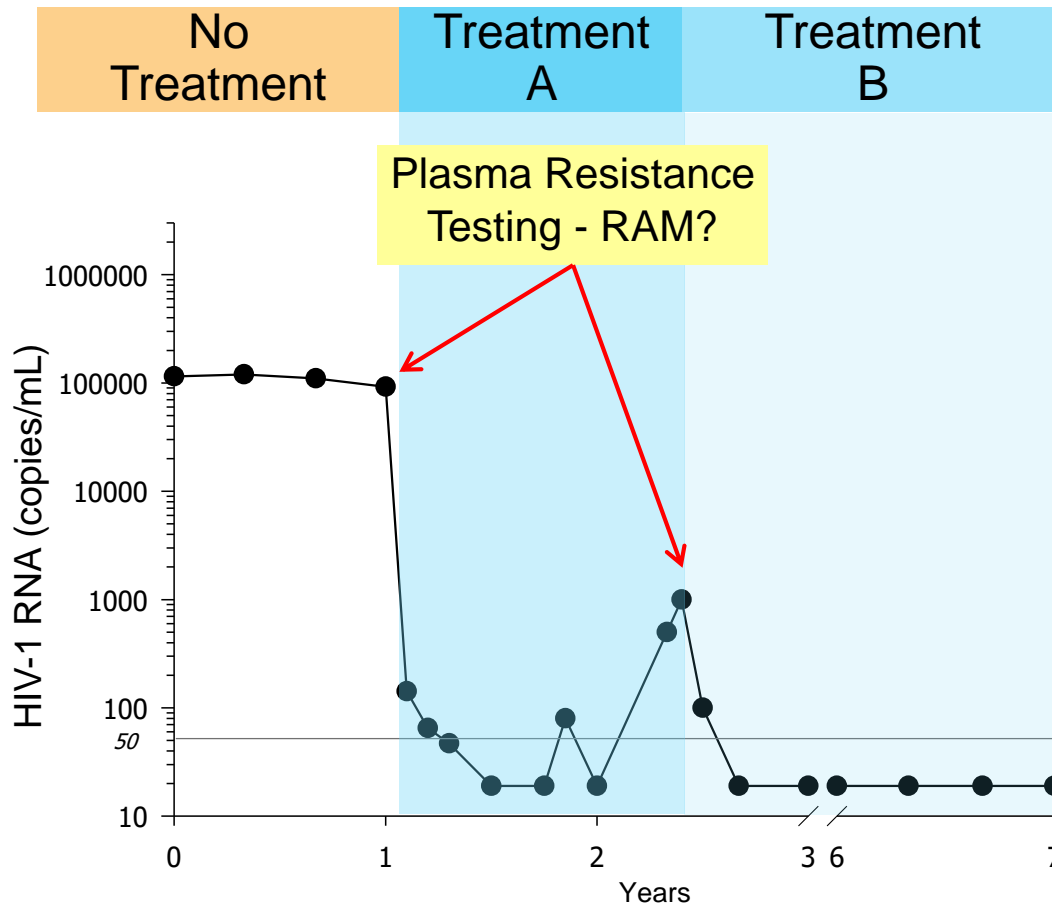


Differential Detection of M184V/I  
Between Plasma Historical HIV Genotypes  
and Proviral DNA from PBMCs

Margot N, Ram R, McNicholl IR, Haubrich R, Callebaut C.  
Gilead Sciences

HIV DART, 27-29 November, 2018, Miami FL

# HIV Resistance Testing and Antiretroviral Therapy



# Suppressed Patients

## Resistance Testing

### Treatment Switch (VL<50 c/mL)

#### Resistance Associated Mutations

- Prior Virologic Failure (VF)
  - i.e. M184V/I, 40-50% patients w/VF (high-level resistance to 3TC and FTC and low-level resistance to ABC)
- Transmitted Drug Resistance
  - K103N, TAMs

*Miller et al AVT, 2012*

*Margot et al JID, 2017*

HIV DNA  
Resistance Testing  
*Integrated Virus*

• Hospital  
laboratory

• Monogram  
• Quest  
• SeqIT

Study 1824: CRO selected  
(*validated assay*)

# Study 1824

## Switch Study

- HIV-1-infected Adults
- Switch from 2 NRTIs + 3<sup>rd</sup> agent
- HIV-1 RNA < 50 c/mL

- Historical Genotype showing M184V/I  
Part 1: M184V/I only  
Part 2: M184V/I ±0-2 TAMs

- No exclusionary mutation in HIV DNA analysis

N = 63

E/C/F/TAF QD

12 weeks  
Primary  
Endpoint\*

24 weeks  
Secondary  
Endpoint\*\*

48 weeks

(\*) Perez-Valero IDRW, 2017

(\*\*) Perez-Valero WorldAIDS, 2018

} 100% Suppression using  
Pure Virologic Failure

Historical reports  
(local lab and  
commercial sources)

GenoSure Archive  
(Monogram)

## Detection of M184V or I (N=87)

Historical report vs. Archive

- Paired historical & Archive data available for 87 screened patients

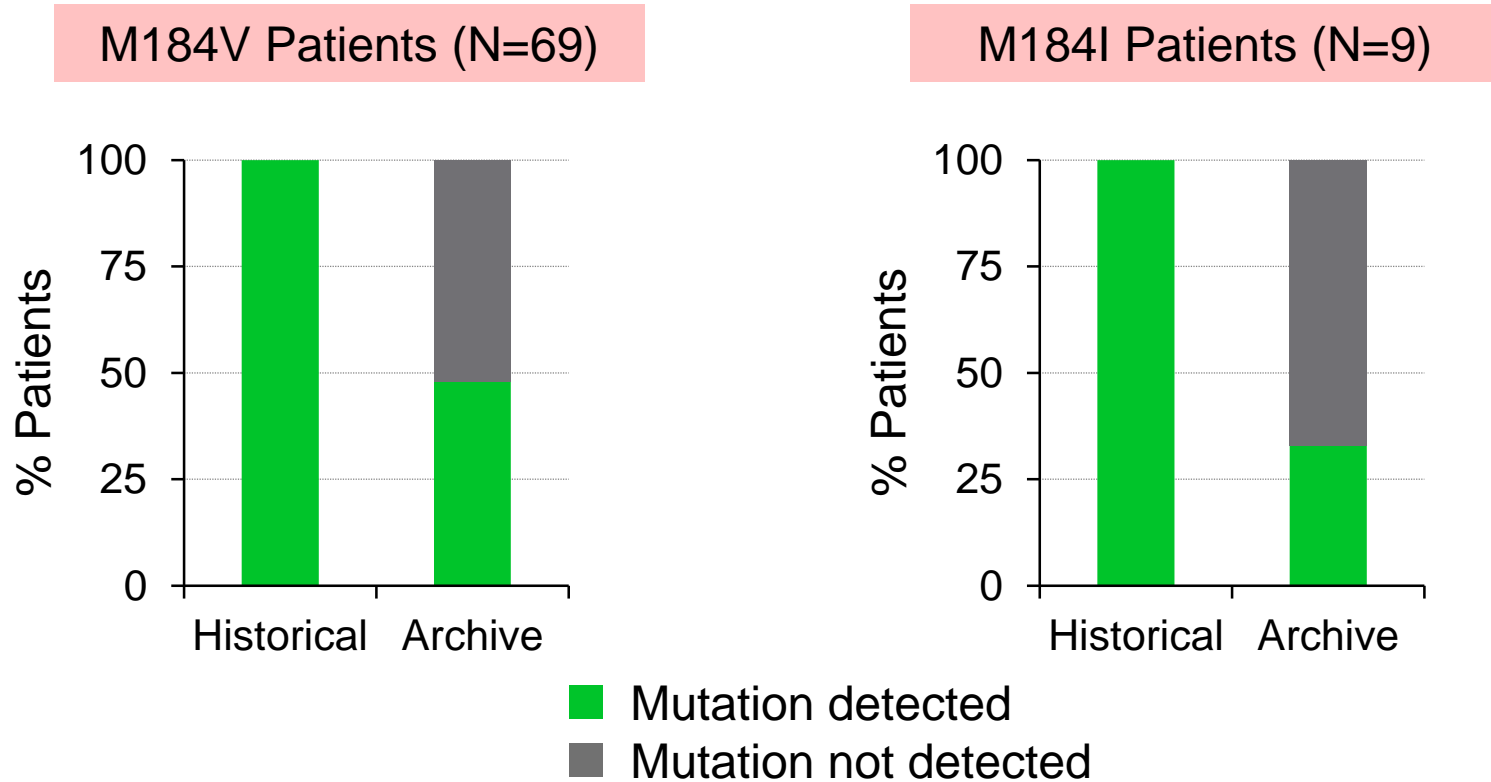
Genotype	“Historical” (plasma; N=87)	“Archive” (HIV DNA; N=87)
M184V	78%	38%
M184I	11%	3%
M184V/I	11%	7%
Assay Failure	N/A	8%
WT	N/A	44%

100% (sum of M184V, M184I, and M184V/I in Historical)  
48% (sum of M184V, M184I, and M184V/I in Archive)

- Archive: Mutation detected in only 48% patients

# Presence of M184V and M184I

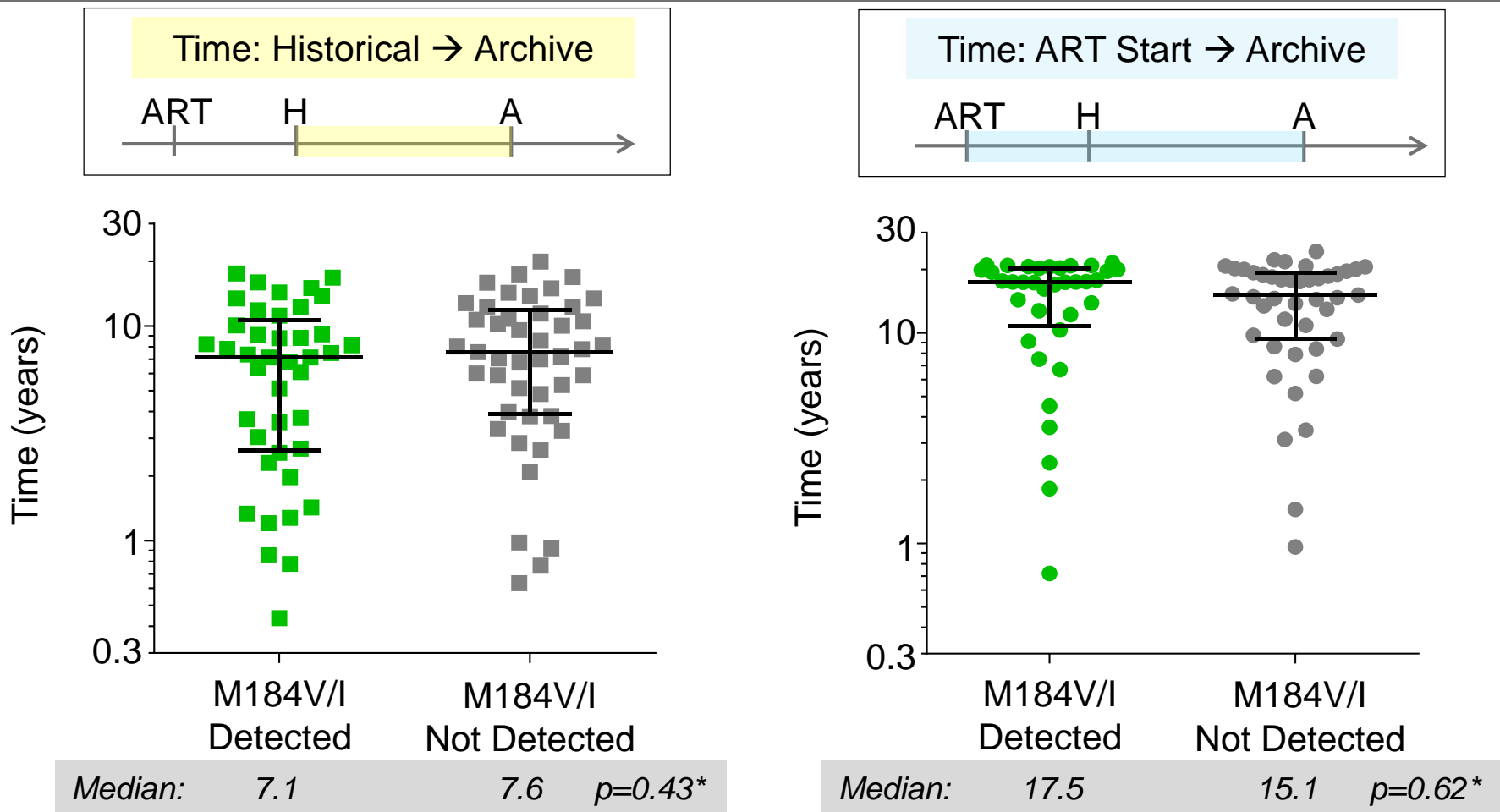
Historical report vs. Archive



- M184V: detected with Archive in 48% patients
- M184I: detected with Archive in 33% patients

# Detection of M184V/I in Archive Assay

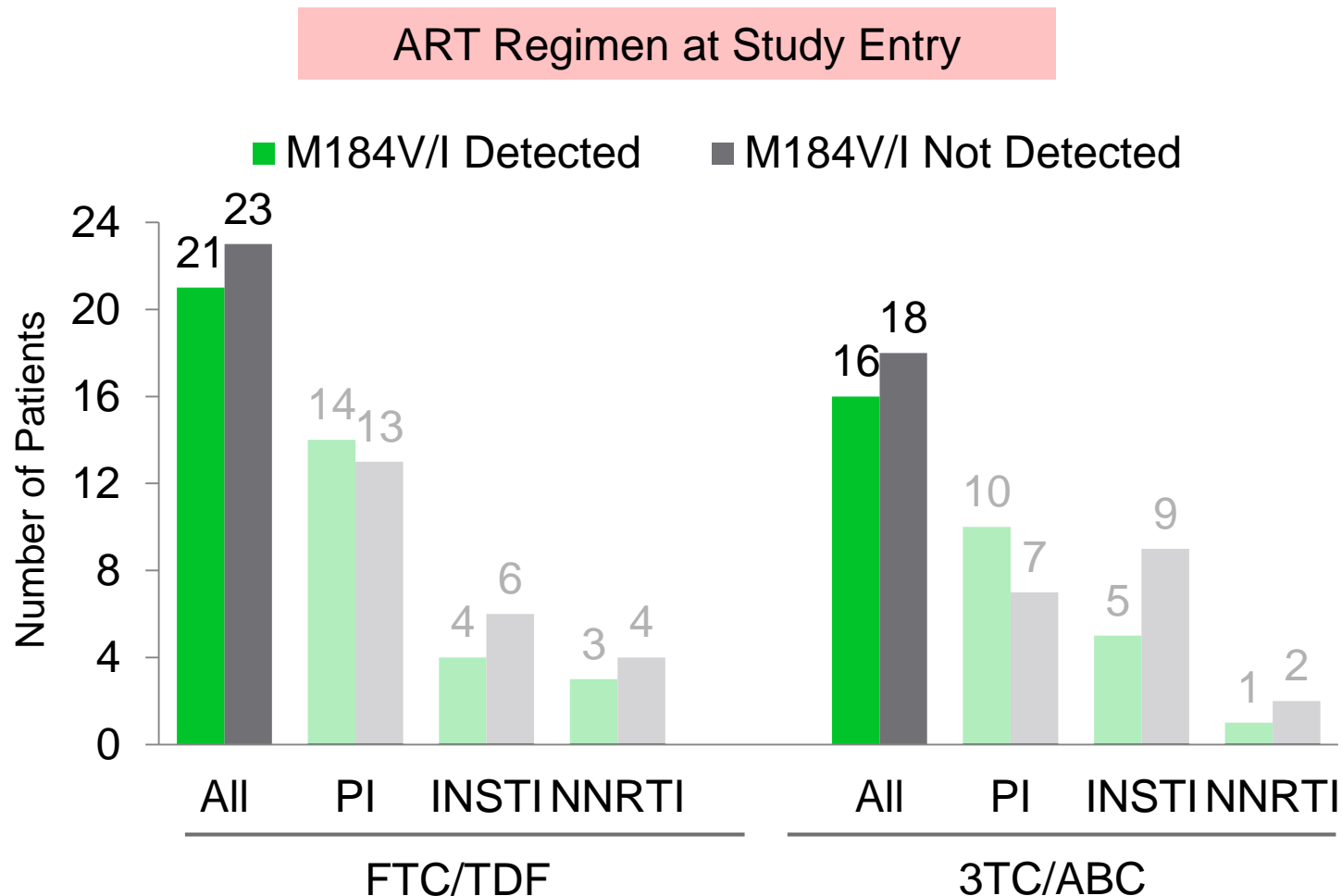
Lack of Detection due to Time from Historical to Archive Sample?



- Differential detection not due to sample timing or time on ART

# Detection of M184V/I in Archive Assay

ART Regimen at Baseline (n=78)



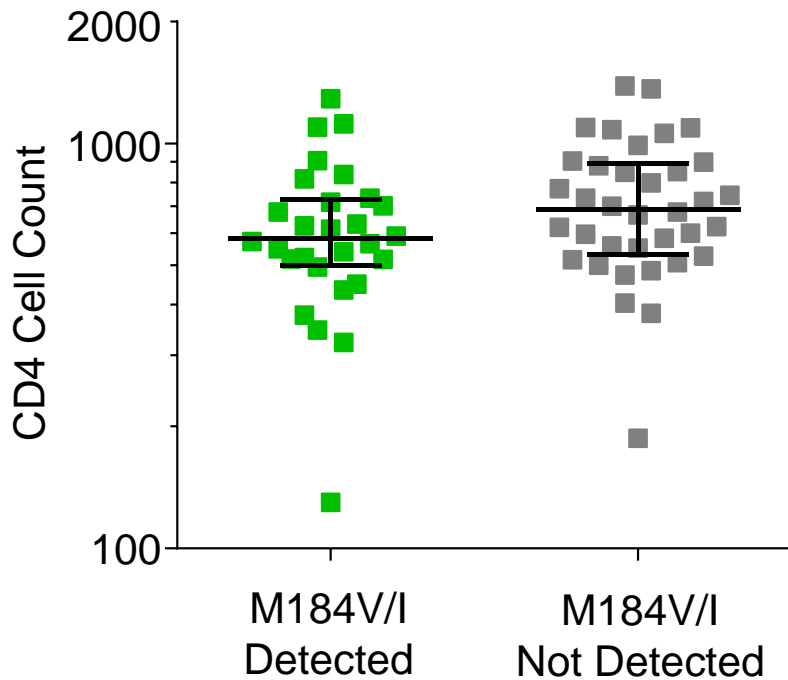
- Differential detection not associated with baseline regimen



# Detection of M184V/I in Archive Assay

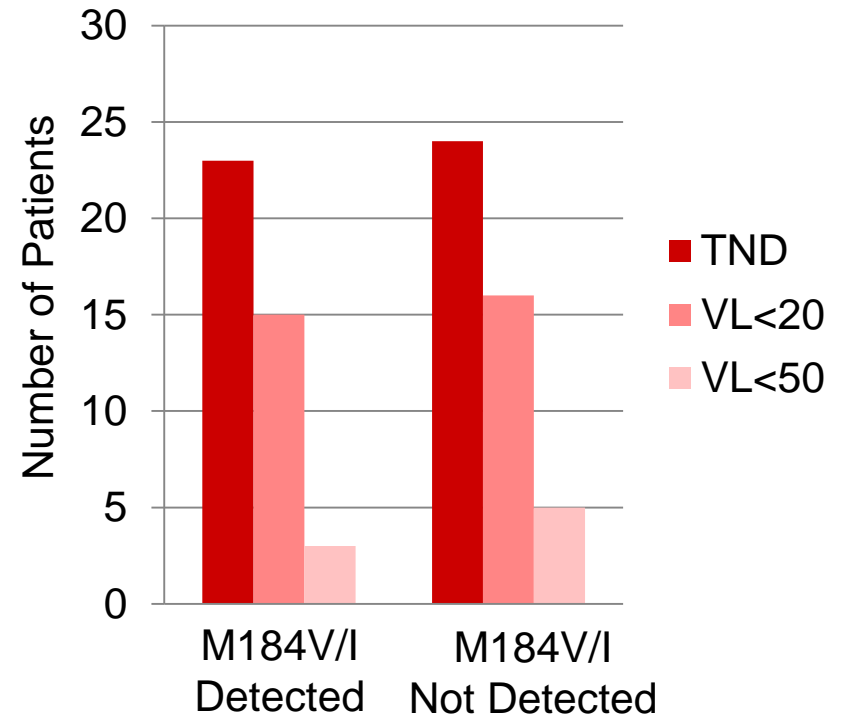
Lack of Detection Linked to CD4 Cell Count or HIV-1 RNA?

CD4 Cell Count at Baseline



Median: 582 689  $p=0.13^*$

HIV-1 RNA at Baseline



- Differential detection not associated with Baseline CD4 count or viral load

# Conclusions

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- In subjects with documented prior M184V/I on historical genotype
  - M184V not detected in 52% with Archive assay
  - M184I not detected in 67% with Archive assay (A3G?)
- Difference in detection of M184V/I not associated with:
  - Time between historical and archived testing
  - Time on ART
  - Prior treatment regimen
  - Baseline CD4 count
  - HIV-1 RNA detection (TND, <20, <50)
- Not detecting M184V/I may have potential clinical consequences when switching patients to 2-drug treatment containing FTC or 3TC
  - Presence of M184V/I confers high-level resistance to FTC and 3TC

# Acknowledgments

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- 1824 Study Investigators and Staff

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- E/C/F/TAF Project Team