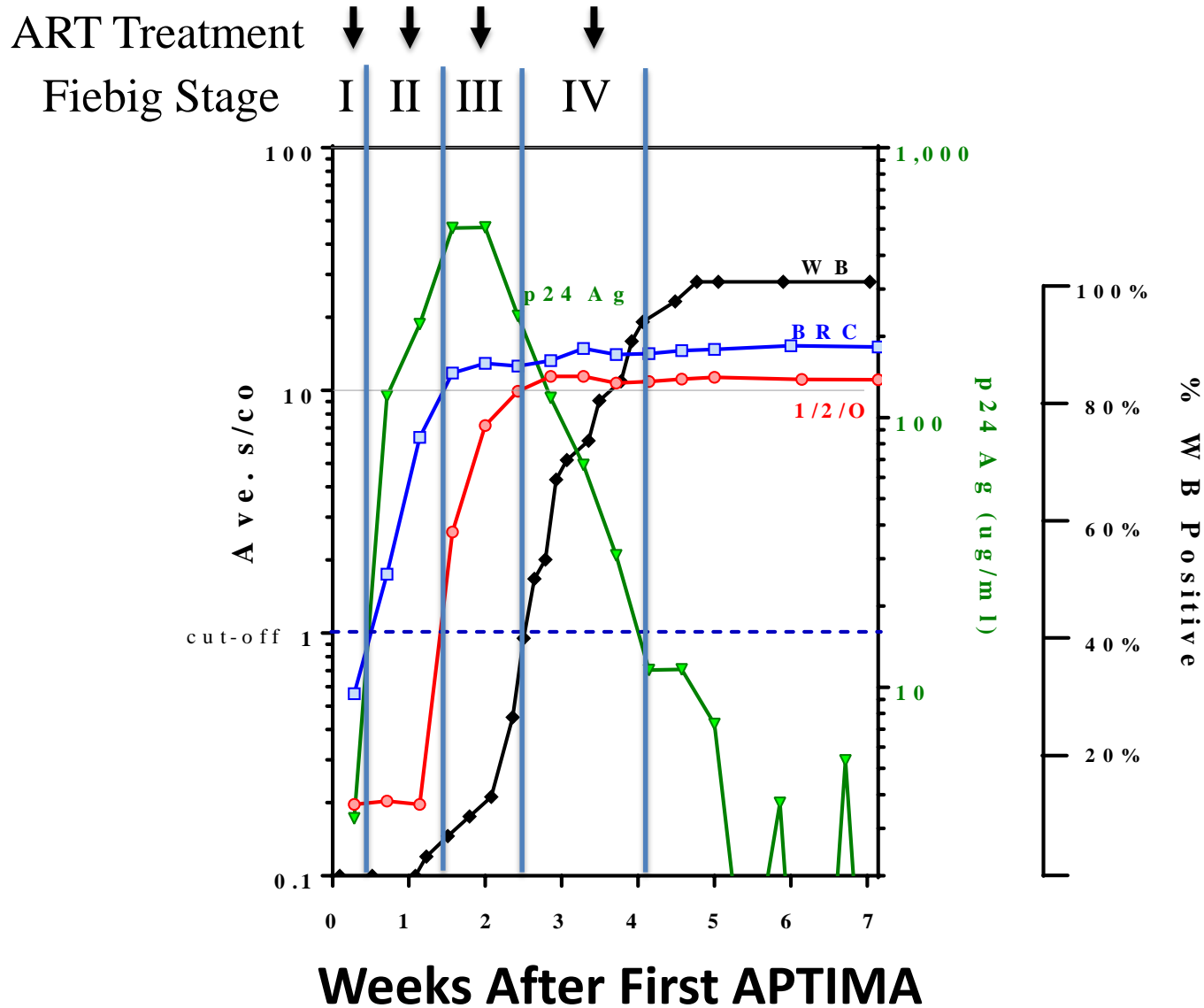
**N = 30**

**Weeks after first APTIMA Reactive**

# Time Course of Serological Markers



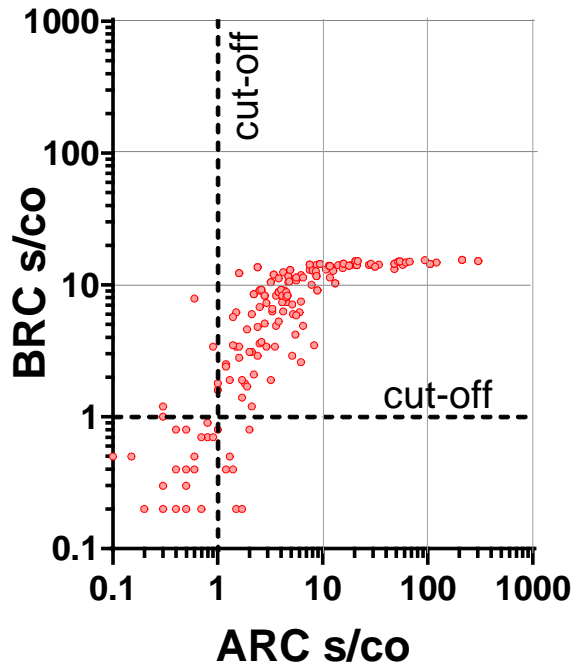
# Time Course of Serological Markers



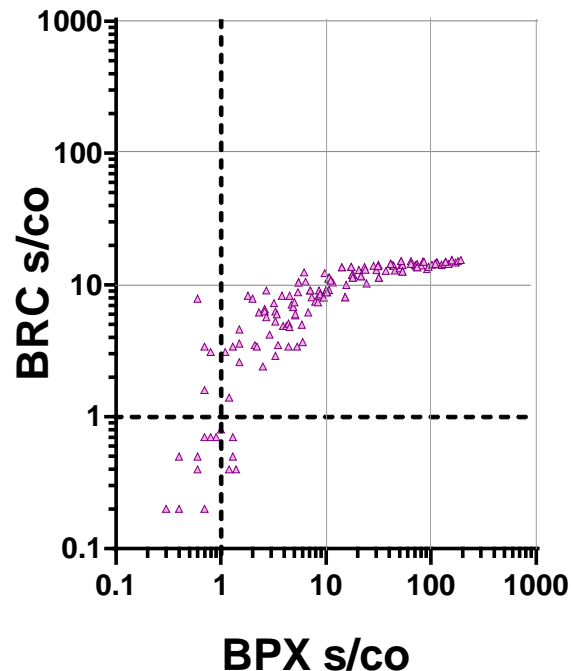


# 4<sup>th</sup> Gen Immunoassays 24 Weeks After ART

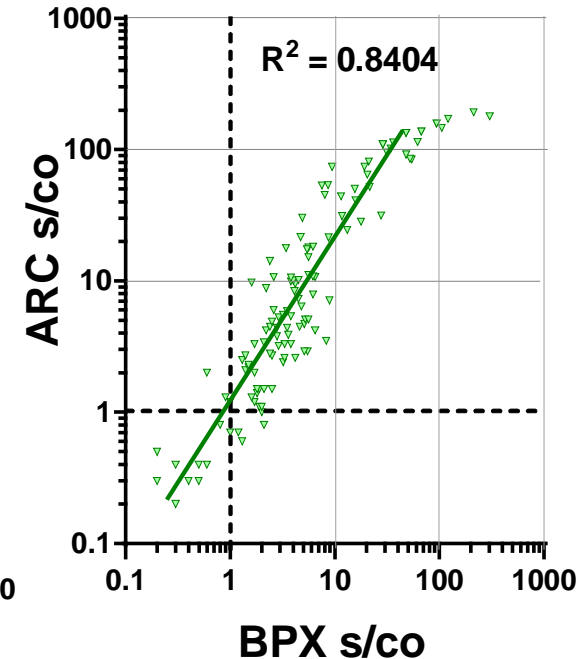
## ARC vs BRC



## BPX vs BRC



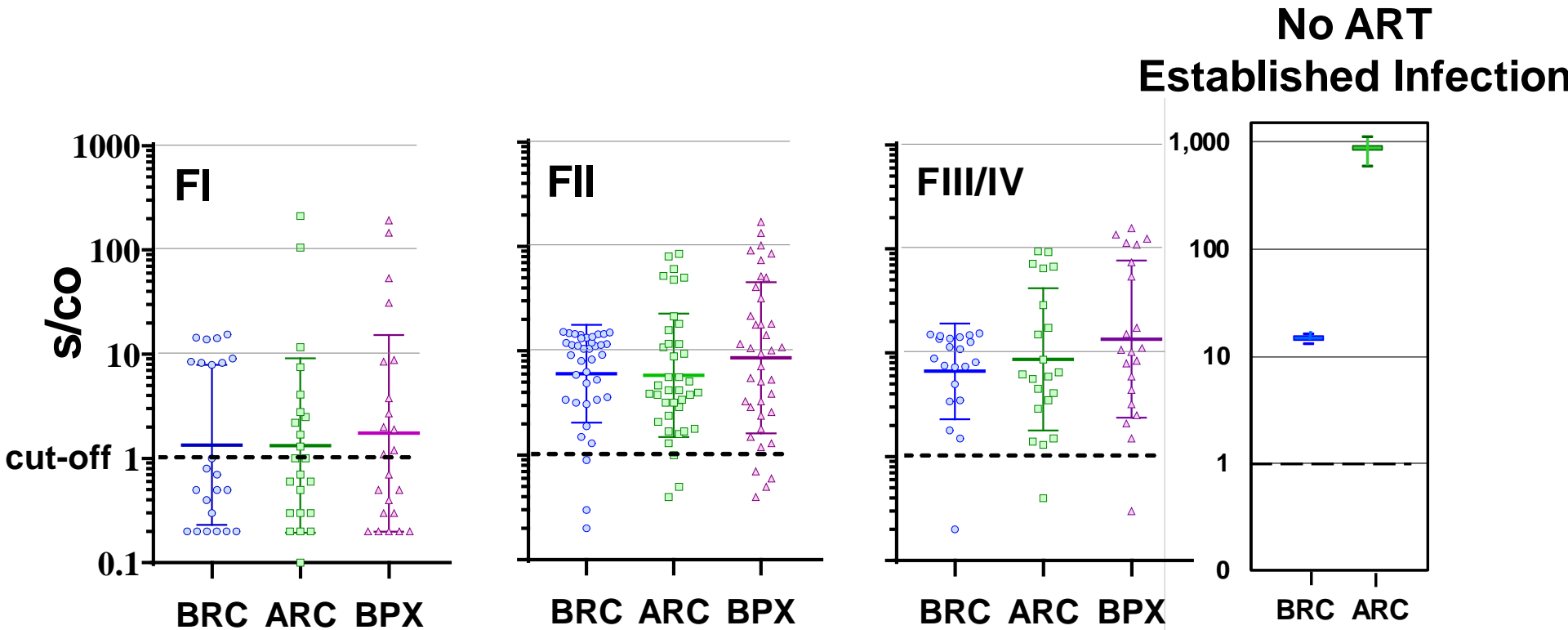
## BPX vs ARC



- BRC reaches max signal at S/CO 14
- ARC and BPX continue to higher S/CO to >100
- ARC and BPX signal highly correlated

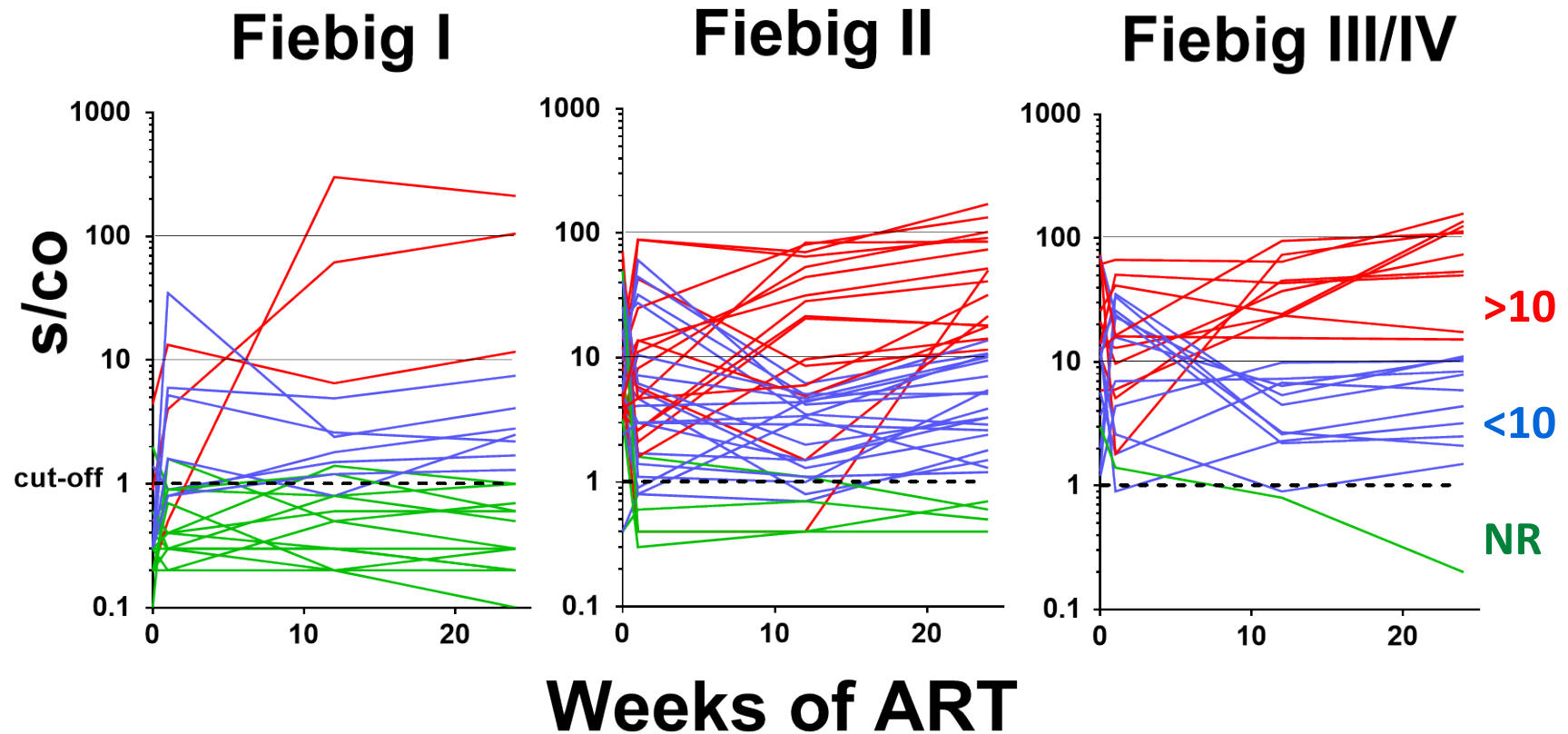
$$R^2 = 0.8404$$

# S/CO at 24 Weeks After Early ART



- FI S/CO remains close to cut-off, most NR
- FII Increased S/CO compared to FI, Fewer NR
- FIII/IV Low, but Reactive S/CO, Very few NR
- No ART Established Infection;  
S/CO BRC 13.5-15.0; ARC 800-1200: BPX >200

# Time Course of BPX Reactivity After ART

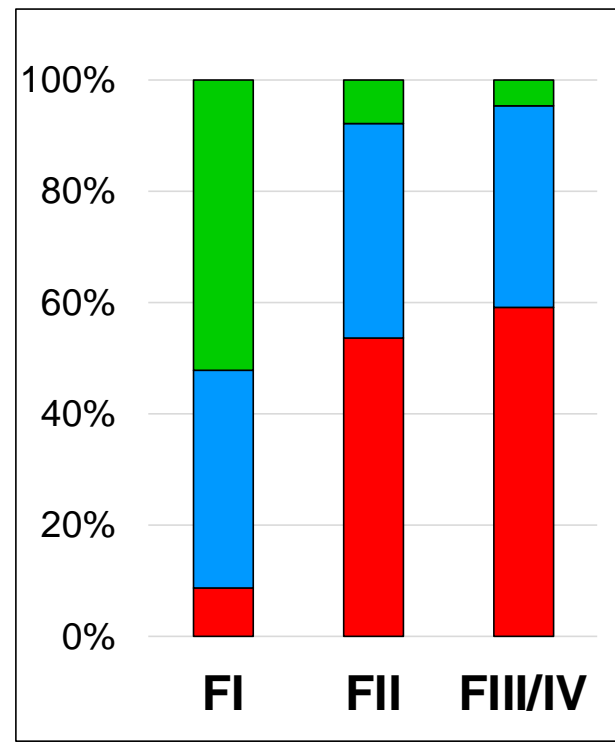
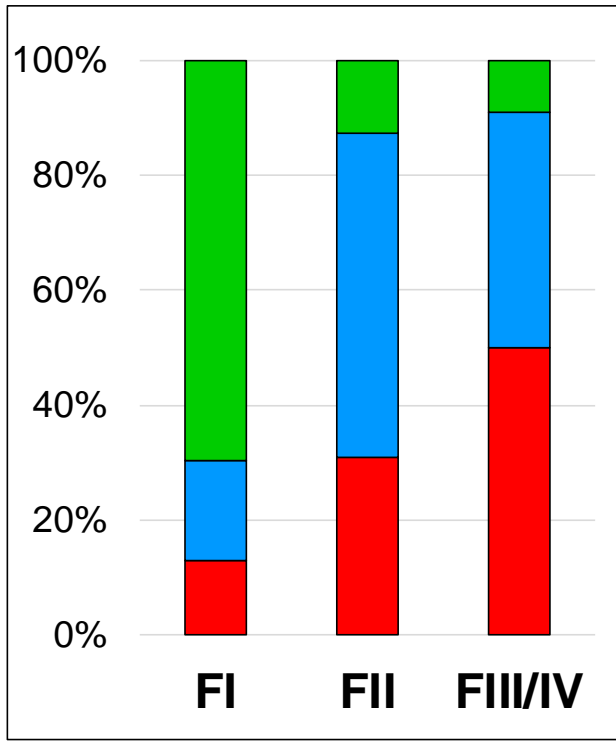


- Transient increase in signal in some individuals at week 1
- Decrease to low level and little increase thereafter
- Seroreversion observed in some individuals

# Reactivity of BPX at 24 weeks after Early ART

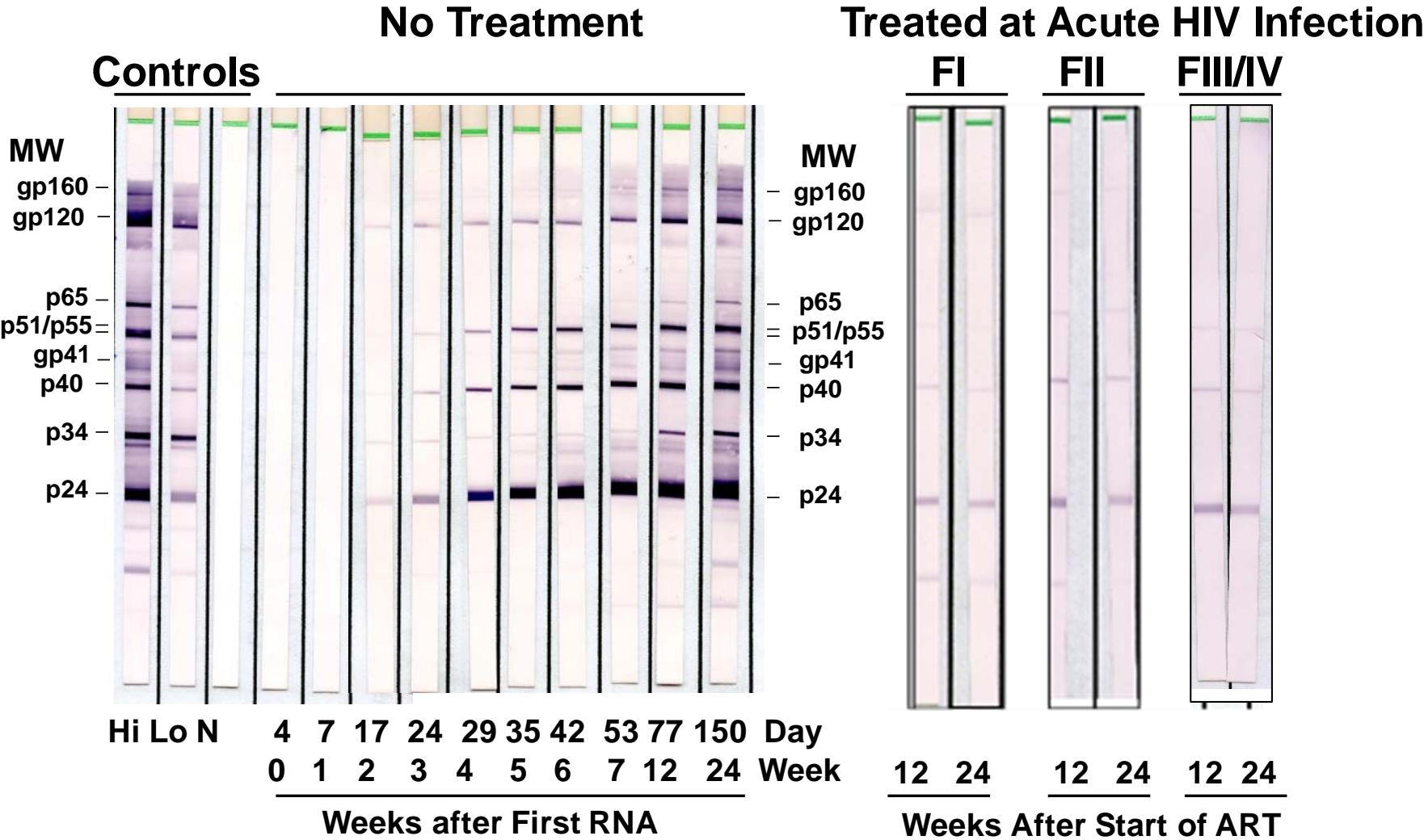
	Week 12		
	FI	FII	FIII/IV
NR	69.6%	12.8%	9.1%
S/CO <10	17.4%	56.4%	40.9%
S/CO >10	13.0%	30.8%	50.0%
Total	100.0%	100.0%	100.0%

	Week 24		
	FI	FII	FIII/IV
NR	52.2%	7.7%	4.5%
S/CO <10	39.1%	38.5%	36.4%
S/CO >10	8.7%	53.8%	59.1%
Total	100.0%	100.0%	100.0%

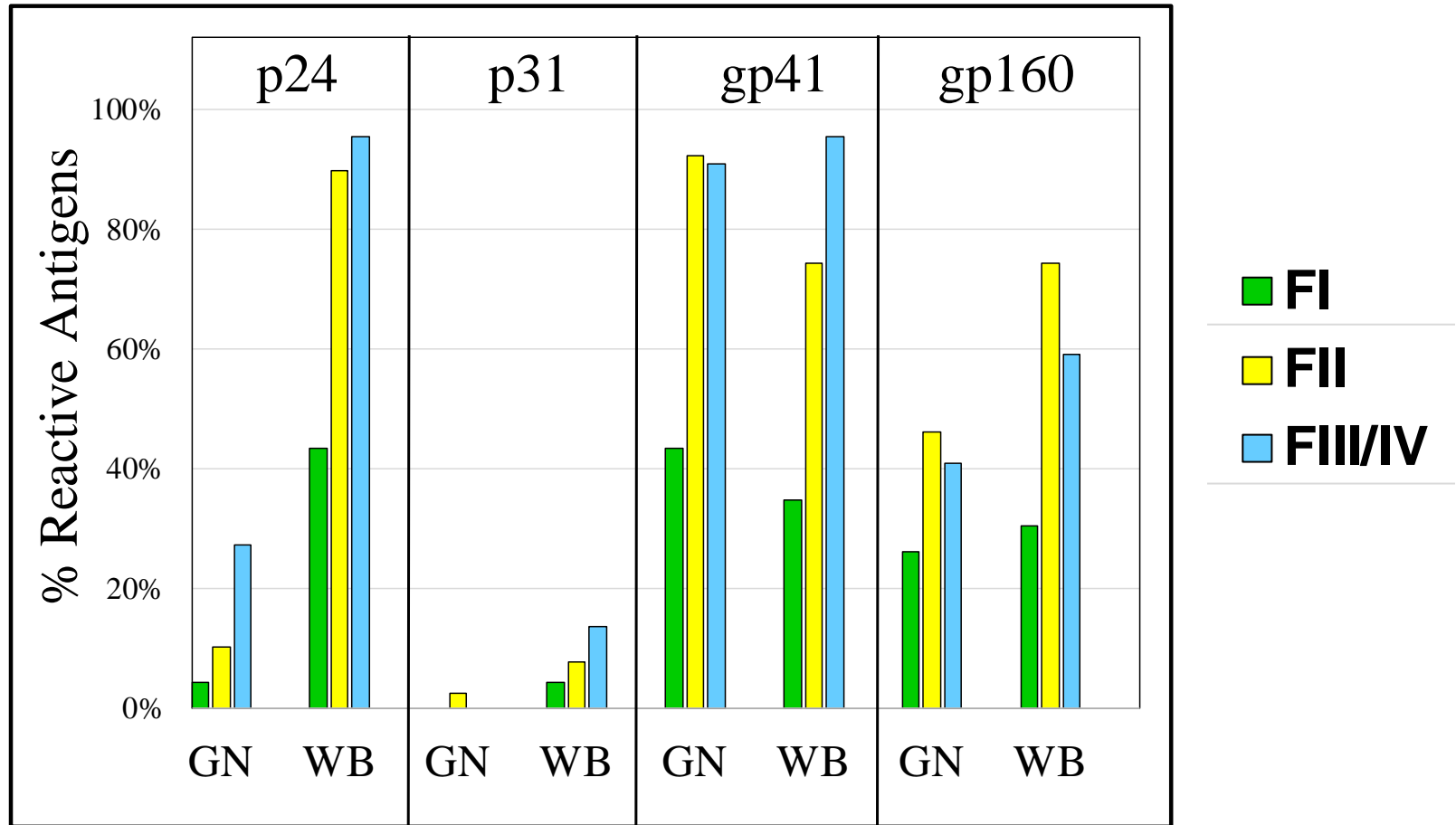


■ NR ■ S/CO <10 ■ S/CO >10

# Evolution of Western Blot Ag Reactivity



# Geenius and WB Ag at 24 Weeks After Early ART

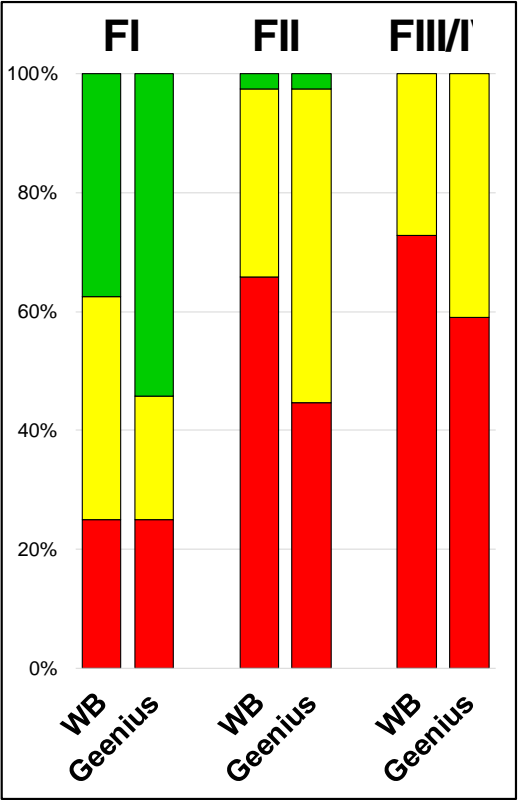


- Geenius and WB have comparable sensitivity for gp41 and gp160
- Geenius is less sensitive for p24 (early Ag)
- Both assays have low sensitivity for p31 (late Ag)

# Genius and WB Reactivity at 12-24 Weeks After ART

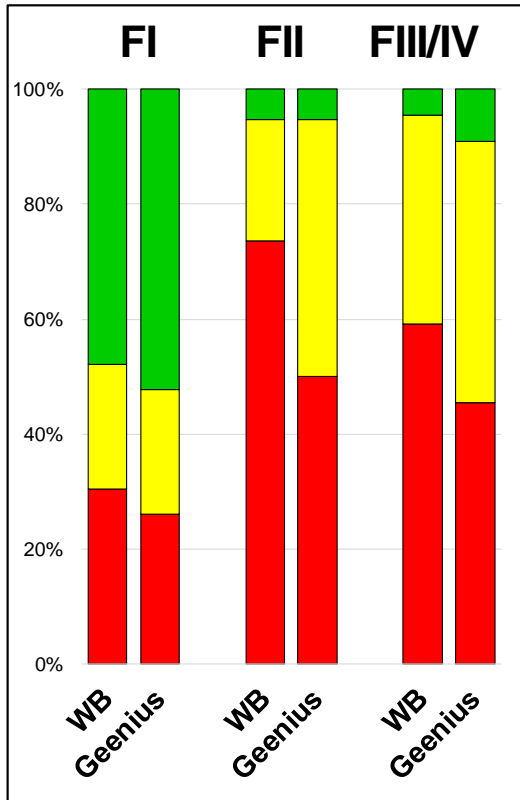
Week 12

	Fiebig I		Fiebig II		Fiebig III/IV	
	WB	Genius	WB	Genius	WB	Genius
R	25.0%	25.0%	65.8%	44.7%	72.7%	59.1%
IND	37.5%	20.8%	31.6%	52.6%	27.3%	40.9%
NR	37.5%	54.2%	2.6%	2.6%	0.0%	0.0%
	100%	100%	100%	100%	100%	100%



Week 24

	Fiebig I		Fiebig II		Fiebig III/IV	
	WB	Genius	WB	Genius	WB	Genius
R	30.4%	26.1%	73.7%	50.0%	59.1%	45.5%
IND	21.7%	21.7%	21.1%	44.7%	36.4%	45.5%
NR	47.8%	52.2%	5.3%	5.3%	4.5%	9.1%
	100%	100%	100%	100%	100%	100%



■ NR ■ IND ■ R

# Conclusions I

- Evolution of serological markers in untreated individuals develops rapidly with time post infection
- Reduction in immune response by early ART can confound the ability of serological assays to correctly classify HIV infectious status
- At 24 Weeks of therapy:
  - 52.2% of those initiating ART at FI, 7.7% at FII, and 4.5% at FIII/IV remain 4<sup>th</sup> Gen NR; 36-39% of samples demonstrated low S/CO (<10)
  - Bio-Rad GS, Abbott Architect, Bio-Rad BioPlex: comparable results
  - Geenius Reactive in only 26.1%, 43.6% and 45.5% of individuals initiating ART at FI, II, and III/IV
  - HIV-1 Western Blot was slightly more sensitive



# Conclusions II

- These results have implications in monitoring individuals who initiate ART in acute infection or participate in programs such as:
  - Treatment as Prevention (TasP)
  - Pre-Exposure Prophylaxis (PrEP)
  - Post Exposure Prophylaxis (PEP)
  - HIV Cure studies.
- Consider a contextual algorithm for testing of ART treated populations
- Alternative approaches such as testing for cell-associated HIV RNA/DNA may be required to rule out HIV-1 infection (Jagodzinski, J Clin Micro 2019)

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## **RV254/SEARCH010**

- SE Asia Research Collaboration with Hawaii

## **RV217 Sites**

- AFRIMS-Thailand
- MUWRP-Uganda
- MMRP-Tanzania
- WRP-Kericho

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