



ORAL ABSTRACT

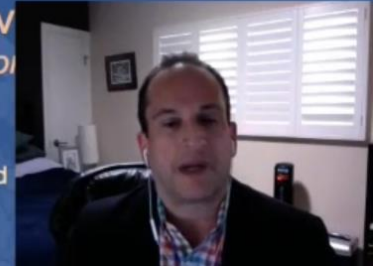
# Laboratory Analysis of HIV Infections in HPTN 083: Injectable CAB for PrEP

Marzinke M, Grinsztejn B, Fogel J, Piwowar-Manning EM, Hanscom B, Coelho L, Cohen MS, Rinehart AR, Rooney JF, Adeyeye A, Anderson P, McCauley M, Landovitz R, Eshleman S, for the HPTN 083 Study Team

**Presenting Author:** Raphael J. Landovitz  
University of California

*Disclosure:*

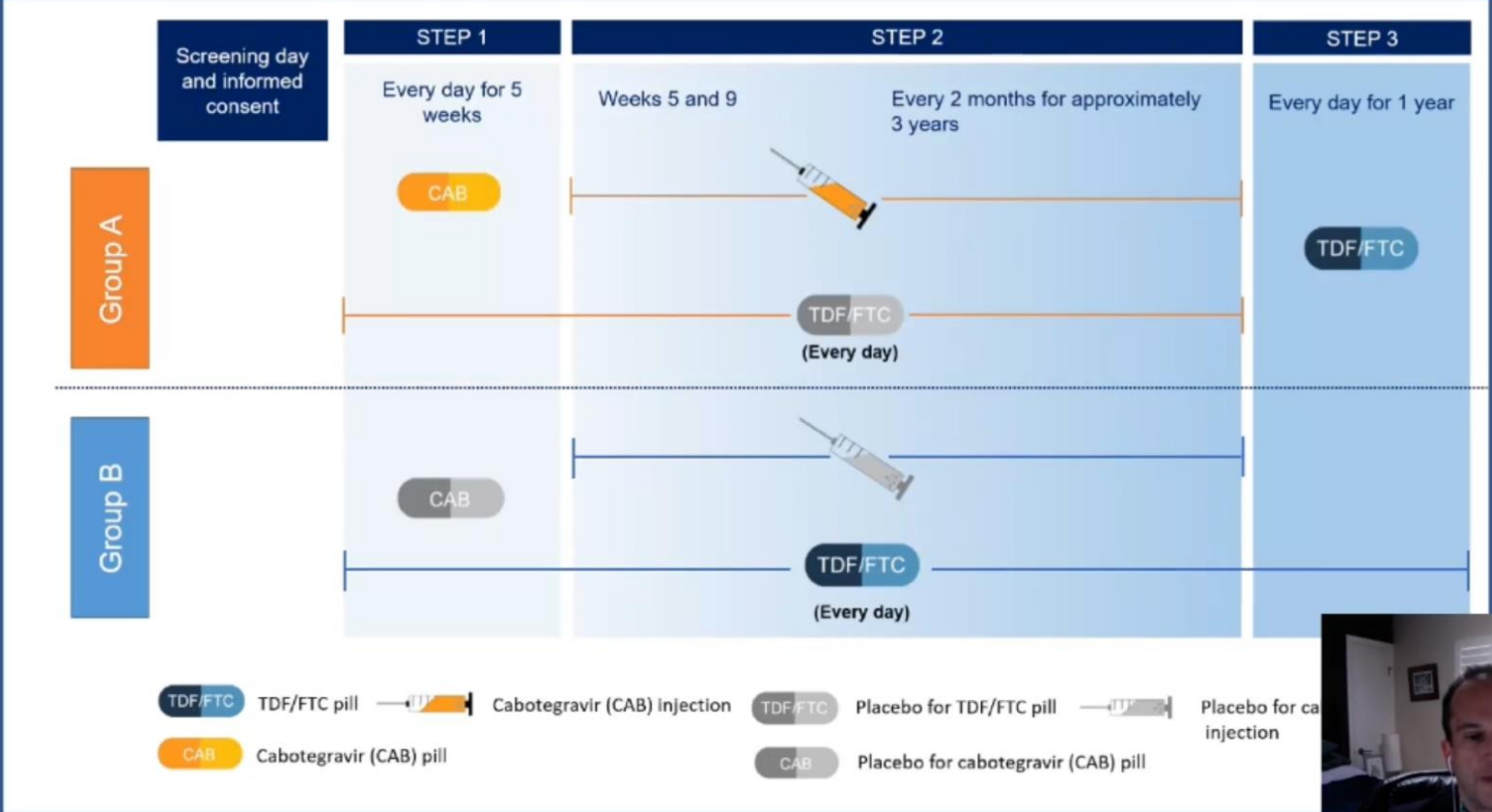
Raphael J. Landovitz has served on scientific advisory boards for Gilead Sciences and Merck Inc, and has received honoraria from Roche, Inc and Janssen.



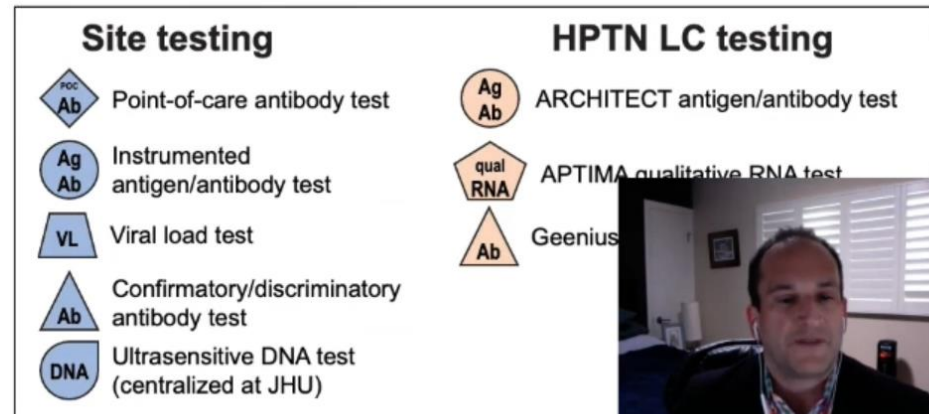
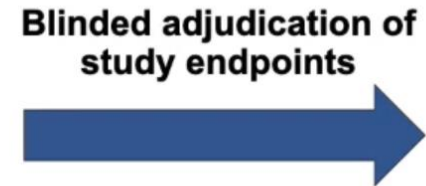
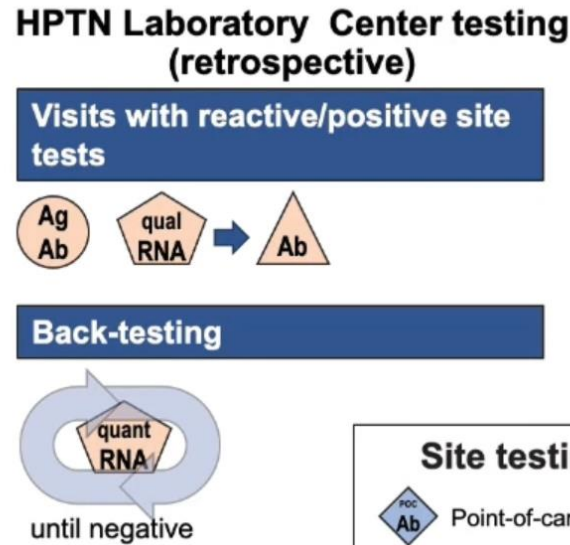
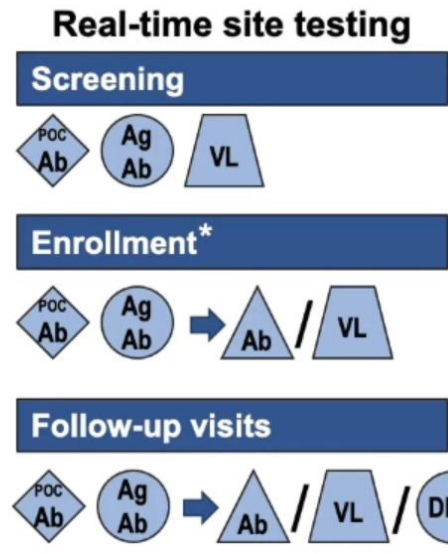


# HPTN 082 Study Design

livestream.com befindet sich jetzt im Vollbildmodus. [Vollbild beenden \(Esc\)](#)



# Pre-specified HIV Testing



\*Selected cases



# Extended HPTN LC Testing

## HIV testing

### Back-testing



**CAB arm:** All visits  
**TDF/FTC arm:** Enrollment, weeks 2, 4, 5



**CAB arm:** Enrollment plus three visits prior to the first RNA pos visit  
**TDF/FTC arm:** Enrollment plus one visit prior to the first RNA pos visit



If Ag/Ab test reactive



If qualitative RNA test reactive



Selected cases/visits

## HIV genotyping (VL >500 c/mL)

### CAB arm

- All study visits

### TDF/FTC arm

- First HIV positive visit
- First site positive visit

## Pharmacology testing

### CAB concentrations

#### CAB arm

Plasma [CAB]: all study visits  
Plasma [TFV]: baseline infections, step 3 infections  
DBS [TFV-DP]: step 3 infections

### TDF/FTC concentrations

Plasma [TFV]: first site pos, first HIV pos, 3 prior visits  
DBS [TFV-DP]: first site pos, 1 prior visit



ARCHITECT antigen/antibody test



APTIMA qualitative RNA test



Geenius discriminatory antibody test



Viral load test

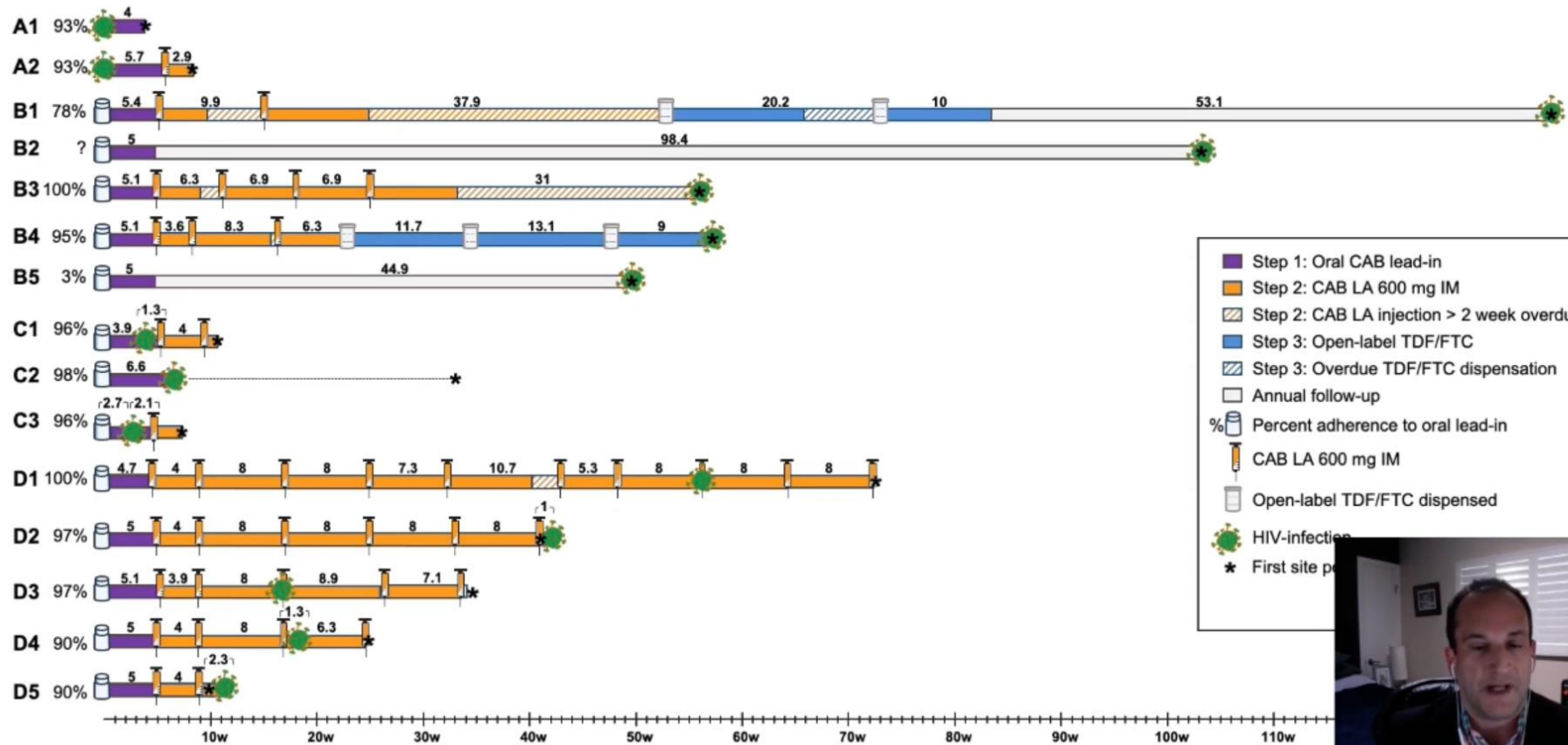


Single copy RNA test





# 13 Incident, 2 baseline Infections: Cabotegravir

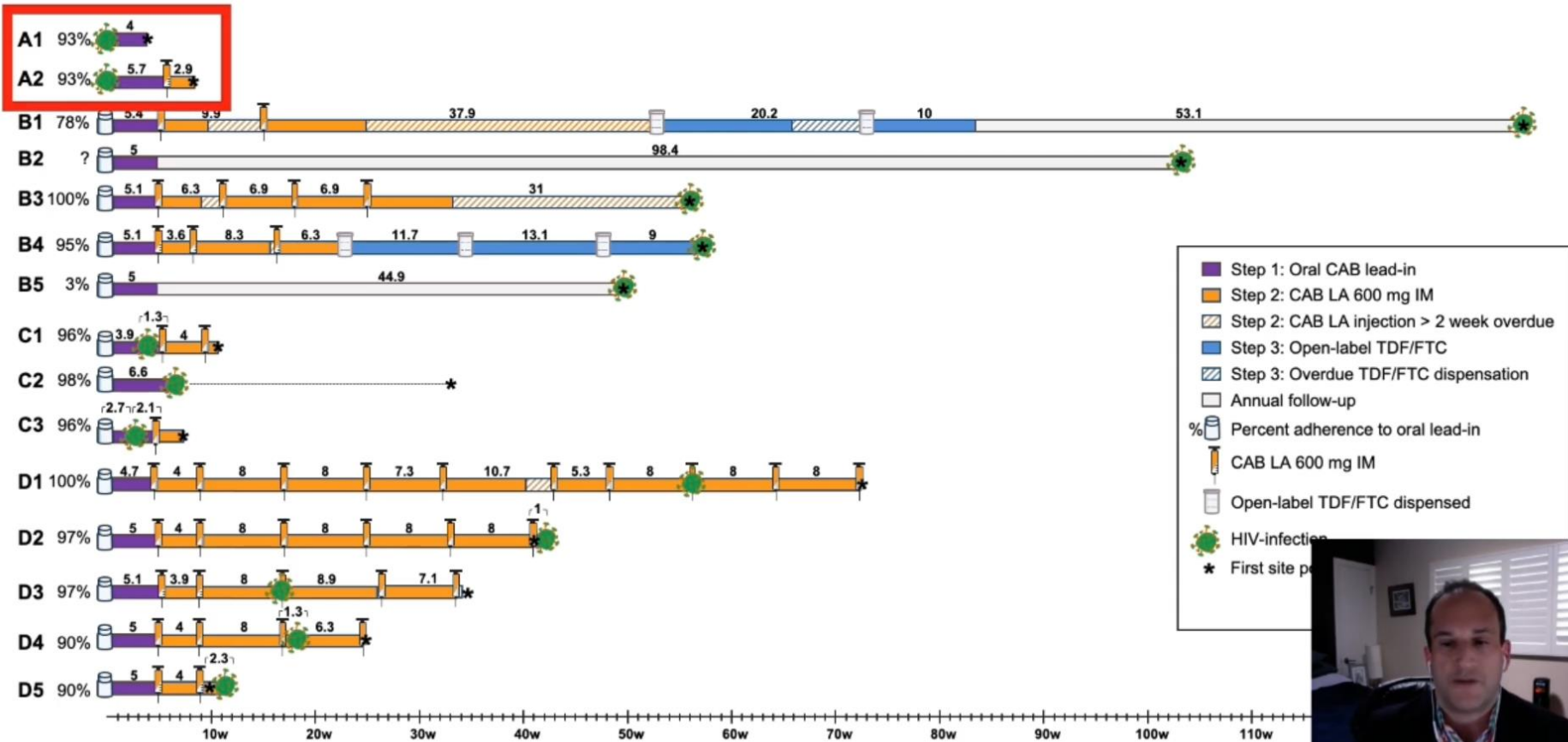


- Step 1: Oral CAB lead-in
- Step 2: CAB LA 600 mg IM
- Step 2: CAB LA injection > 2 week overdue
- Step 3: Open-label TDF/FTC
- Step 3: Overdue TDF/FTC dispensation
- Annual follow-up
- Percent adherence to oral lead-in
- CAB LA 600 mg IM
- Open-label TDF/FTC dispensed
- HIV-infection
- First site positive



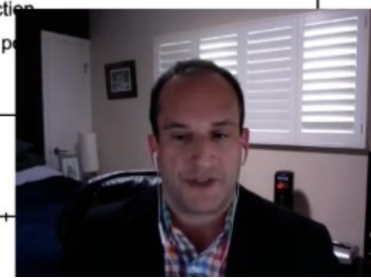
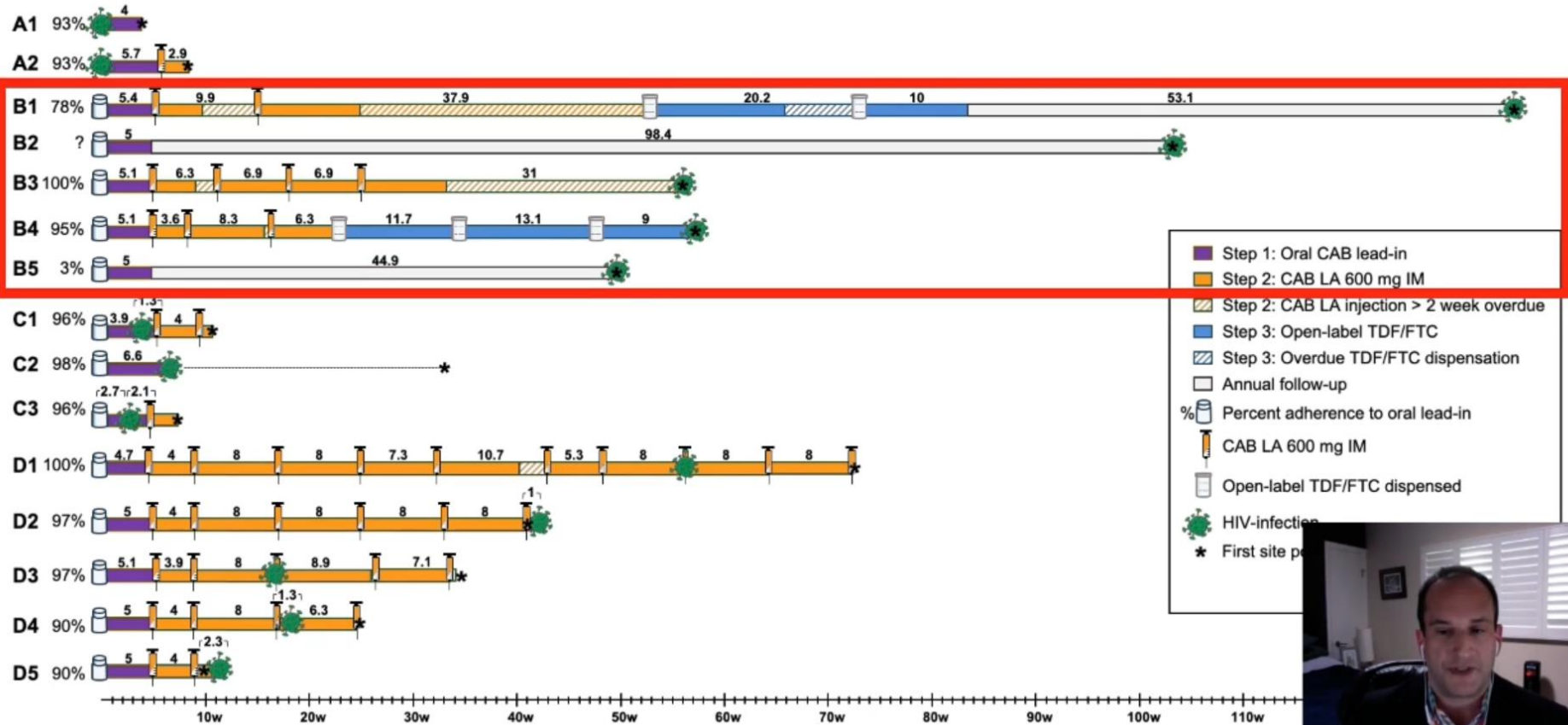


# 13 Incident, 2 baseline Infections: Cabotegravir



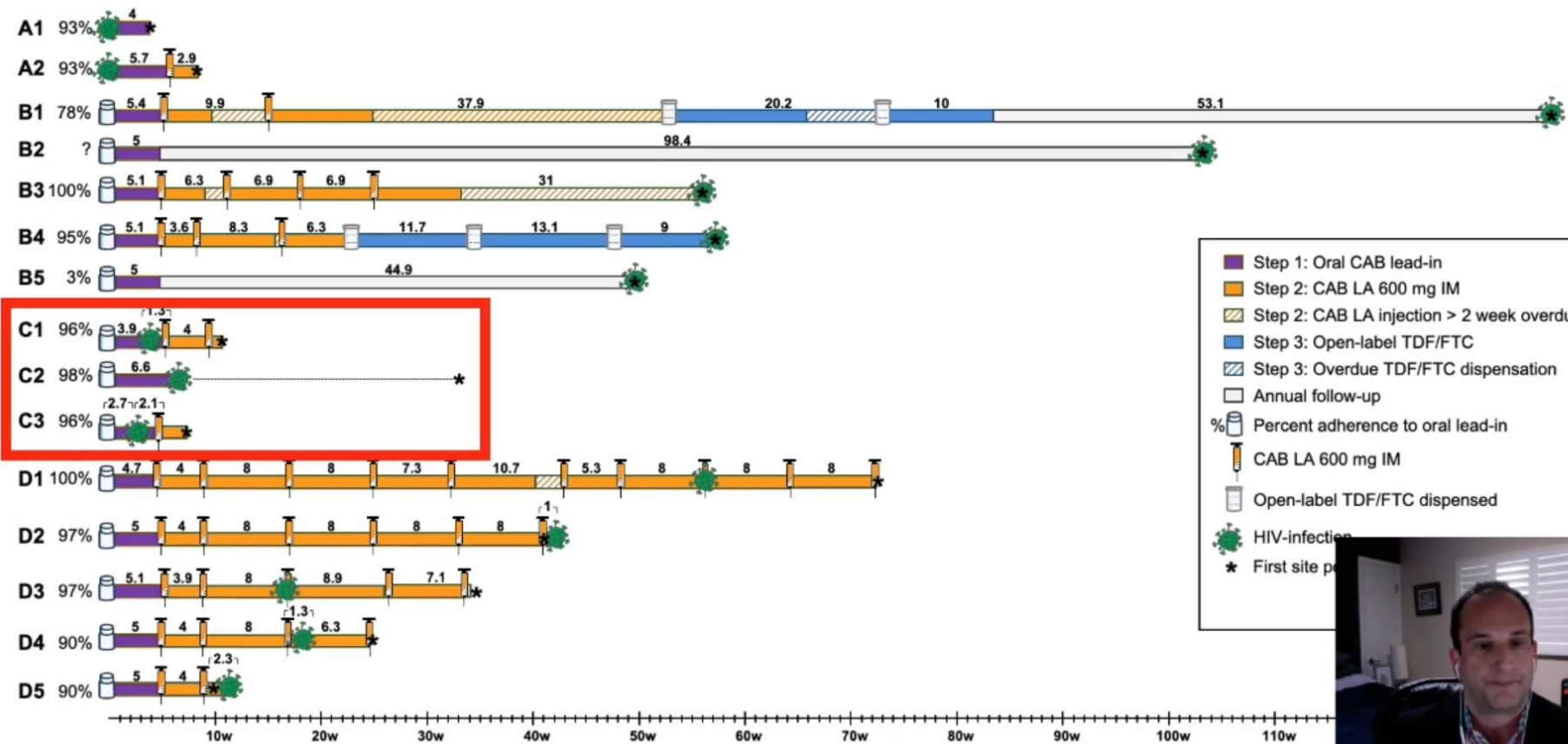


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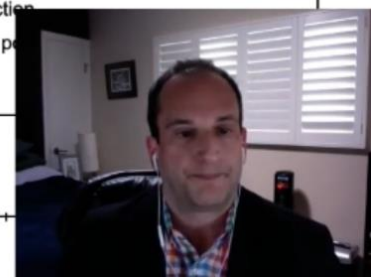




# 13 Incident, 2 baseline Infections: Cabotegravir



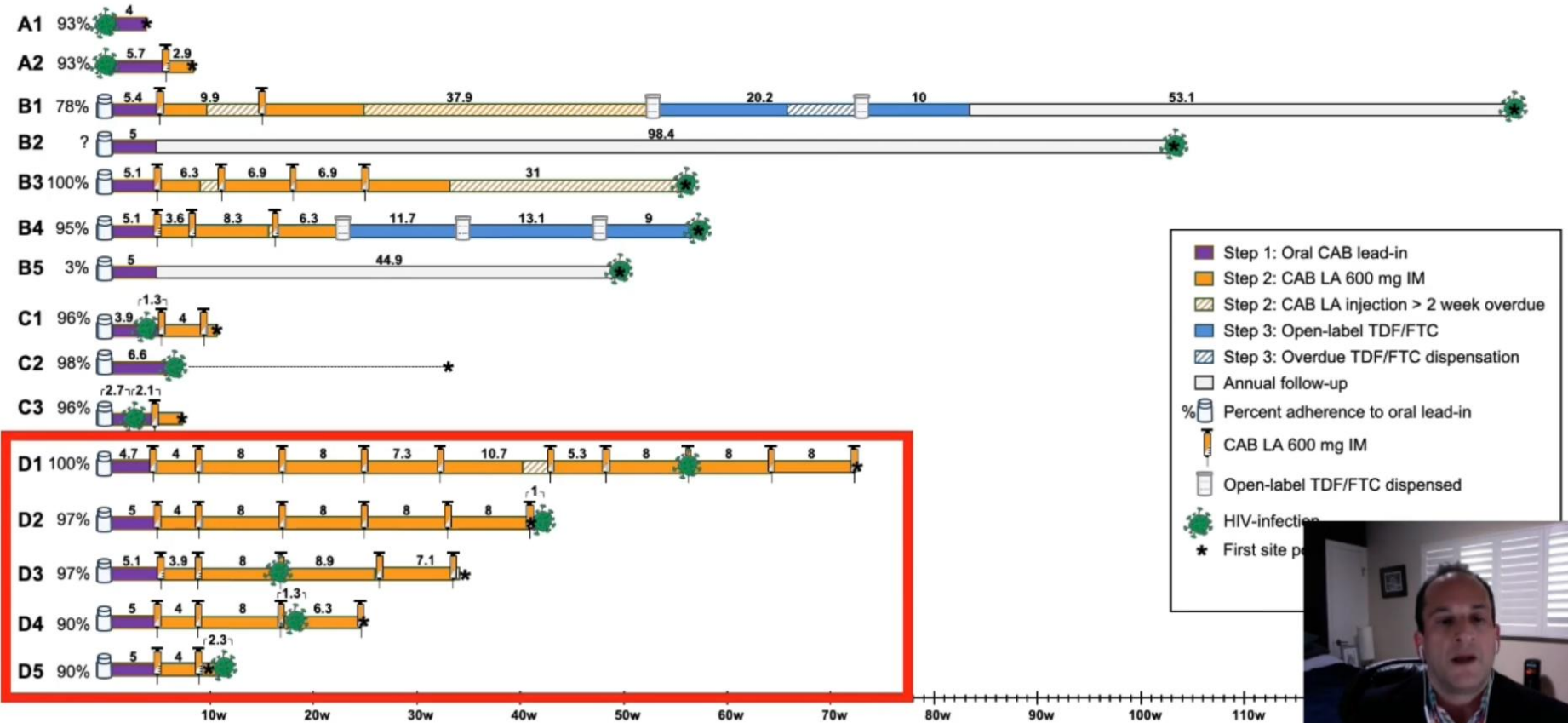
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- CAB LA 600 mg IM
- Open-label TDF/FTC dispensed
- HIV-infection
- \* First site positive





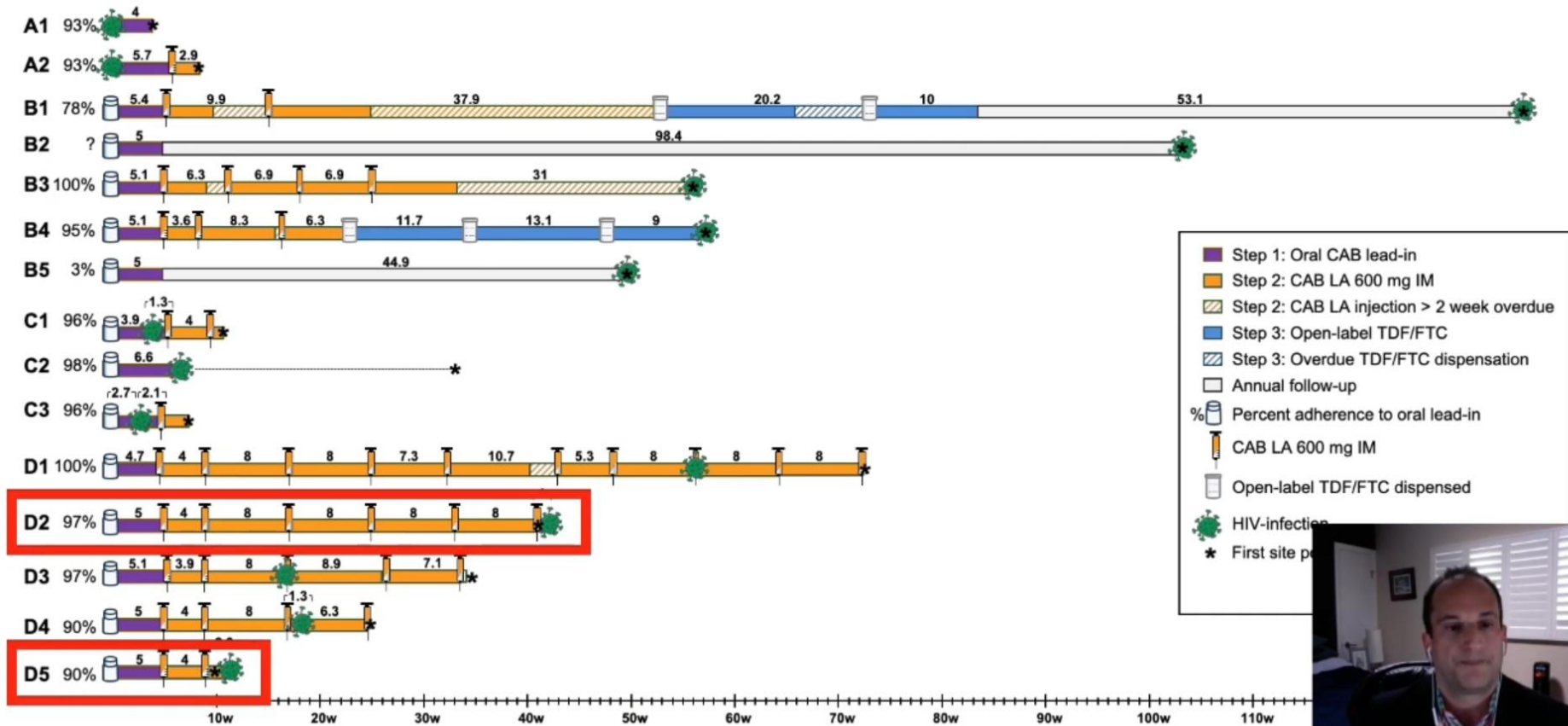


# 13 Incident, 2 baseline Infections: Cabotegravir



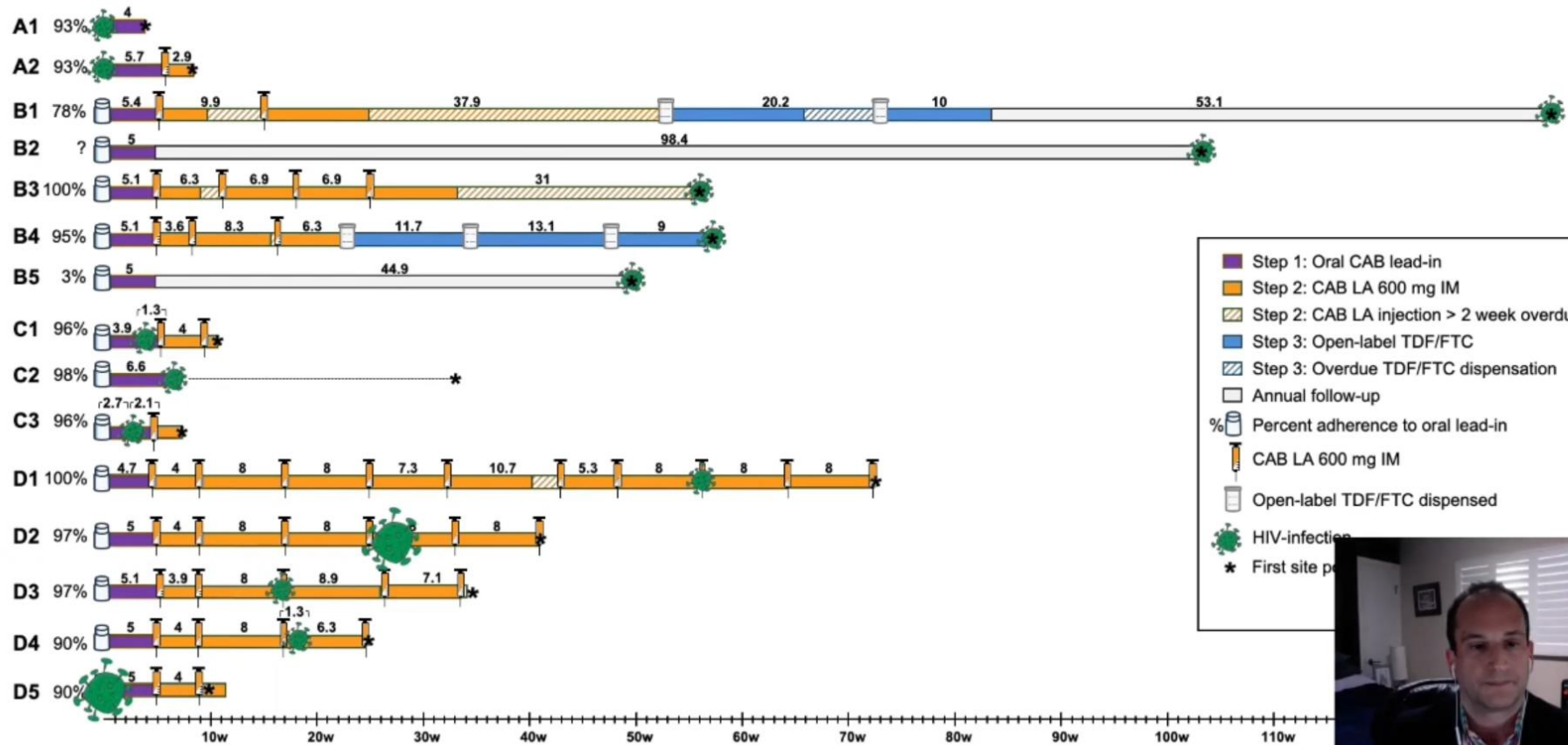


# 13 Incident, 2 baseline Infections: Cabotegravir





# 13 Incident, 2 baseline Infections: Cabotegravir

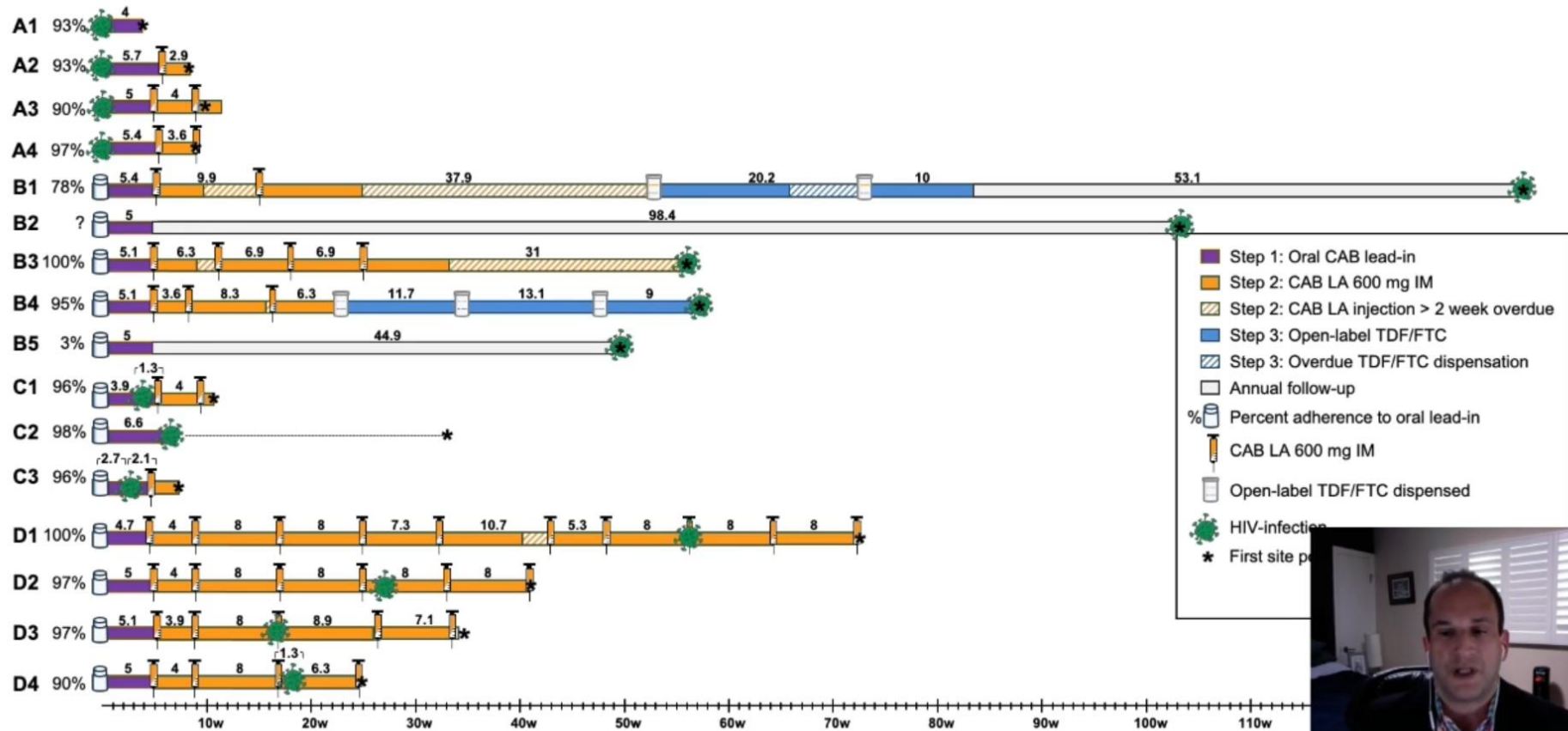


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- % Percent adherence to oral lead-in
- CAB LA 600 mg IM
- Open-label TDF/FTC dispensed
- HIV-infection
- First site positive



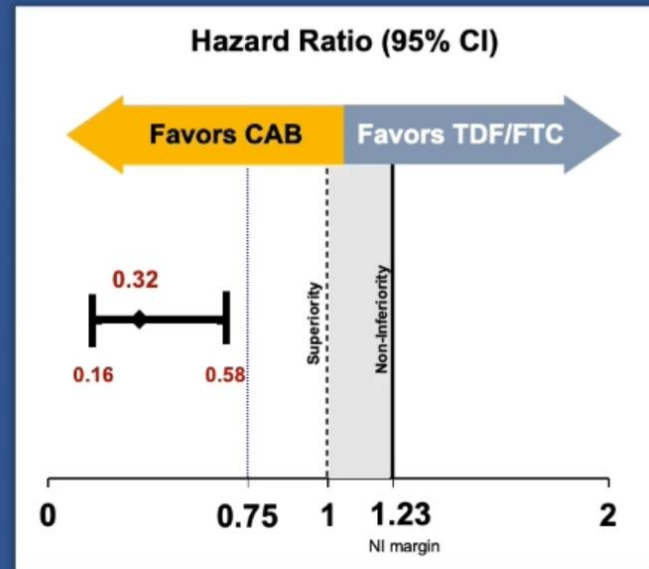
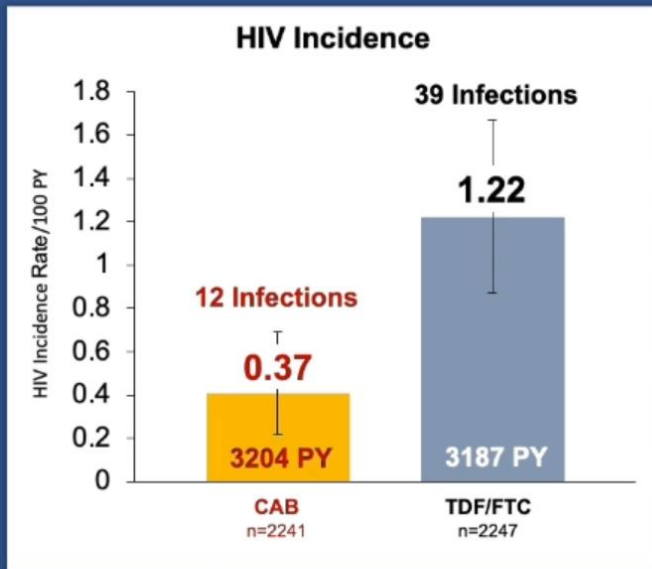


# 12 Incident, 4 baseline Infections: Cabotegravir





# HIV Incidence: CAB vs. TDF/FTC

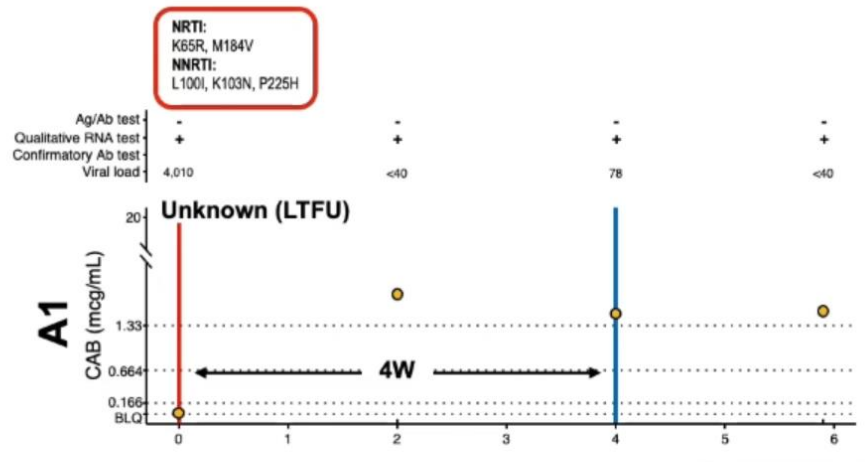


CI, confidence interval

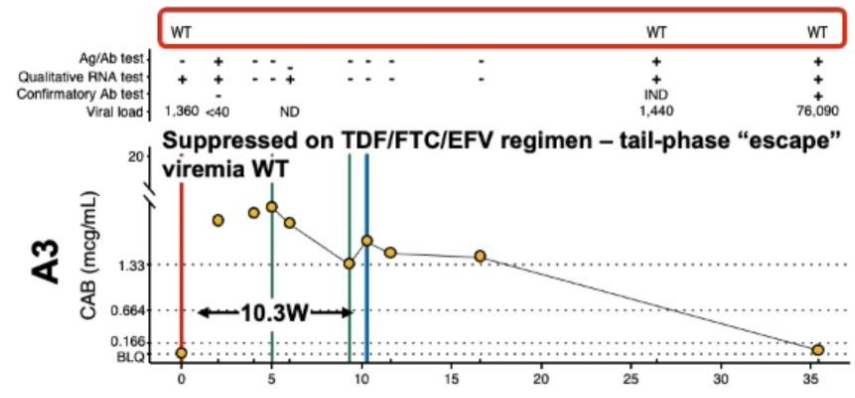


**CAB arm, Group A**  
HIV positive at study enrollment

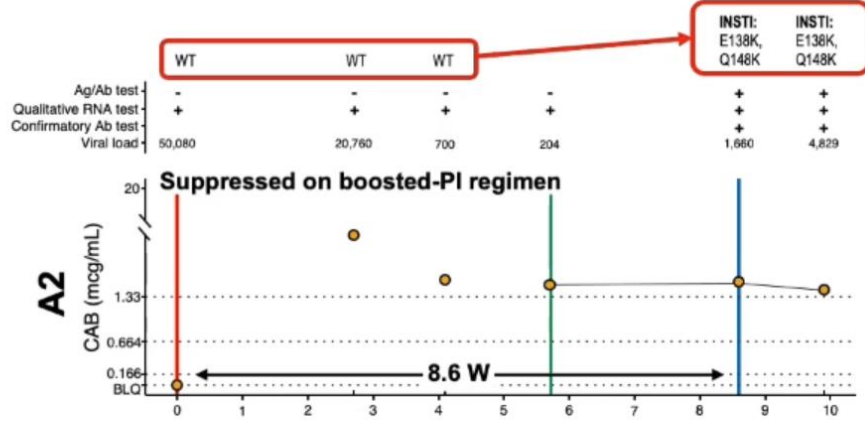




**NRTI:**  
K65R, M184V  
**NNRTI:**  
L100I, K103N, P225H



**WT** **WT** **WT**



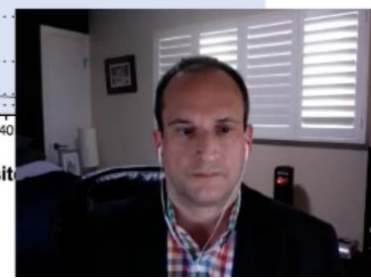
**INSTI:**  
E138K,  
Q148K

**WT** **WT** **WT**

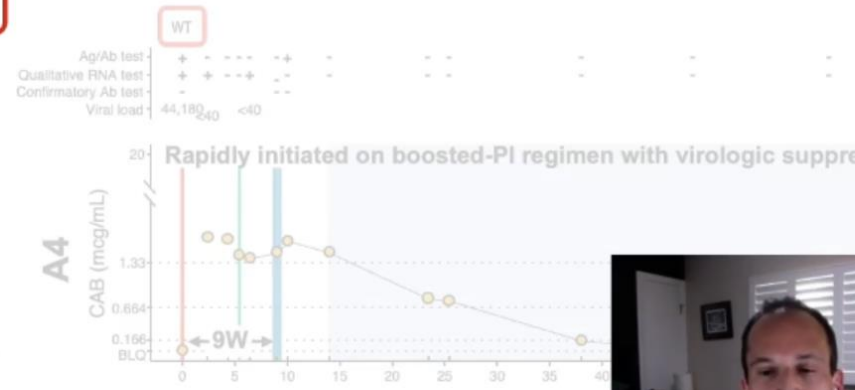
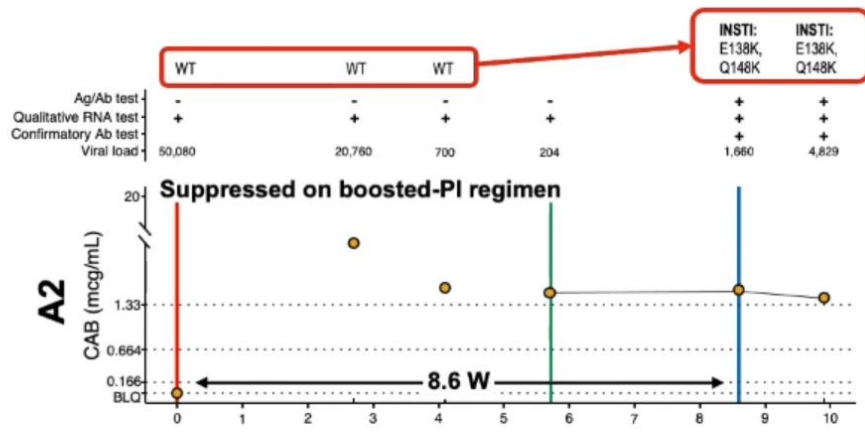
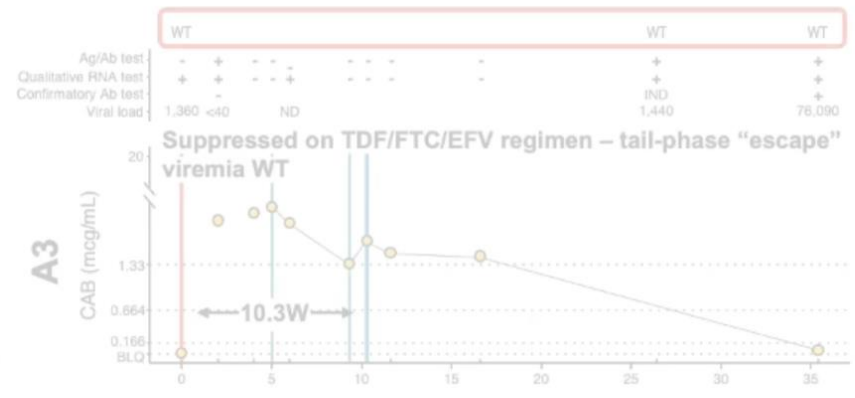
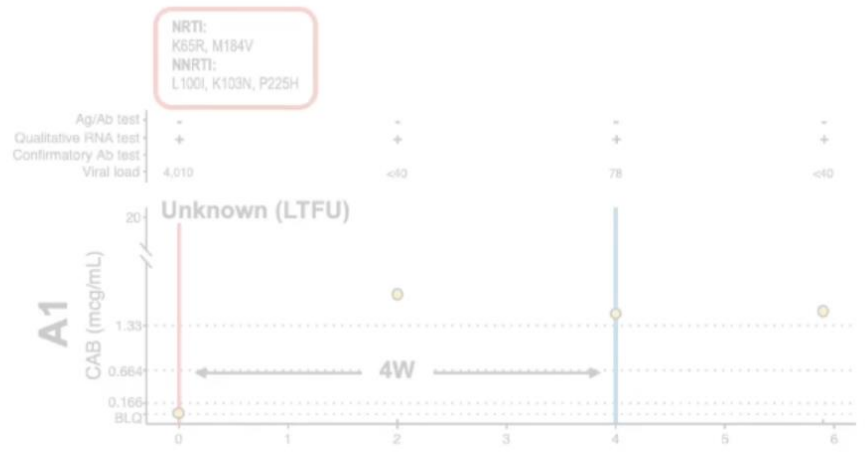


**WT**

● CAB concentration    — CAB injection    — First HIV positive visit    — First site positive visit    — First HIV positive visit and first site positive visit  
 ← # → Weeks between first HIV positive visit and the first site positive test



The x-axis represents weeks since enrollment. The shaded area represents time on ART.

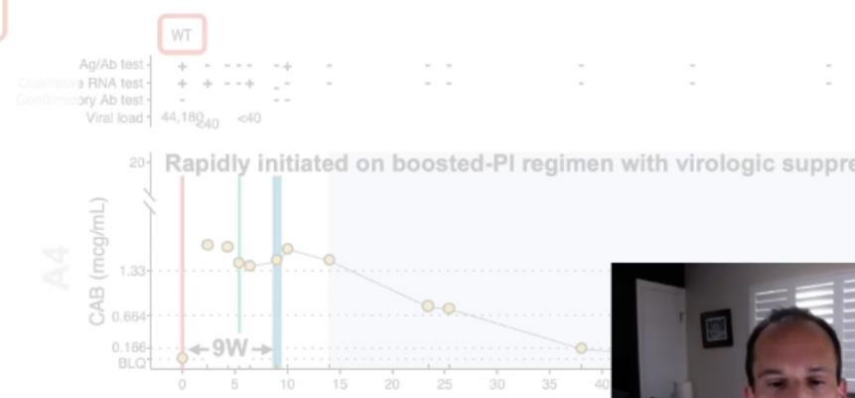
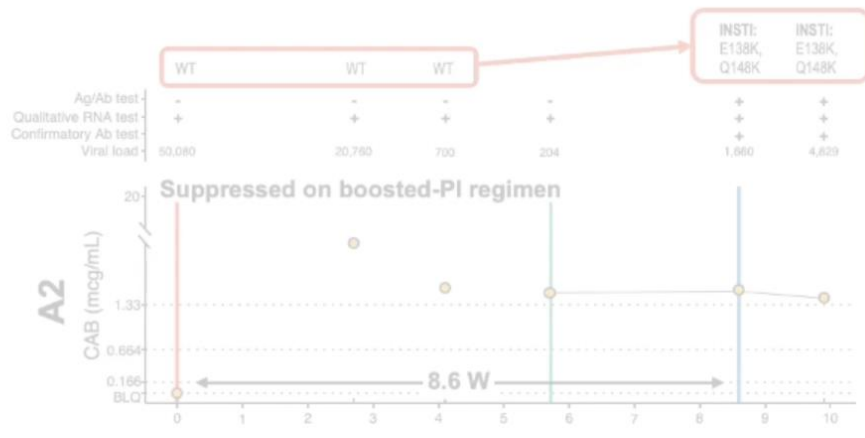
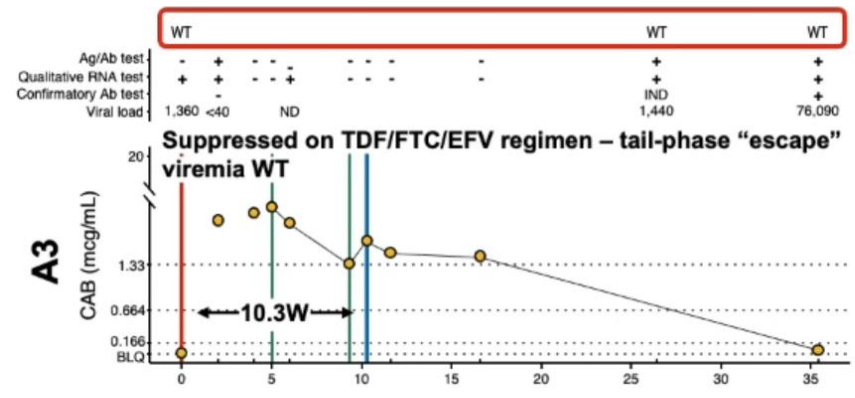
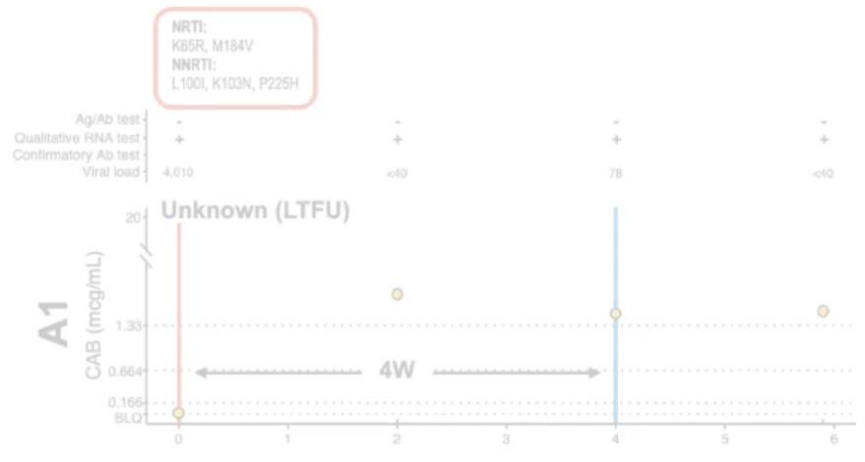


● CAB concentration   
 — CAB injection   
 — First HIV positive visit   
 — First site positive visit   
 — First HIV positive visit and first site positive visit  
 ← # → Weeks between first HIV positive visit and the first site positive test



The x-axis represents weeks since enrollment. The shaded area represents time on ART.





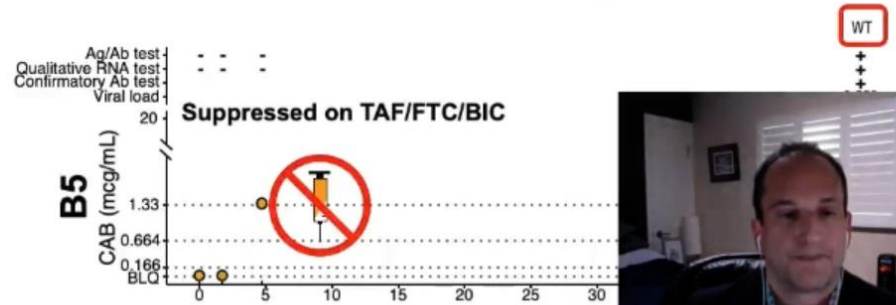
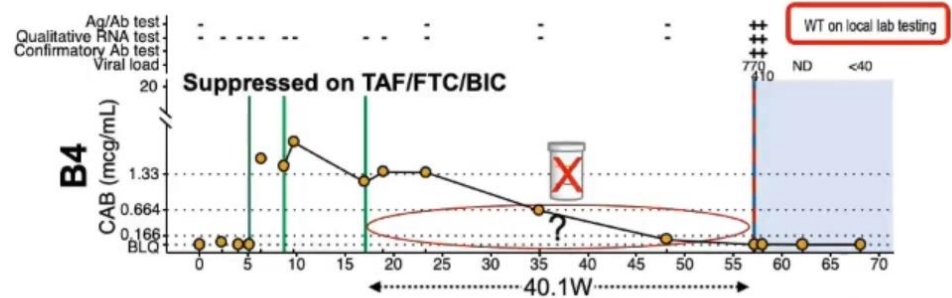
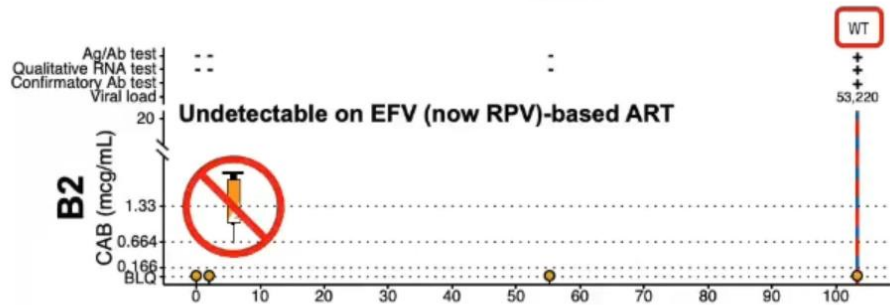
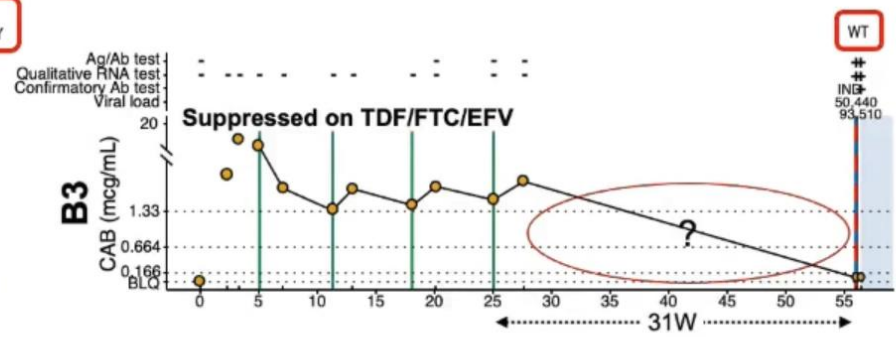
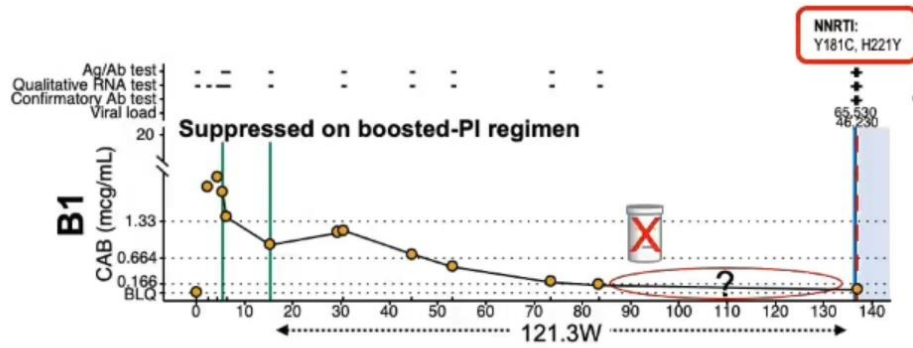
● CAB concentration    ■ CAB injection    ■ First HIV positive visit    ■ First site positive visit    ■ First HIV positive visit and first site positive visit  
 ← # → Weeks between first HIV positive visit and the first site positive test



The x-axis represents weeks since enrollment. The shaded area represents time on ART.

**CAB arm, Group B**  
No recent CAB exposure

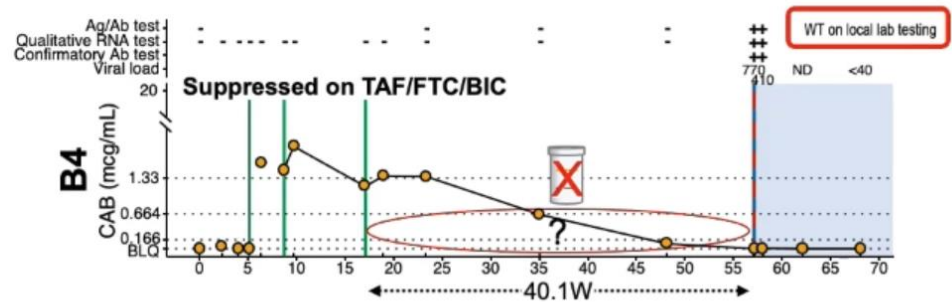
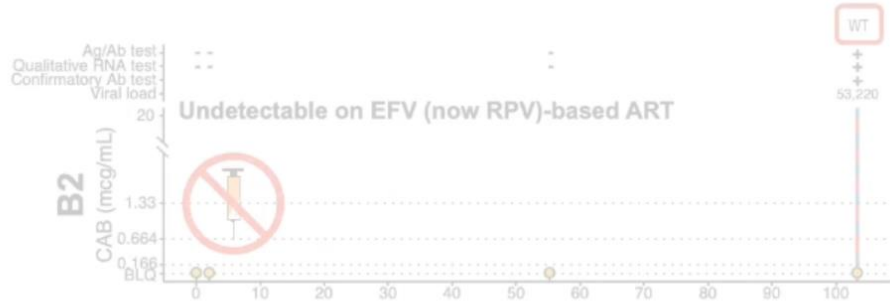
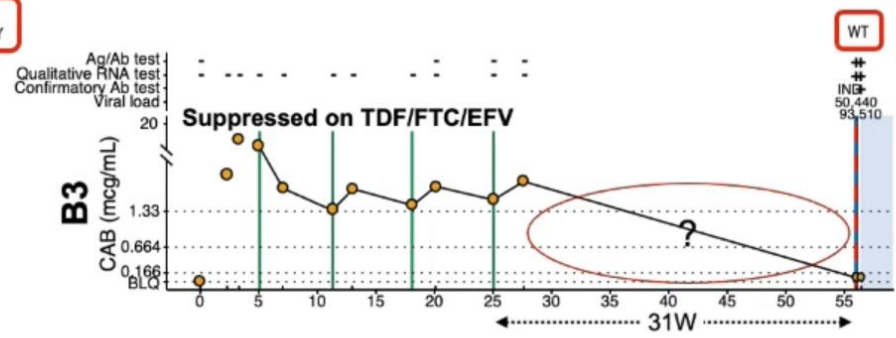
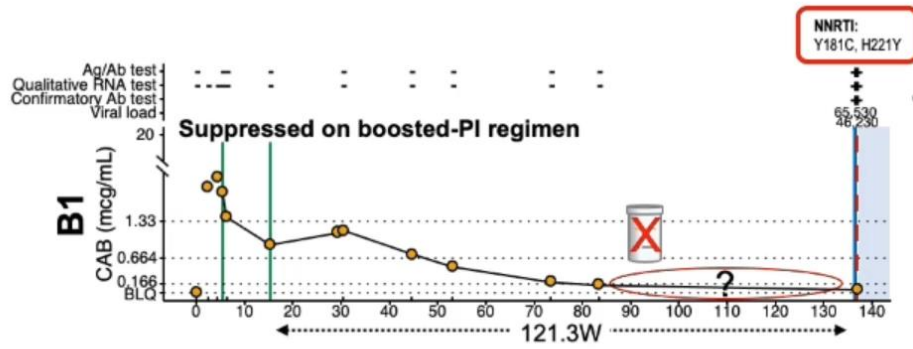




● CAB concentration    ■ CAB injection    — First HIV positive visit  
 — First site positive visit    — First HIV positive visit and first site positive visit  
 ← # → Weeks between last injection and the first HIV positive test

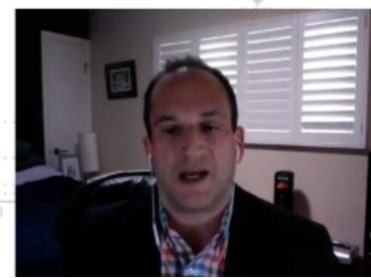
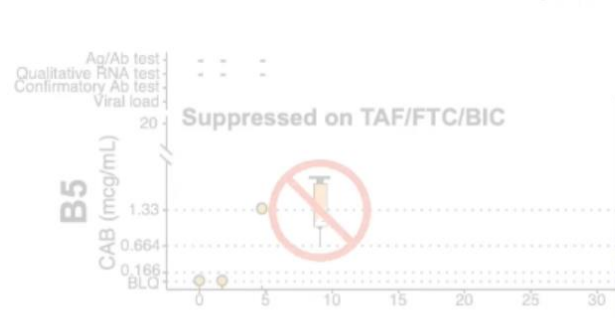
The x-axis represents weeks since enrollment. The shaded area represents time on ART.





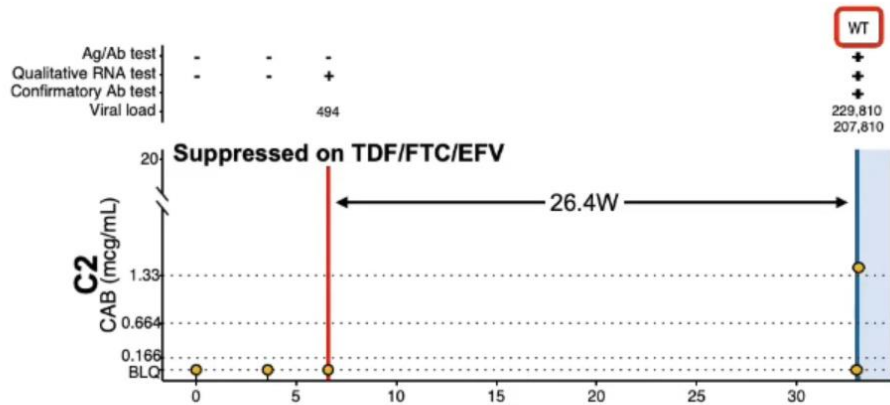
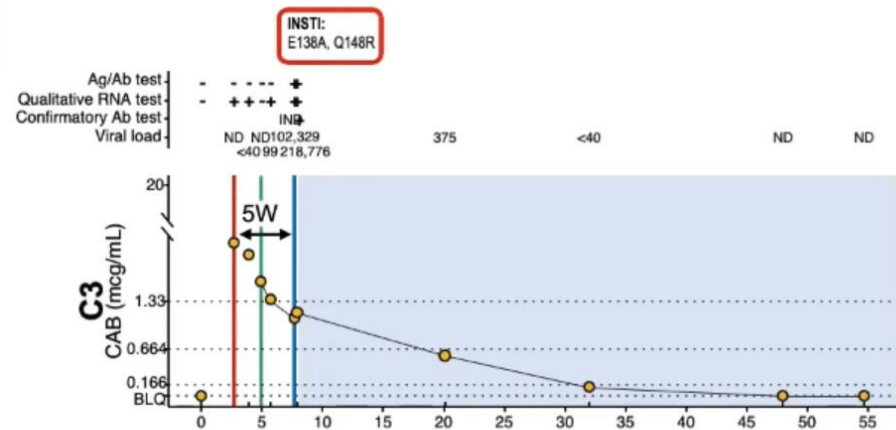
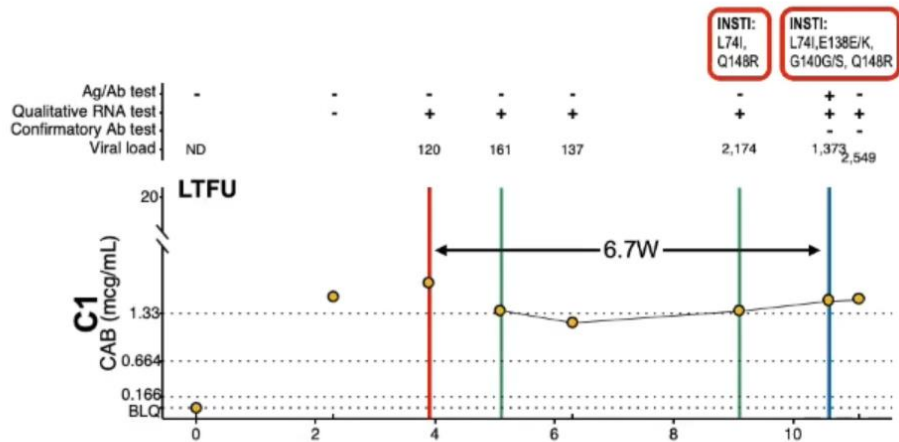
● CAB concentration    ■ CAB injection    — First HIV positive visit  
 — First site positive visit    — First HIV positive visit and first site positive visit  
 ← # → Weeks between last injection and the first HIV positive test

The x-axis represents weeks since enrollment. The shaded area represents time on ART.



**CAB arm, Group C**  
Infected during the CAB oral lead-in period

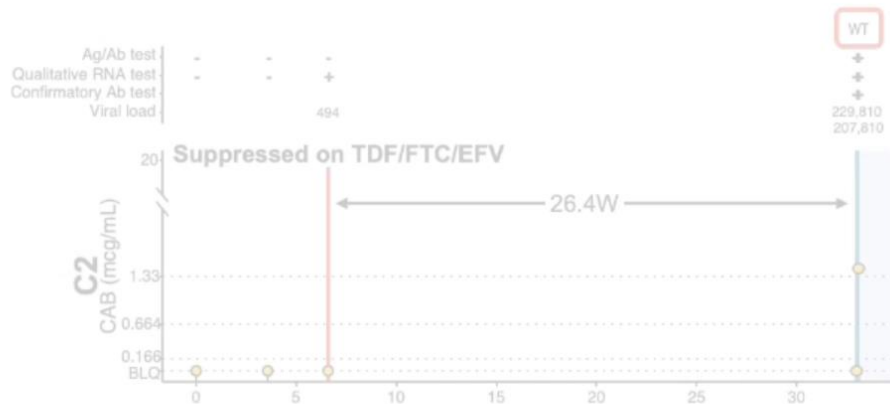
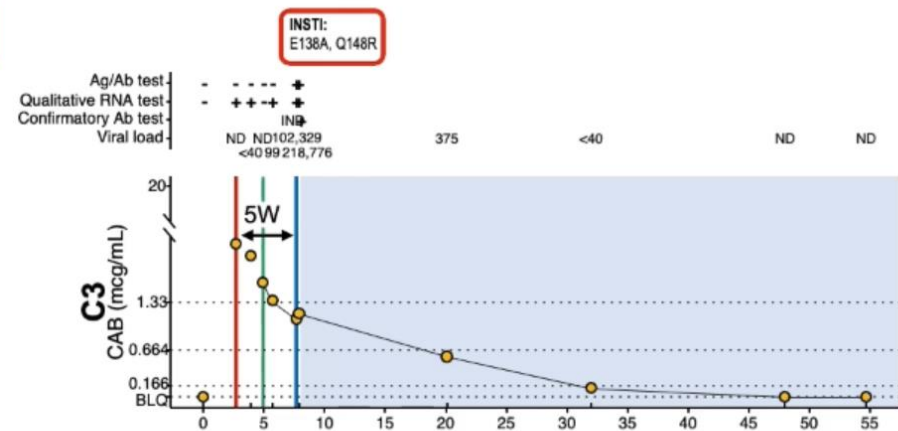
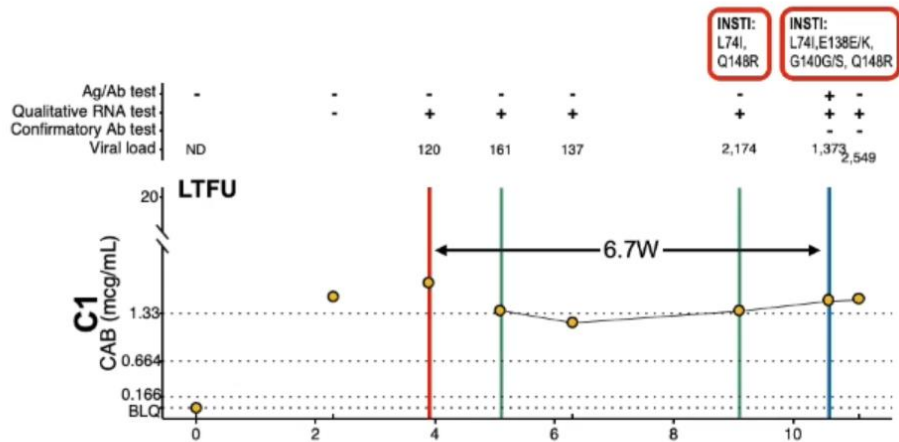




- CAB concentration      ■ CAB injection      ■ First HIV positive visit
- First site positive visit      ■ First HIV positive visit and first site positive visit
- ← # → Weeks between first HIV positive visit and first site positive visit

The x-axis represents weeks since enrollment. Time on ART.



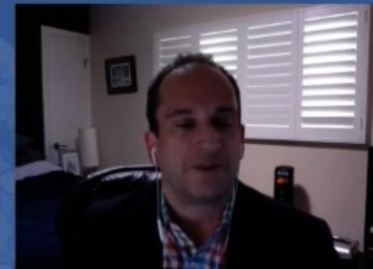


- CAB concentration    ■ CAB injection    ■ First HIV positive visit
- First site positive visit    ■ First HIV positive visit and first site positive visit
- ← # → Weeks between first HIV positive visit and first site positive visit

The x-axis represents weeks since enrollment. Time on ART.

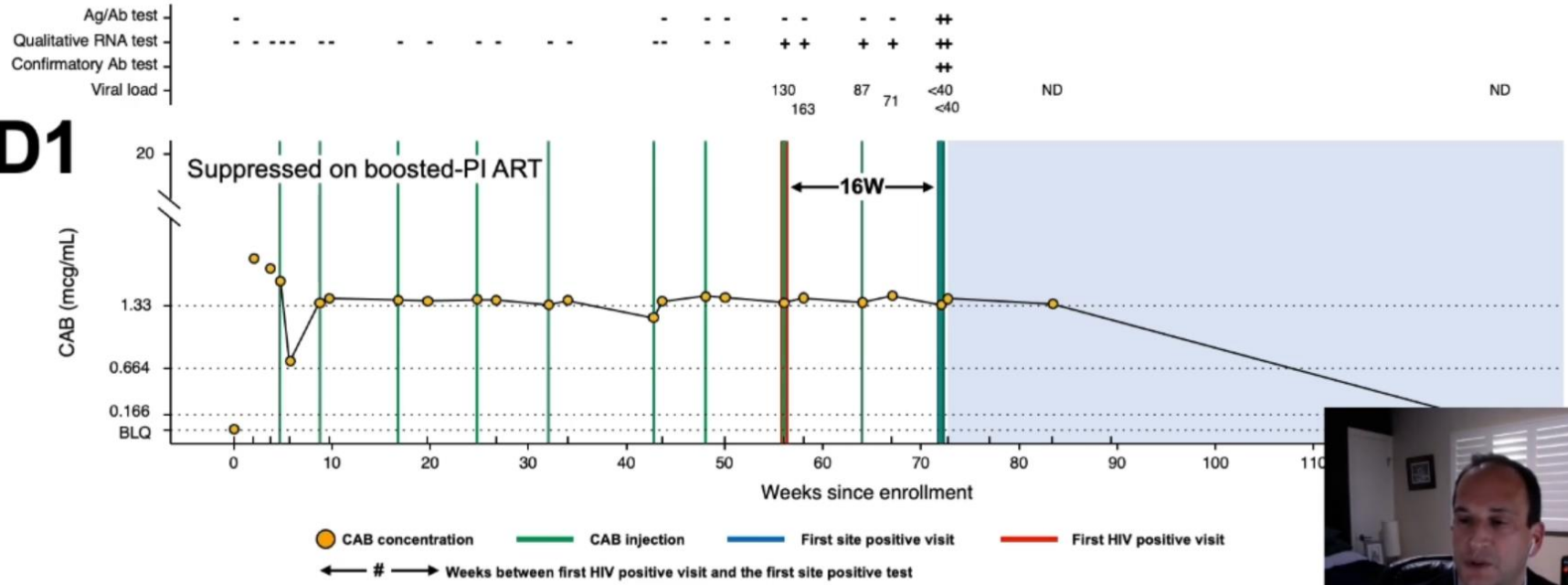


**CAB arm, Group D**  
Infected in the setting of on-time CAB  
injections





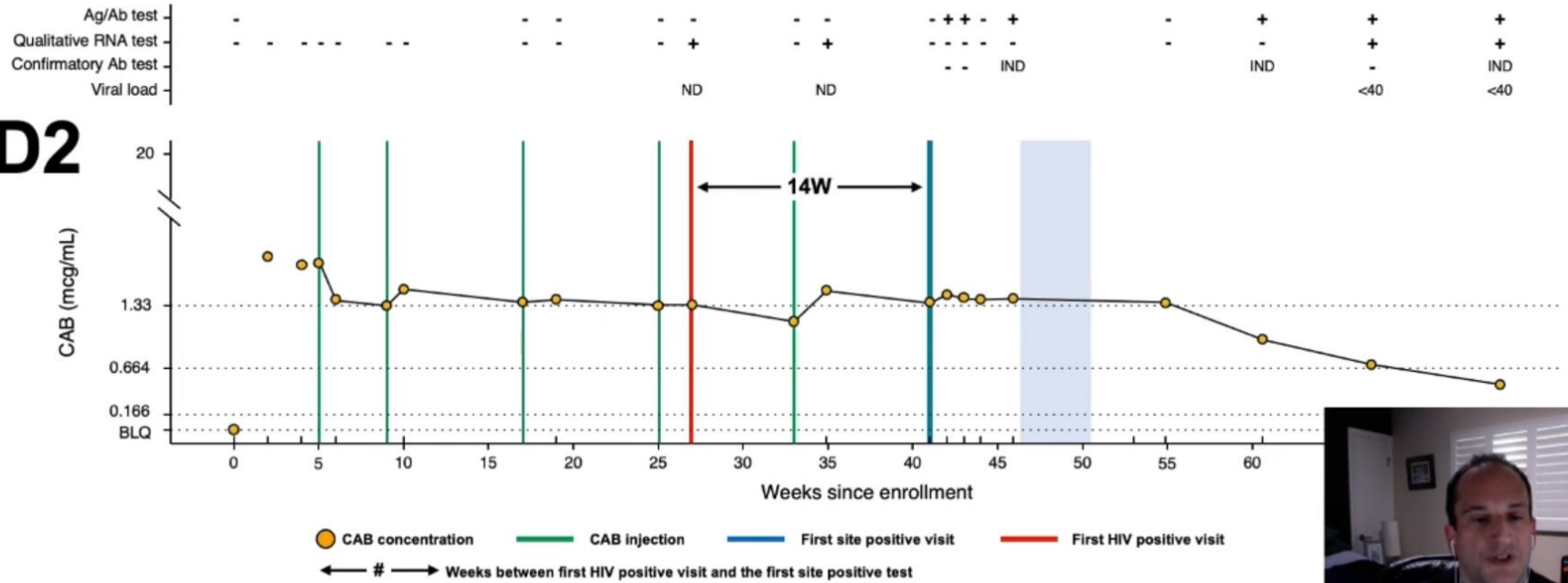
**D1**



The shaded area represents time on ART.



# D2

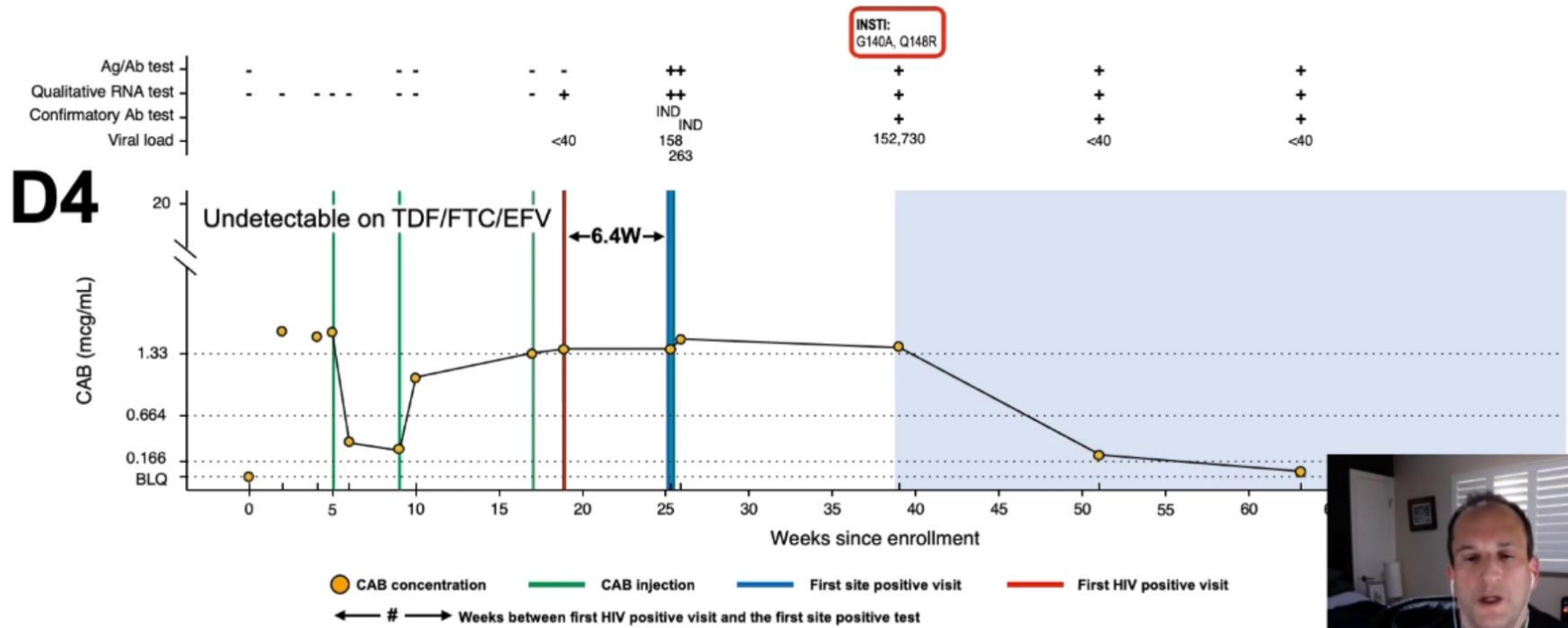


The shaded area represents time on ART.

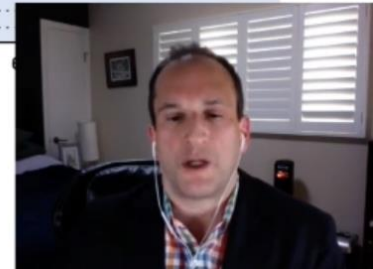




# A Cautionary Tale



The shaded area represents time on ART.





## Key virology findings - CAB arm

- Extended testing identified earlier infection dates in many cases
- Virus loads were often low at the first HIV positive visit
- There was often a prolonged period of viral suppression after infection
- Antibody expression was diminished / delayed in many cases
- In some cases, RNA and Ab tests reverted to negative/non-reactive early in infection

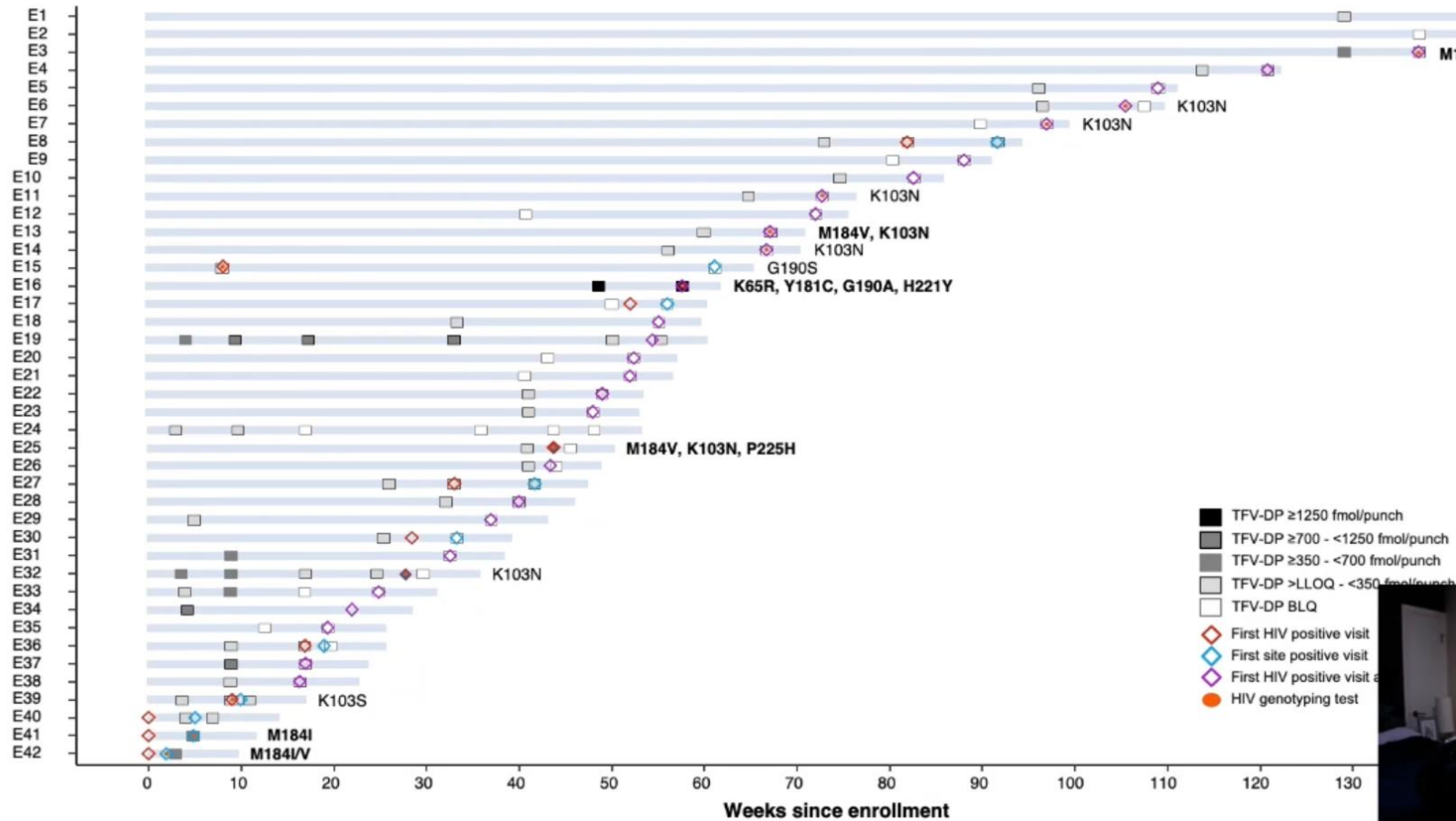


# TDF/FTC arm





# 39 Incident, 3 Baseline Infections: TDF/FTC





# Key Observations & Conclusions

## Key observations:

- 4 incident infections in the CAB arm occurred despite target plasma CAB concentrations; evaluation of correlates of protection is ongoing
- CAB-LA can delay detection of infection using standard HIV testing algorithms
- INI resistance seen when viremic “escape” occurs at higher CAB concentrations
- INI resistance was not seen in 3 tail-phase infections or 1 tail “escape” case
- 37/39 in the TDF/FTC arm with incident infection had suboptimal or non-adherence

## Conclusions:

- Oral lead-in will be optional in 083 OLE
- Use of VL testing as a primary screen for HIV infection will be assessed in 083 OLE
- In the setting of CAB-LA, prompt diagnosis and ART initiation are needed to prevent resistance

**In HPTN 083, CAB-LA and TDF/FTC were both highly effective for HIV PrEP in H...  
CAB-LA was superior to daily oral TDF/FTC for HIV PrEP in H...**





# Acknowledgements

## Sponsor

- U.S. National Institute of Allergy and Infectious Diseases (NIAID), National Institute of Mental Health (NIMH), National Institute on Drug Abuse (NIDA), and the National Institute of Child Health and Human Development (NICHD) all components of the U.S. National Institutes of Health (NIH)
- Additional funding from ViiV Healthcare

## HIV Prevention Trials Network (HPTN)

- Laboratory Center (Johns Hopkins University)
- Statistical Center for HIV/AIDS Research and Prevention (SCHARP), Fred Hutchinson Cancer Research Center
- Leadership and Operations Center, FHI 360
- HPTN Leadership

## Pharmaceutical Support

- ViiV Healthcare
- Gilead Sciences, Inc.

## HPTN 083 Study Team

**Community Program Managers  
Community Educators & Recruiters,  
CAB Members**

**Our 43 Sites in 7 countries**

**...and our Study Participants!**

Questions? Email [rlandovitz@mednet.ucla.edu](mailto:rlandovitz@mednet.ucla.edu) or



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