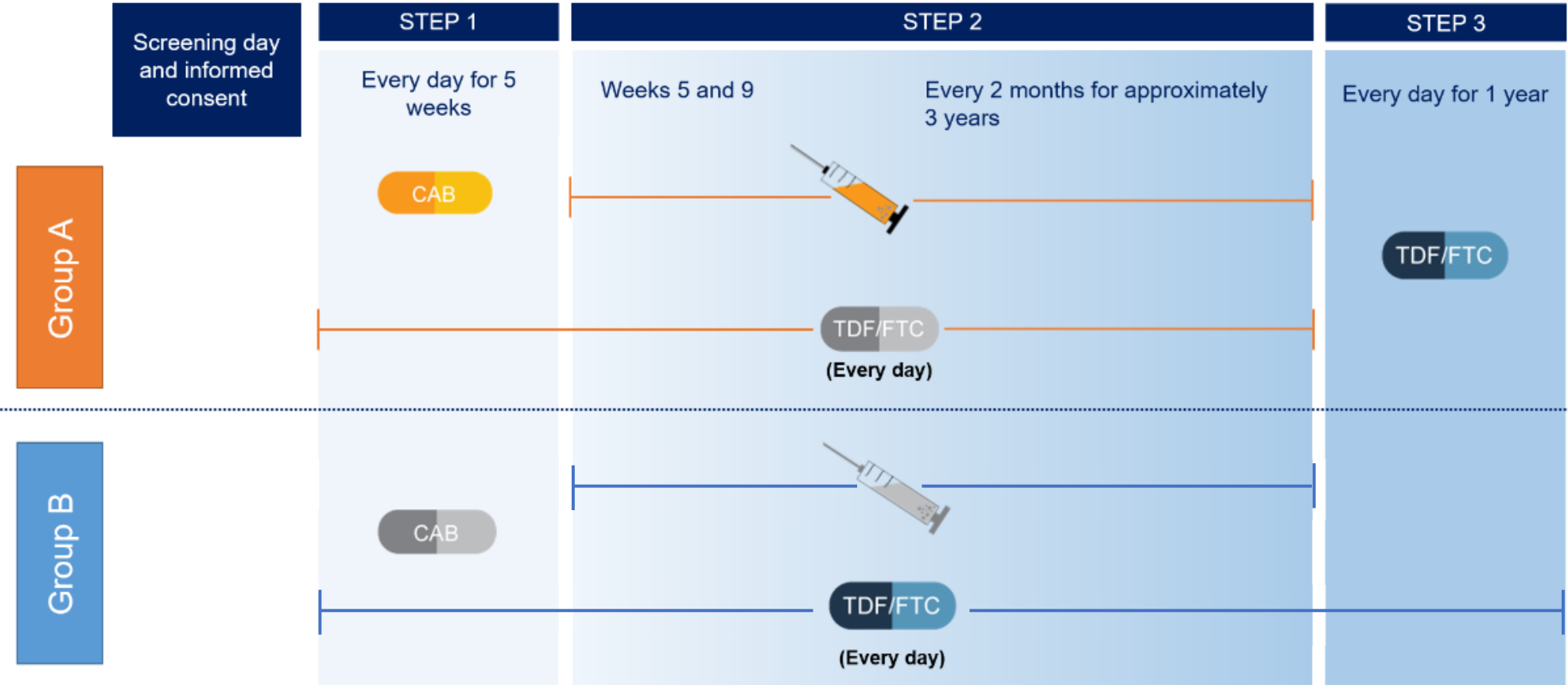


# Laboratory Analysis of HIV Infections in HPTN 083: Injectable CAB for PrEP

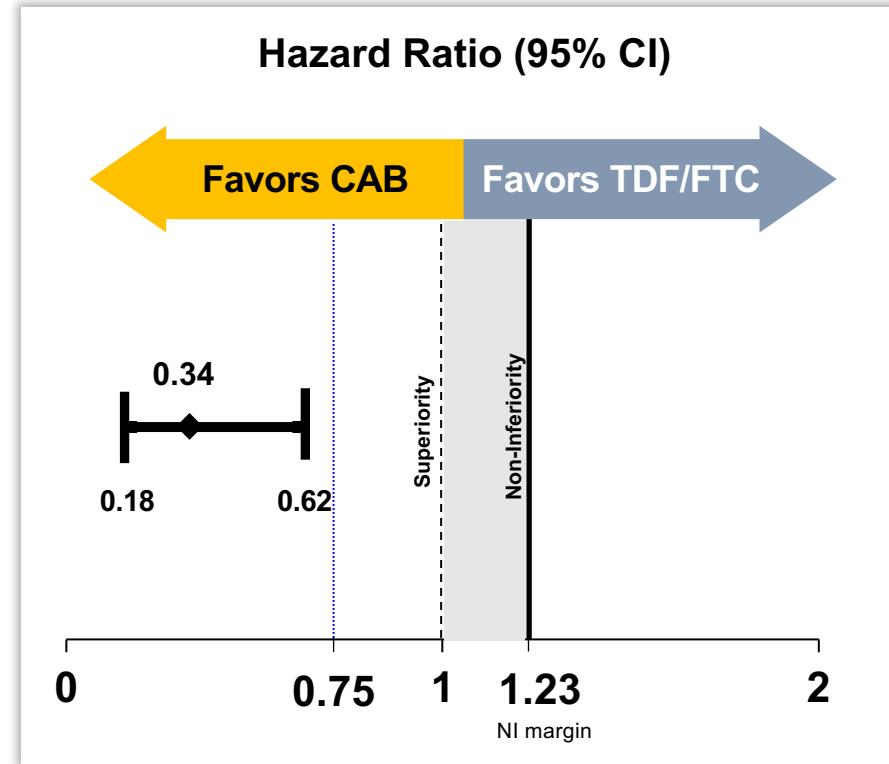
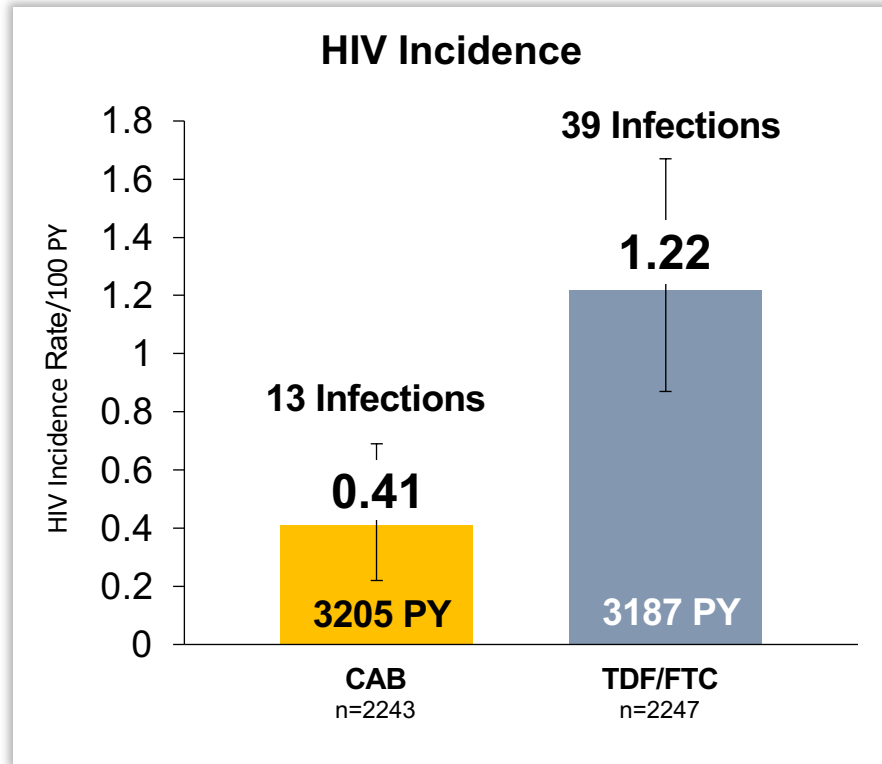
Marzinke M, Grinsztejn B, Fogel J, Piwowar-Manning EM, Hanscom B, Coelho L, Cohen MS, Rinehart AR, Rooney JF, Adeyeye A, Anderson P, McCauley M, [Landovitz R](#), Eshleman S, for the HPTN 083 Study Team

# HPTN 083 Study Design



 TDF/FTC pill    
  Cabotegravir (CAB) injection    
  Placebo for TDF/FTC pill    
  Placebo for cabotegravir (CAB) injection  
 Cabotegravir (CAB) pill    
  Placebo for cabotegravir (CAB) pill

# HIV Incidence: CAB vs. TDF/FTC



CI, confidence interval

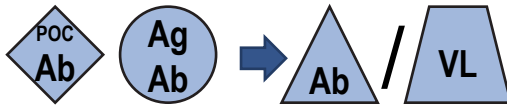
# Pre-specified HIV Testing

## Real-time site testing

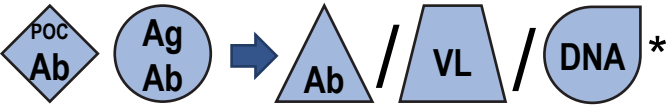
### Screening



### Enrollment\*



### Follow-up visits

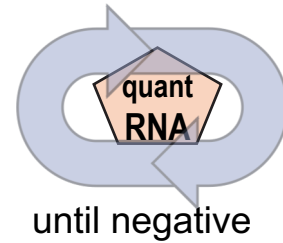


## HPTN Laboratory Center testing (retrospective)

### Visits with reactive/positive site tests








### Back-testing






## Blinded adjudication of study endpoints



### Site testing

-  Point-of-care antibody test
-  Instrumented antigen/antibody test
-  Viral load test
-  Confirmatory/discriminatory antibody test
-  Ultrasensitive DNA test (centralized at JHU)

### HPTN LC testing

-  ARCHITECT antigen/antibody test
-  APTIMA qualitative RNA test
-  Geenius discriminatory antibody test

\*Selected cases

# Extended HPTN LC Testing

## HIV testing

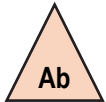
### Back-testing



**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

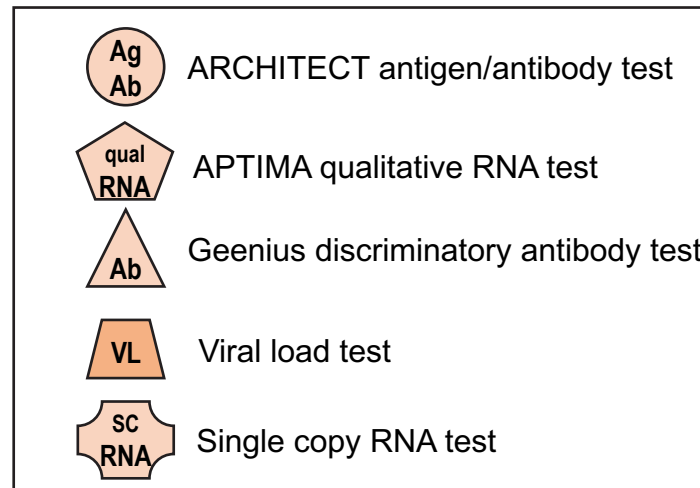
### CAB concentrations

#### CAB arm

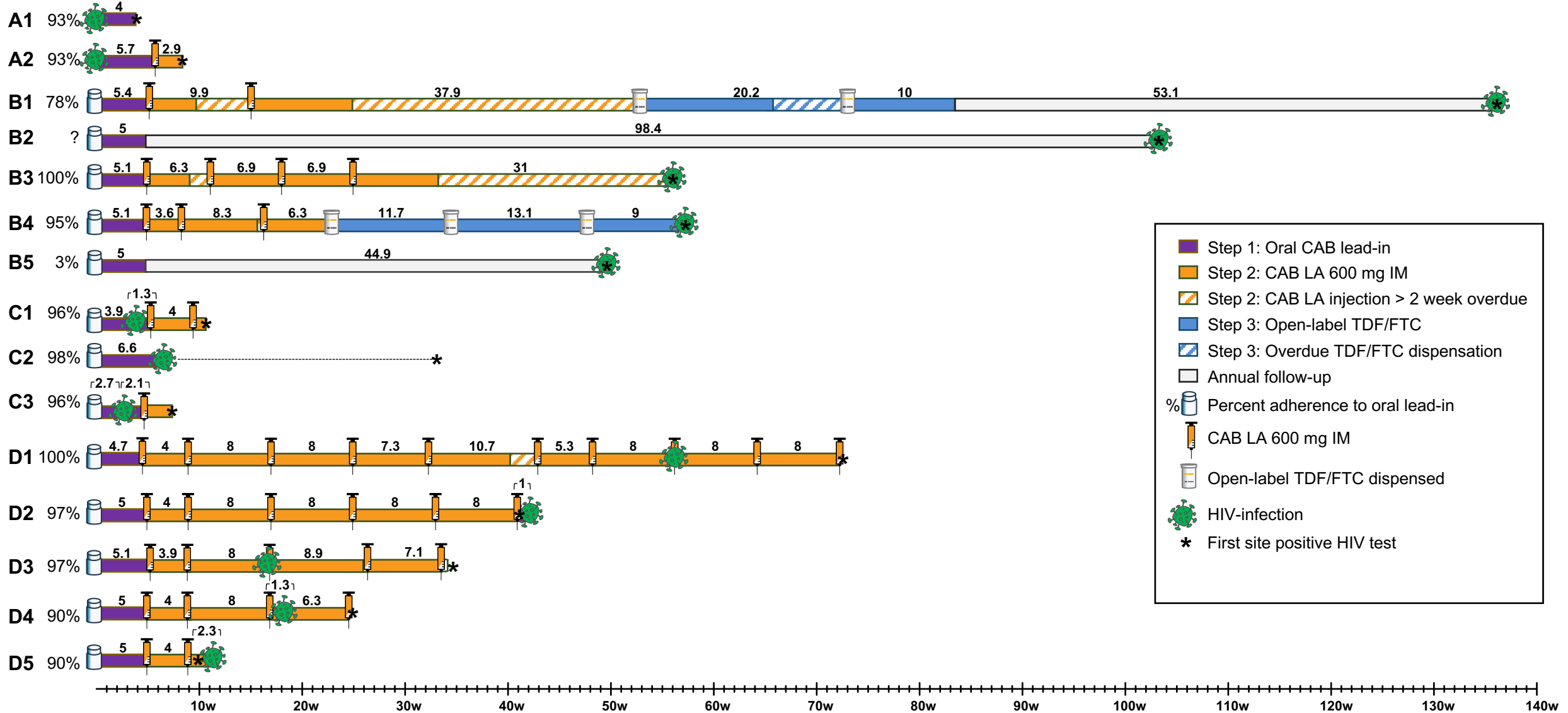
Plasma [CAB]: all study visits  
 Plasma [TFV]: baseline infections, step 3 infections  
 DBS [TFV-DP]: step 3 infections

### TDF/FTC concentrations

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



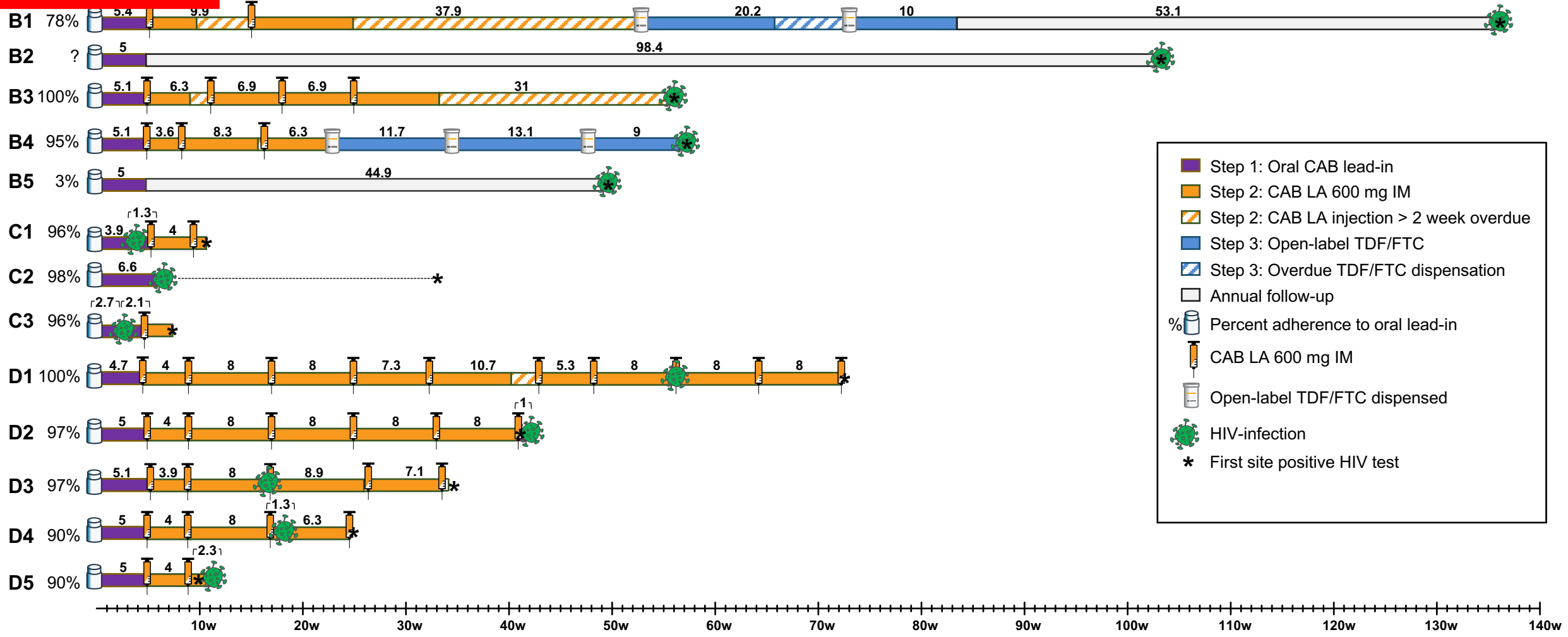
# 13 Incident, 2 baseline Infections: Cabotegravir



# 13 Incident, 2 baseline Infections: Cabotegravir

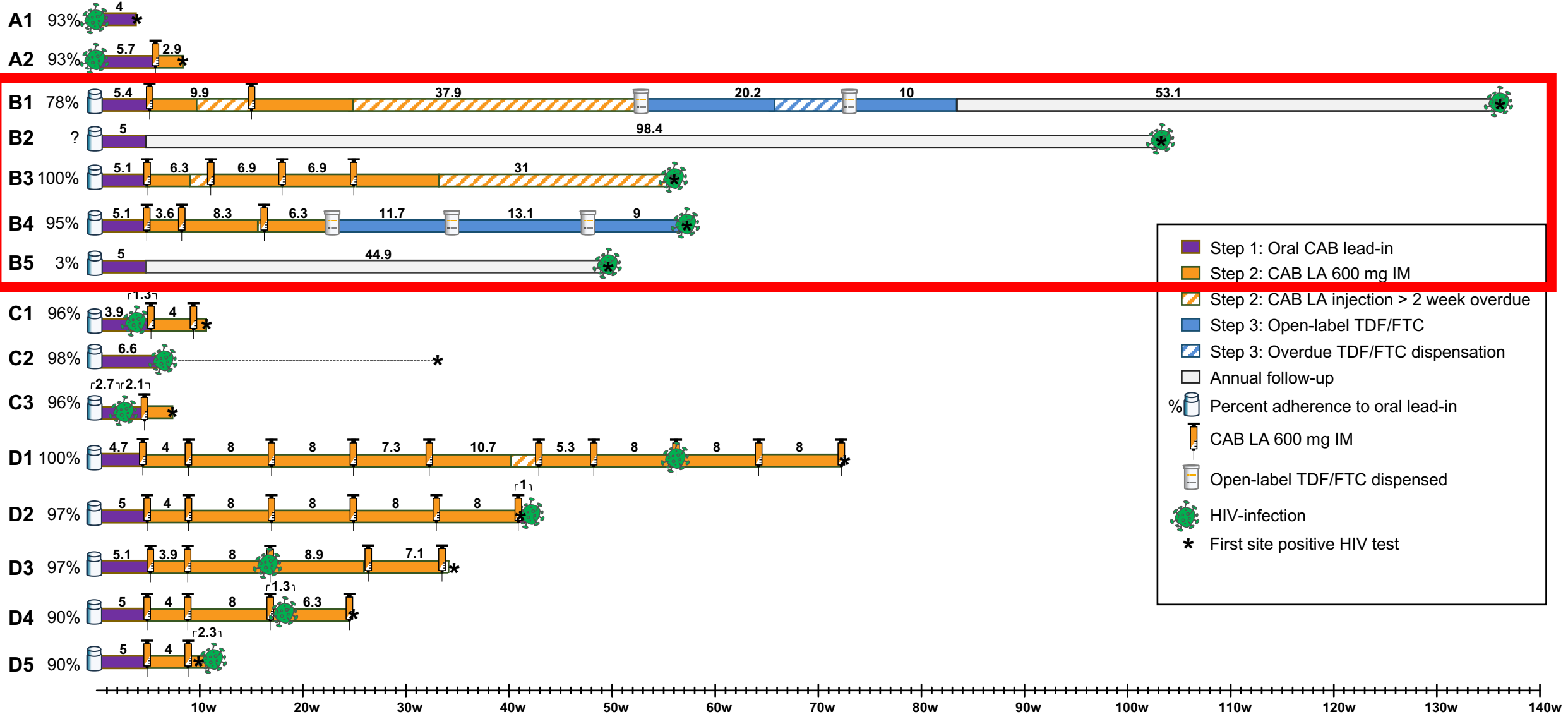
**A1** 93% 4 \*

**A2** 93% 5.7 2.9 \*



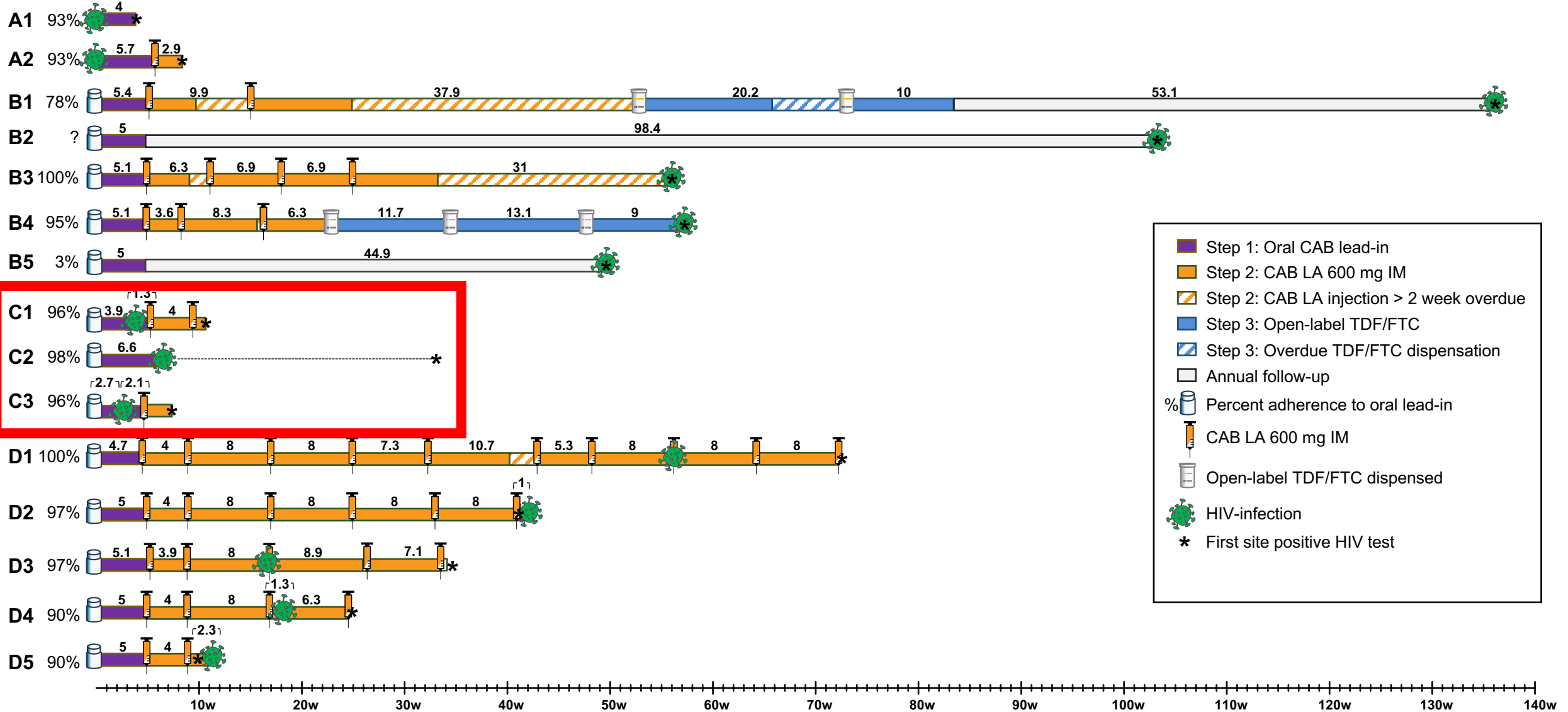
- Step 1: Oral CAB lead-in
- Step 2: CAB LA 600 mg IM
- Step 2: CAB LA injection > 2 week overdue
- Step 3: Open-label TDF/FTC
- Step 3: Overdue TDF/FTC dispensation
- Annual follow-up
- Percent adherence to oral lead-in
- CAB LA 600 mg IM
- Open-label TDF/FTC dispensed
- HIV-infection
- First site positive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

# 13 Incident, 2 baseline Infections: Cabotegravir

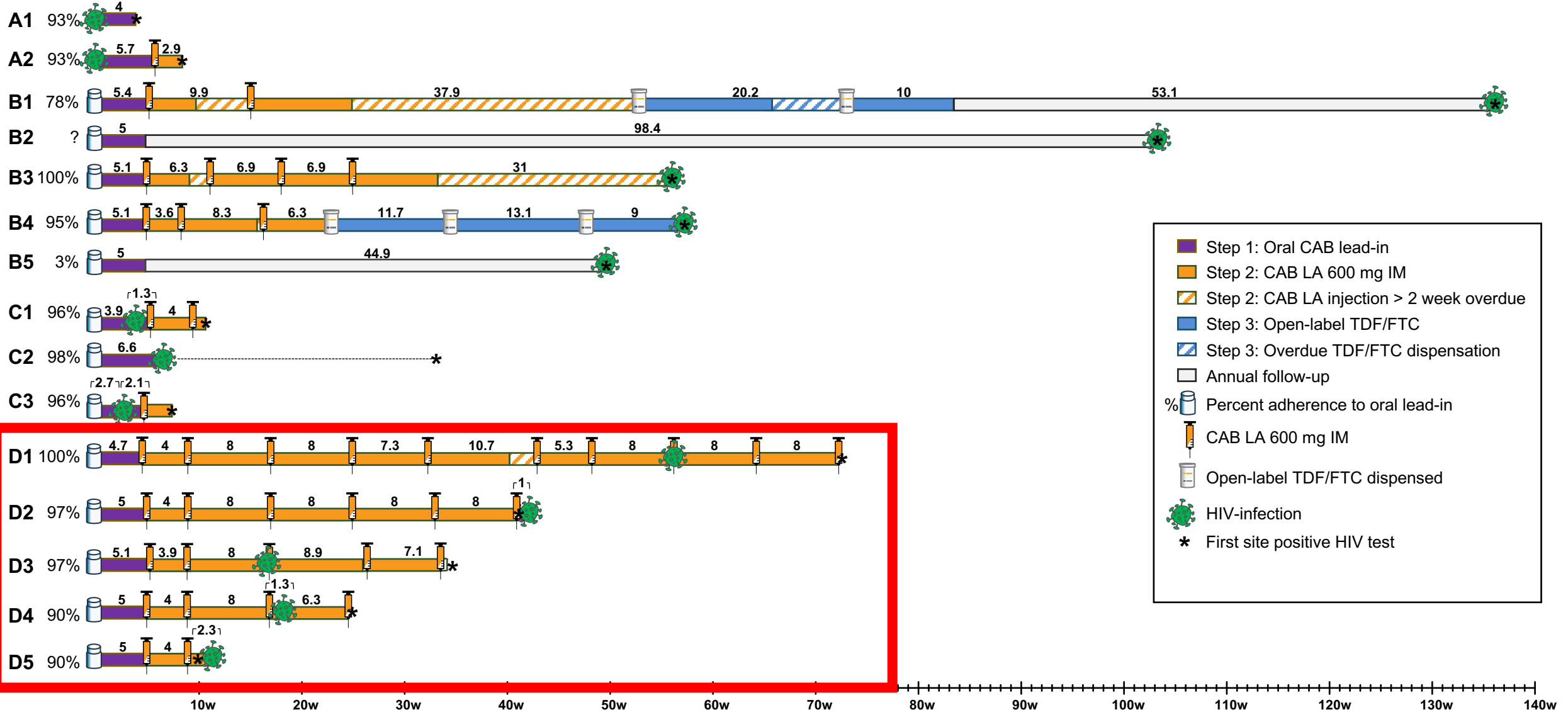




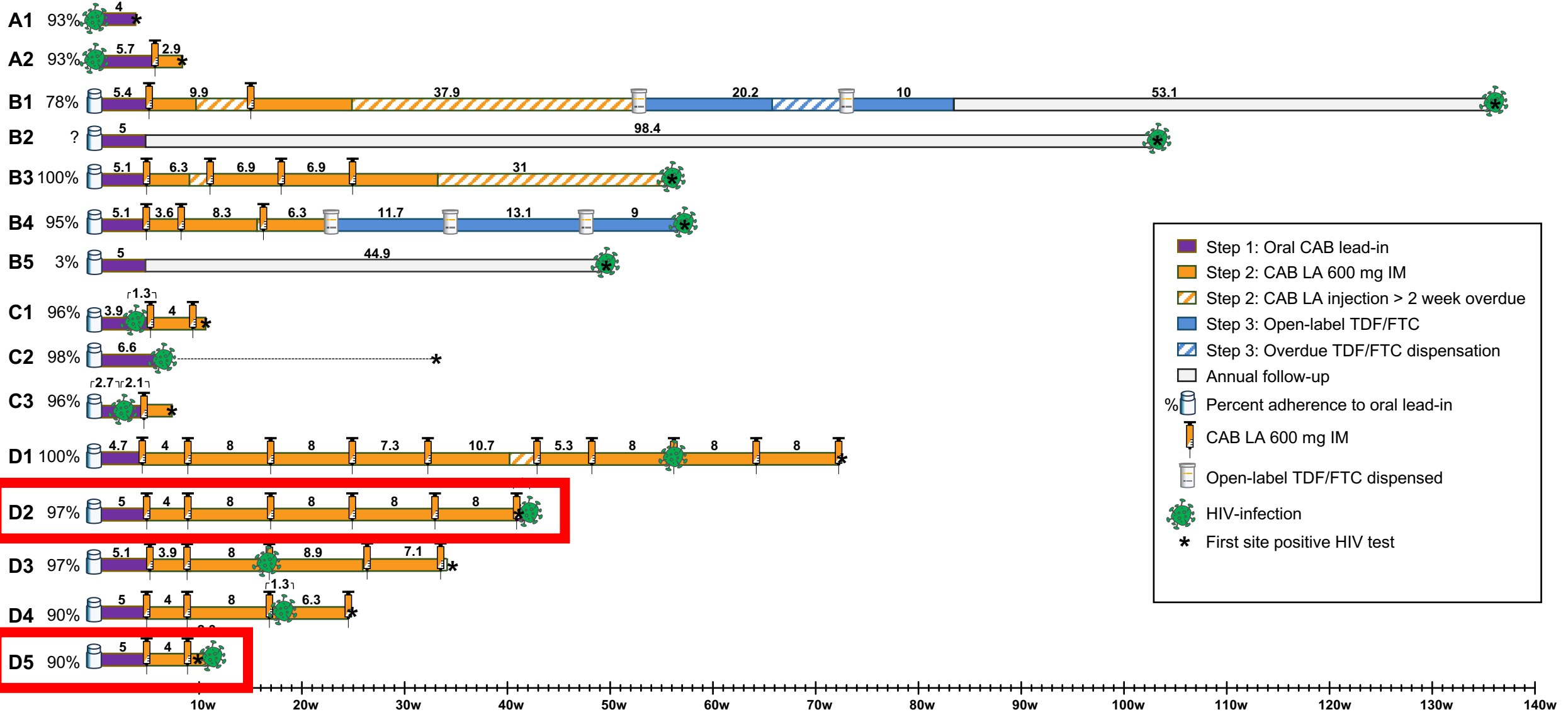
# 13 Incident, 2 baseline Infections: Cabotegravir



# 13 Incident, 2 baseline Infections: Cabotegravir

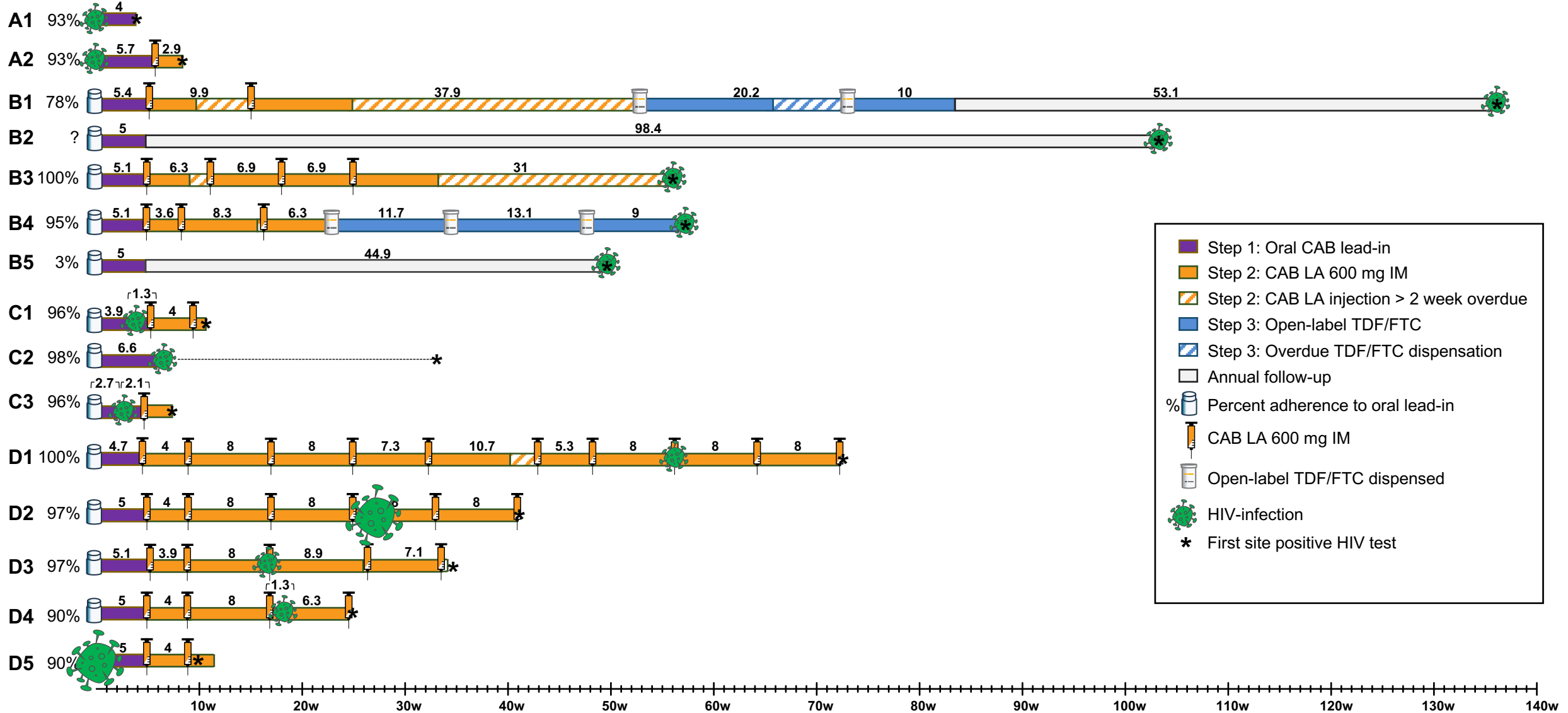


# 13 Incident, 2 baseline Infections: Cabotegravir



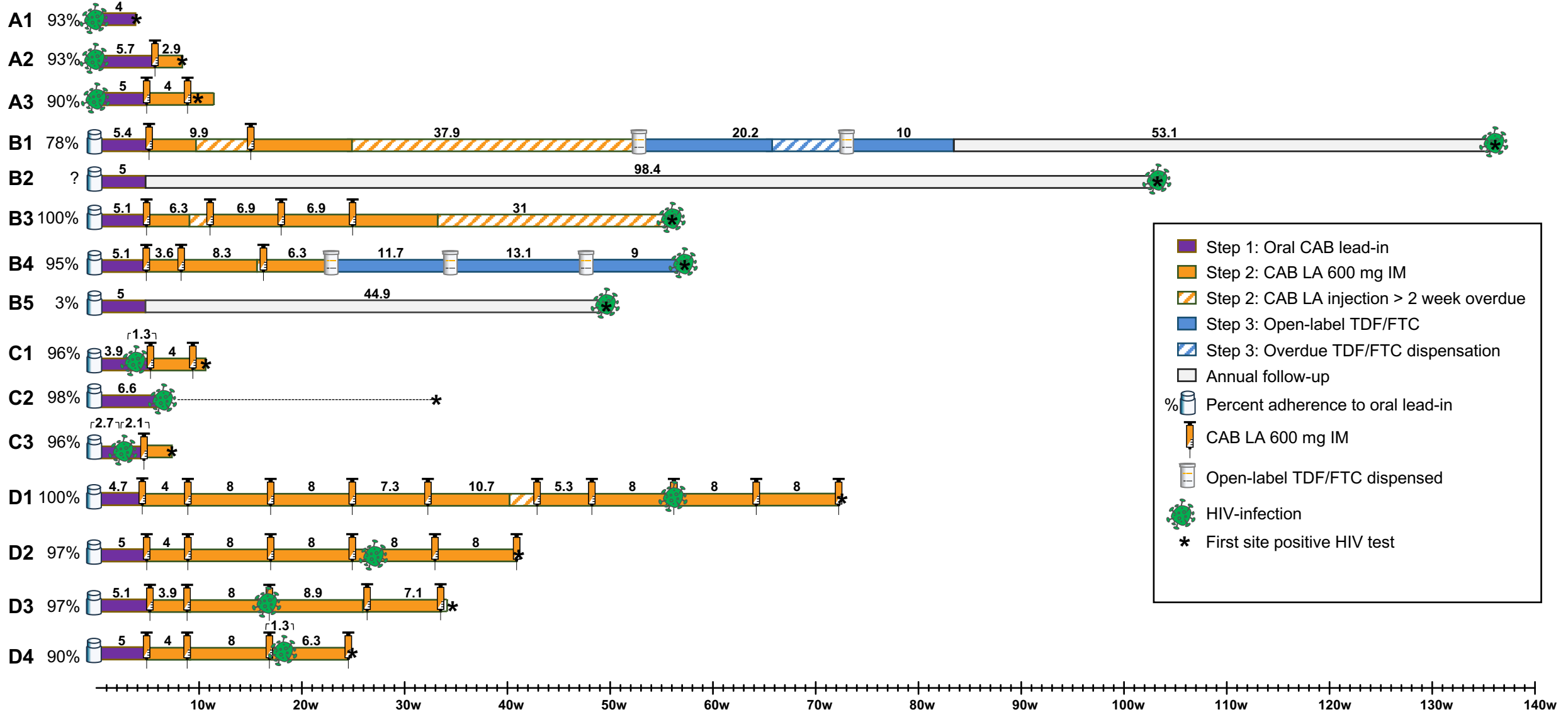
- Step 1: Oral CAB lead-in
- Step 2: CAB LA 600 mg IM
- Step 2: CAB LA injection > 2 week overdue
- Step 3: Open-label TDF/FTC
- Step 3: Overdue TDF/FTC dispensation
- Annual follow-up
- % Percent adherence to oral lead-in
- CAB LA 600 mg IM
- Open-label TDF/FTC dispensed
- HIV-infection
- \* First site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

# 13 Incident, 2 baseline Infections: Cabotegravir

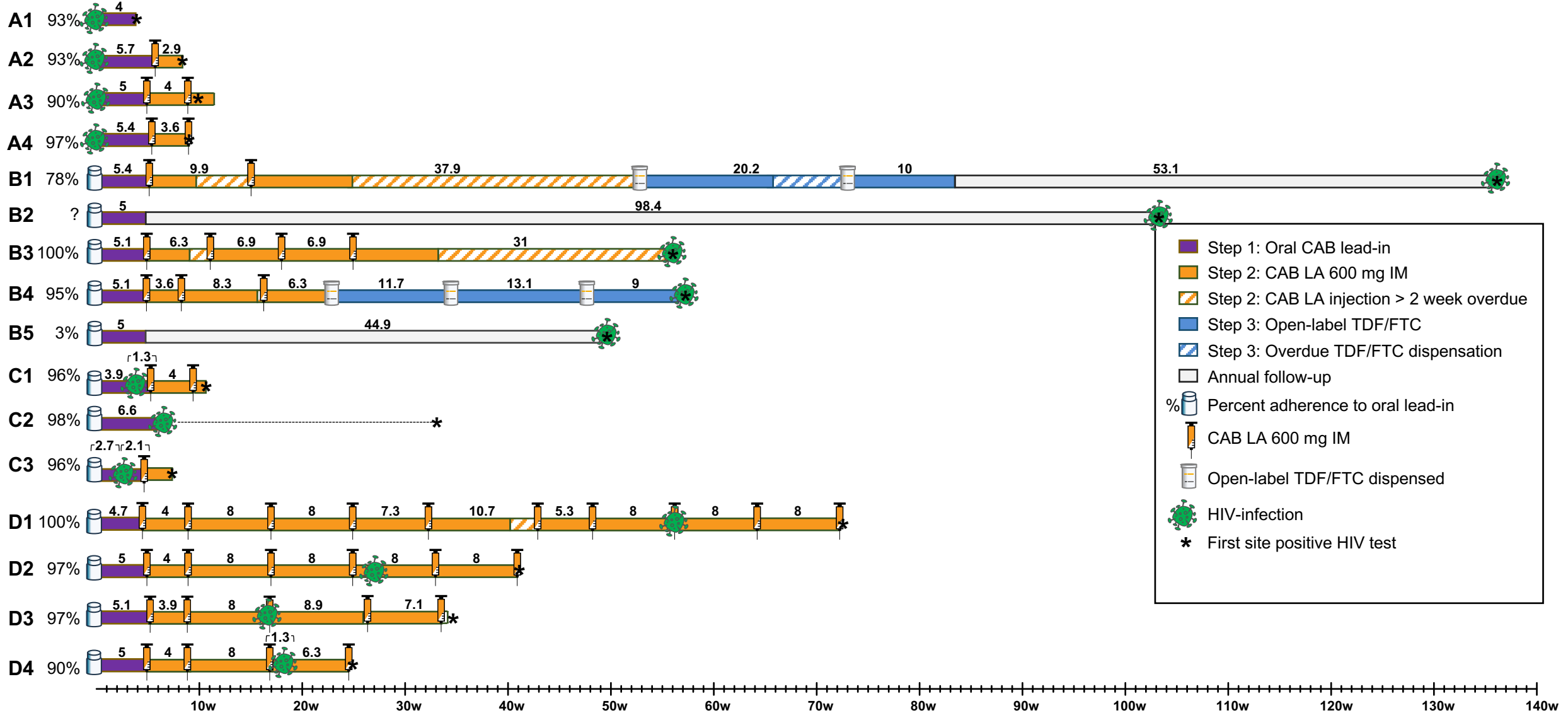


- Step 1: Oral CAB lead-in
- Step 2: CAB LA 600 mg IM
- Step 2: CAB LA injection > 2 week overdue
- Step 3: Open-label TDF/FTC
- Step 3: Overdue TDF/FTC dispensation
- Annual follow-up
- % Percent adherence to oral lead-in
- CAB LA 600 mg IM
- Open-label TDF/FTC dispensed
- HIV-infection
- \* First site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

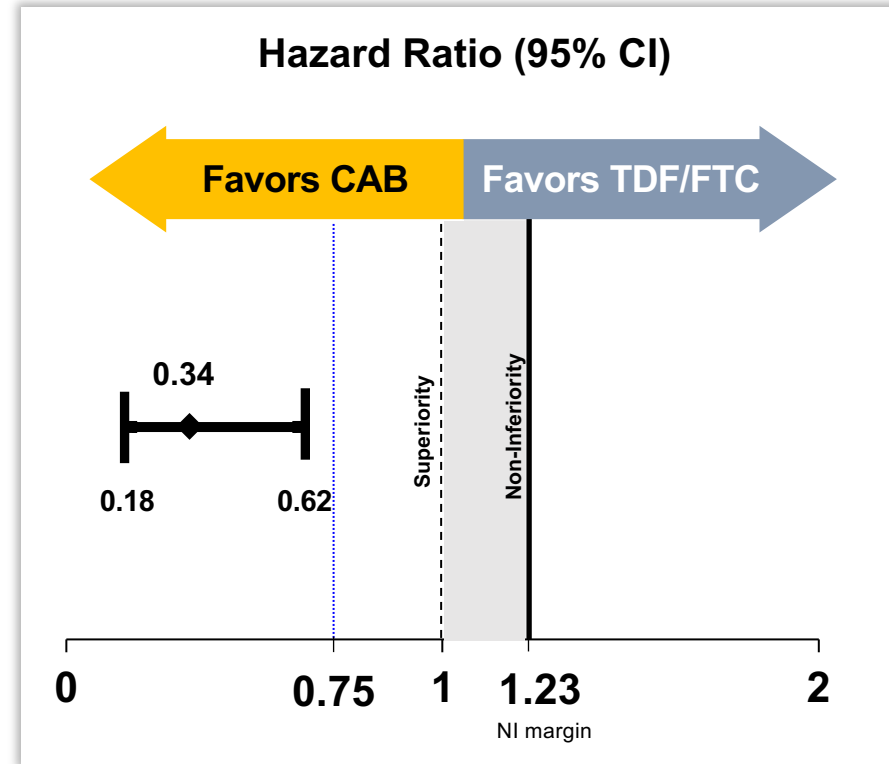
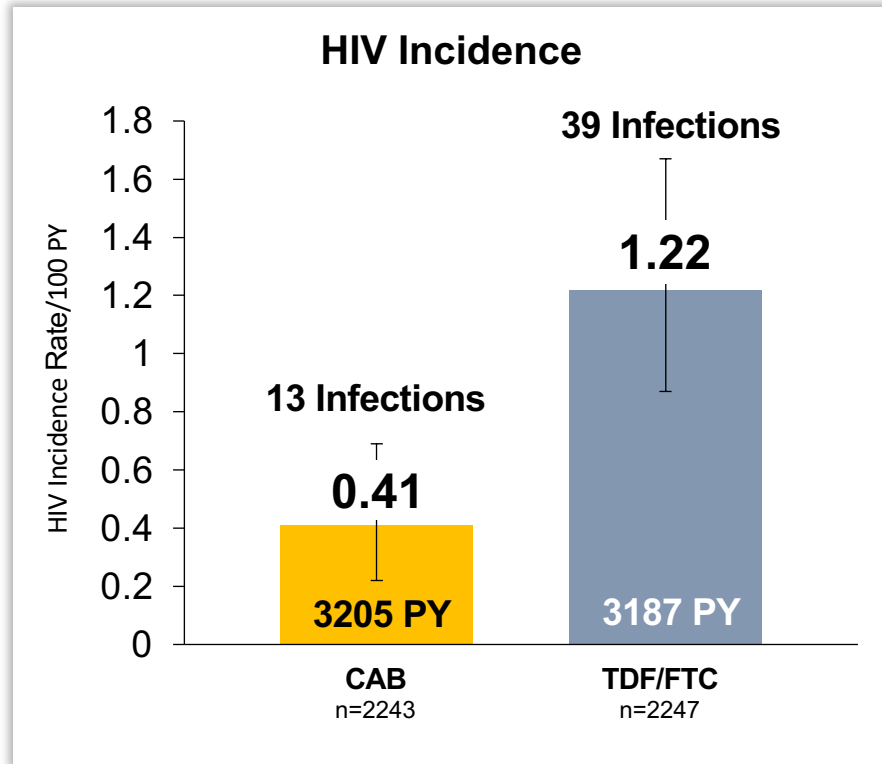
# 13 Incident, 3 baseline Infections: Cabotegravir



# 13 Incident, 4 baseline Infections: Cabotegravir

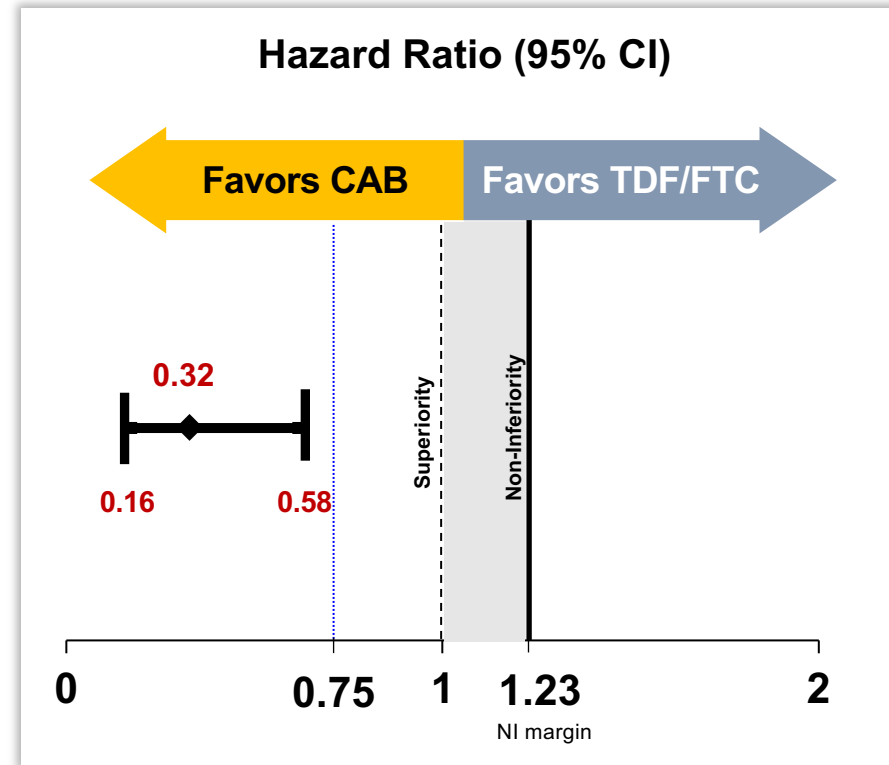
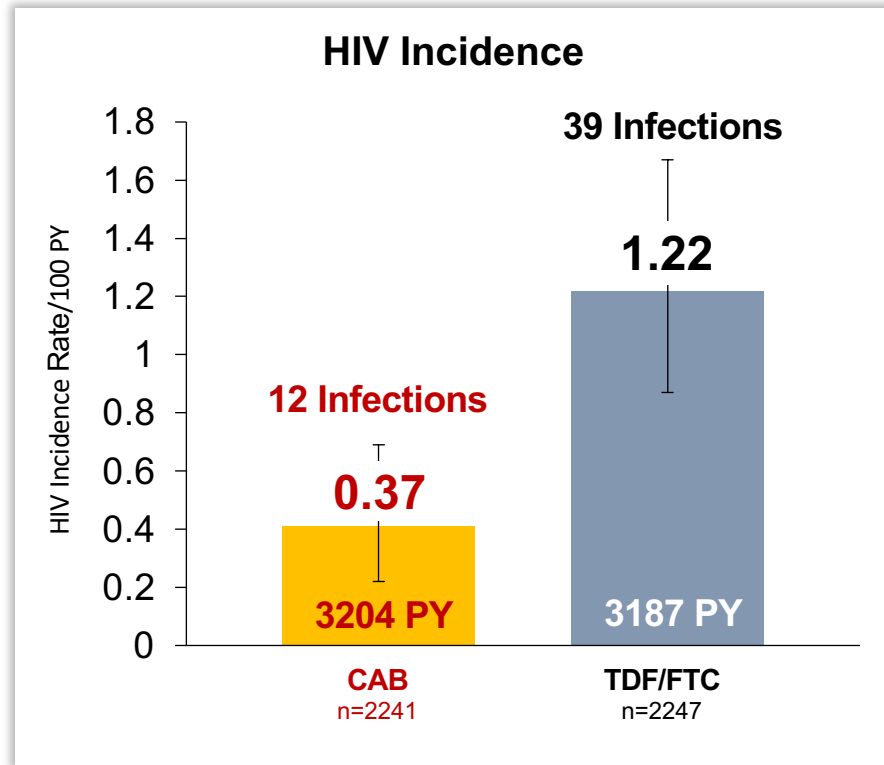


# HIV Incidence: CAB vs. TDF/FTC



CI, confidence interval

# HIV Incidence: CAB vs. TDF/FTC



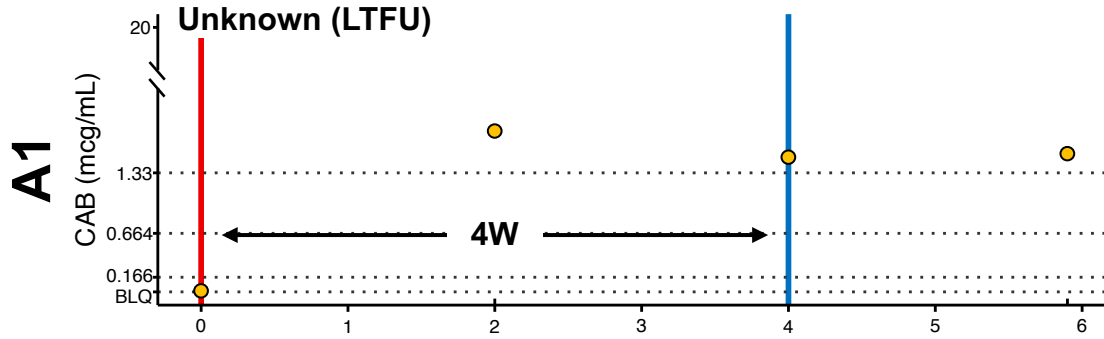
CI, confidence interval



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

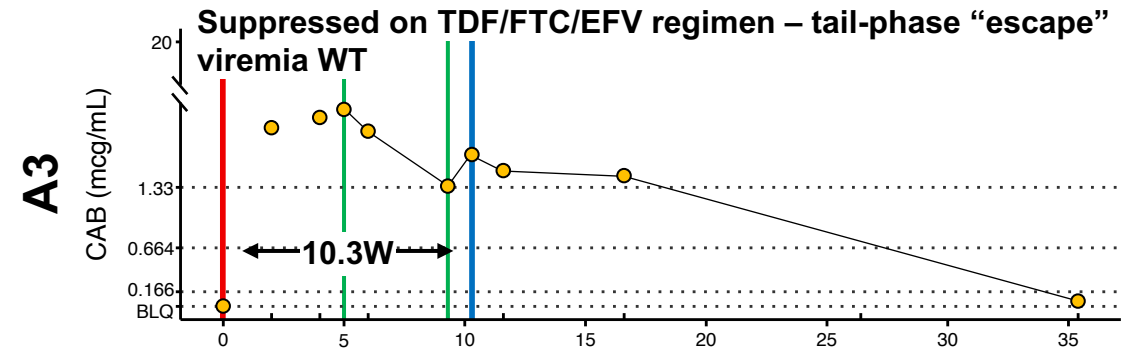
**NRTI:**  
K65R, M184V  
**NNRTI:**  
L100I, K103N, P225H

Ag/Ab test	-	-	-	-
Qualitative RNA test	+	+	+	+
Confirmatory Ab test	-	-	-	-
Viral load	4,010	<40	78	<40



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

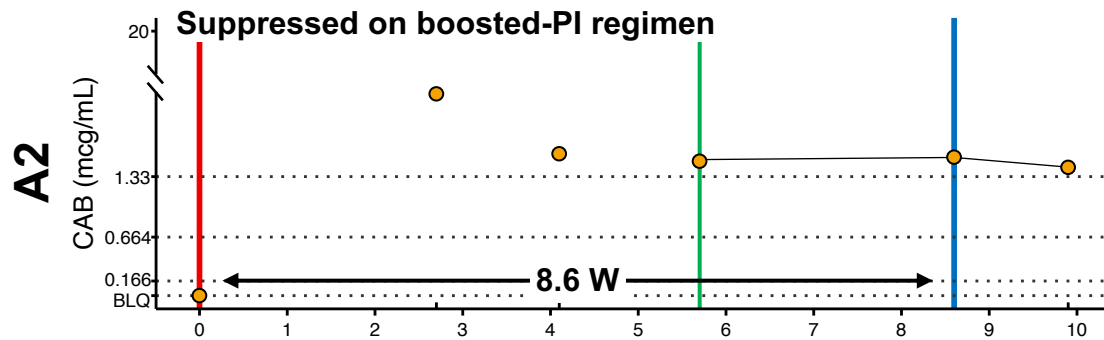
Ag/Ab test	-	+	-	-	-	-	-	+	+
Qualitative RNA test	+	+	-	-	+	-	-	+	+
Confirmatory Ab test	-	-	-	-	-	-	-	IND	+
Viral load	1,360	<40	ND	ND	ND	ND	ND	1,440	76,090



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

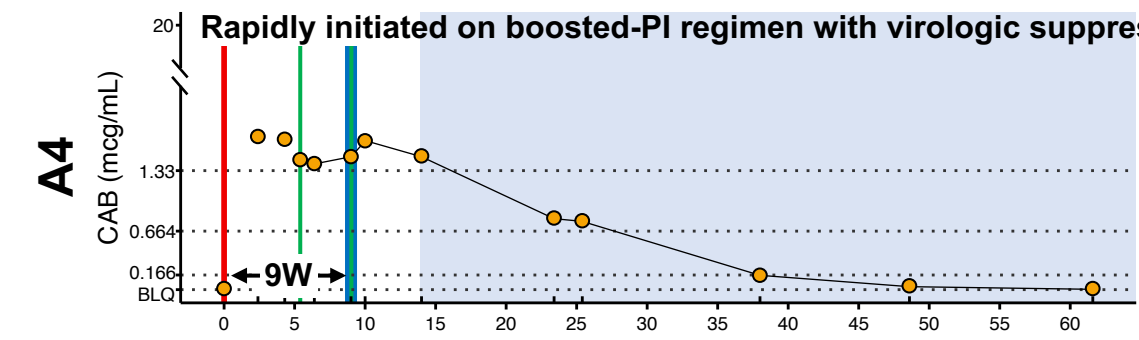
**INSTI:**  
E138K,  
Q148K **INSTI:**  
E138K,  
Q148K

Ag/Ab test	-	-	-	-	+	+
Qualitative RNA test	+	+	+	+	+	+
Confirmatory Ab test	-	-	-	-	+	+
Viral load	50,080	20,760	700	204	1,660	4,829



**WT**

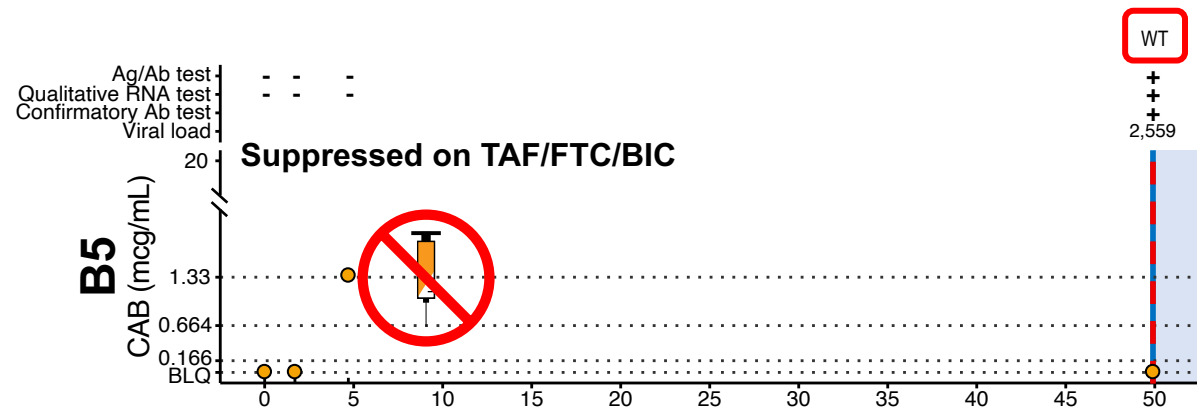
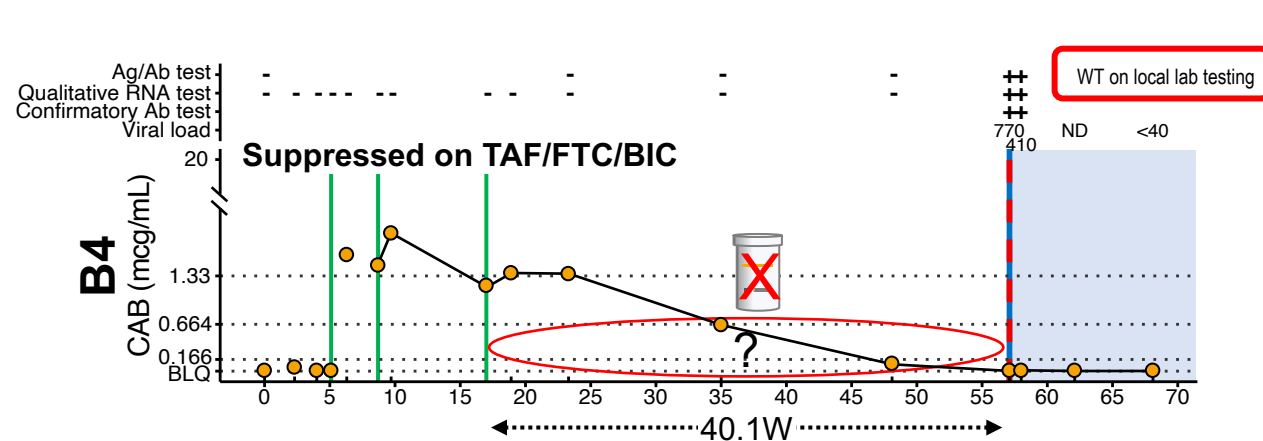
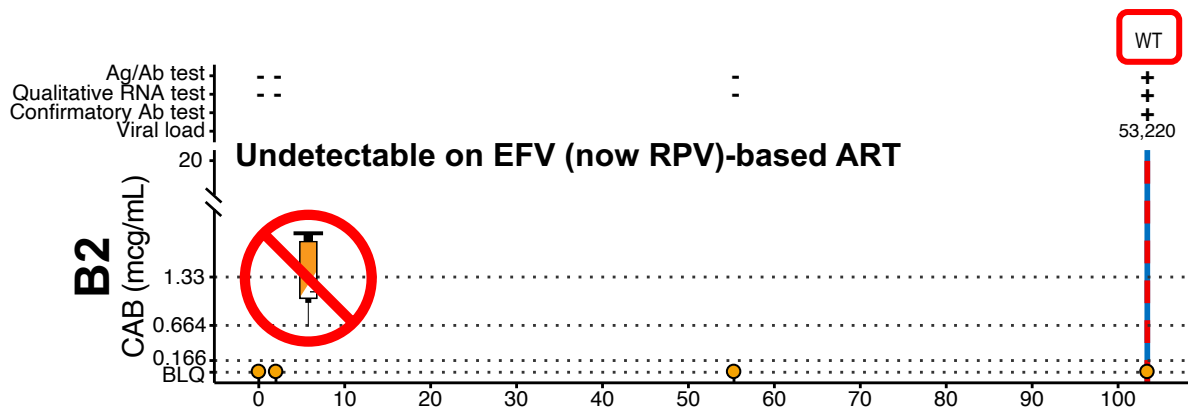
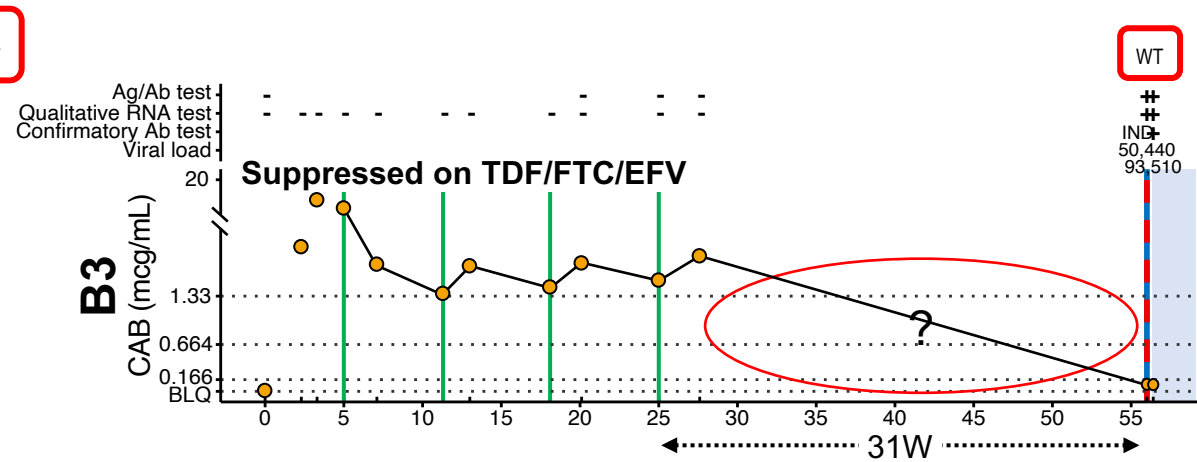
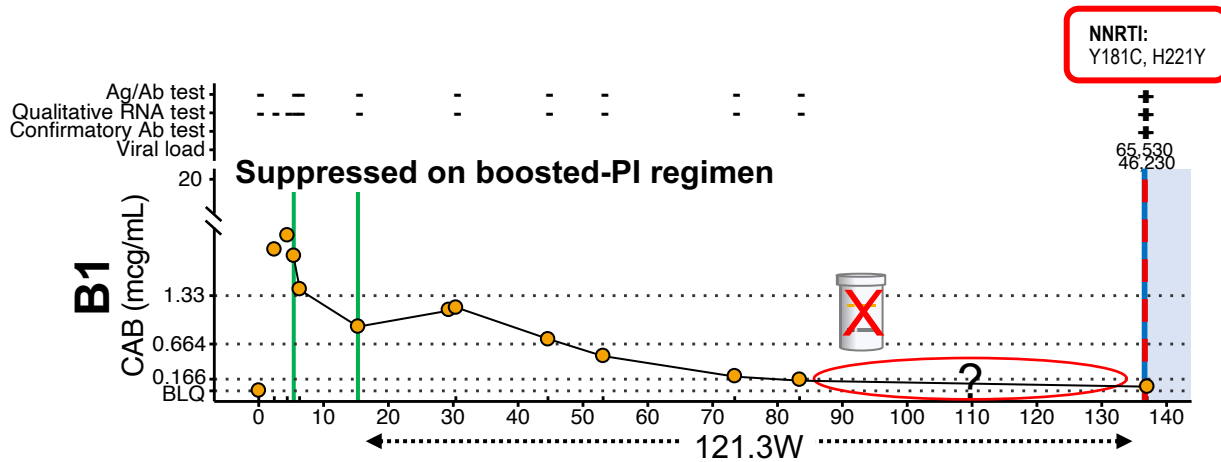
Ag/Ab test	+	-	-	-	+	-	-	-	-	-
Qualitative RNA test	+	+	+	+	-	-	-	-	-	-
Confirmatory Ab test	-	-	-	-	-	-	-	-	-	-
Viral load	44,180	<40	<40	<40	<40	<40	<40	<40	<40	<40



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

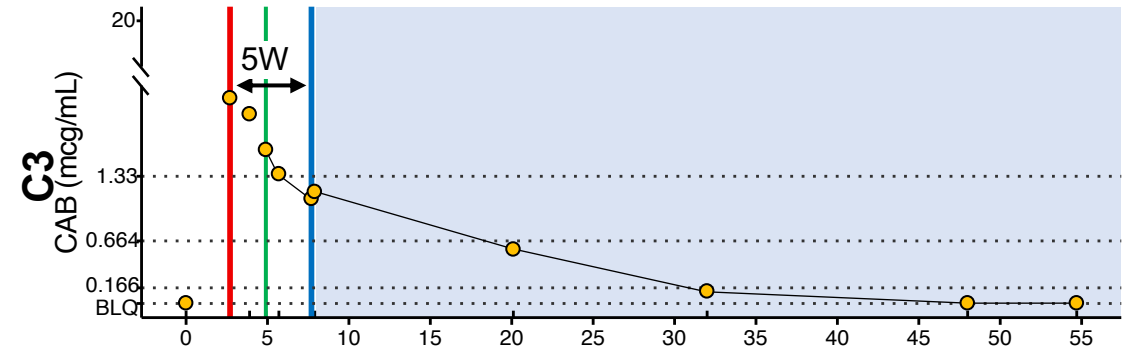
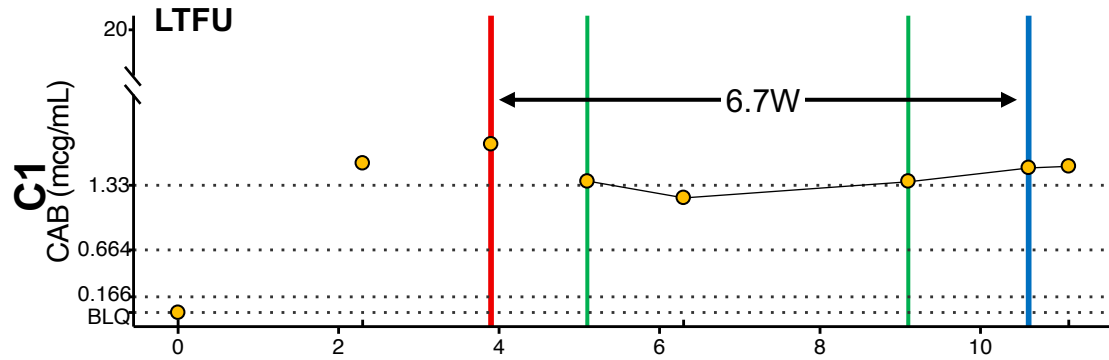
Ag/Ab test	-	-	-	-	-	-	+	-
Qualitative RNA test	-	-	+	+	+	+	+	+
Confirmatory Ab test	-	-	-	-	-	-	-	-
Viral load	ND		120	161	137	2,174	1,373	2,549

**INSTI:**  
L74I,  
Q148R

**INSTI:**  
L74I,E138E/K,  
G140G/S, Q148R

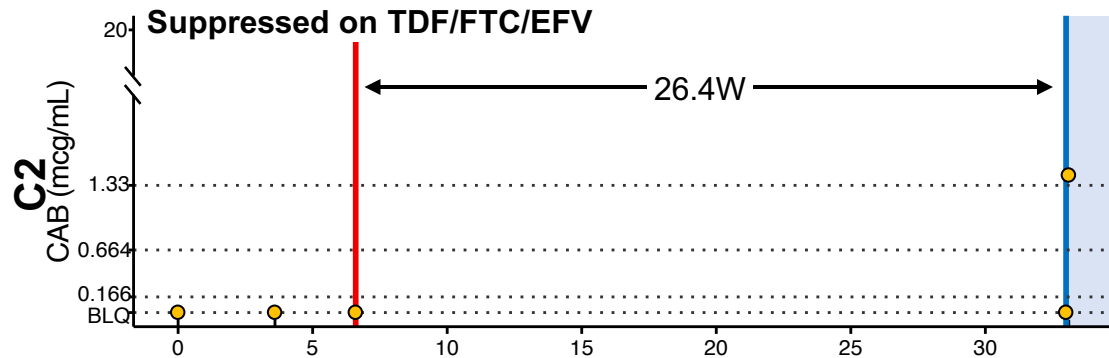
Ag/Ab test	-	-	-	-	+
Qualitative RNA test	-	+	+	+	+
Confirmatory Ab test	-	-	-	-	-
Viral load	ND	ND	102,329	375	<40
			99,218,776		

**INSTI:**  
E138A, Q148R



Ag/Ab test	-	-	-	+
Qualitative RNA test	-	-	+	+
Confirmatory Ab test	-	-	-	+
Viral load			494	229,810 207,810

**WT**

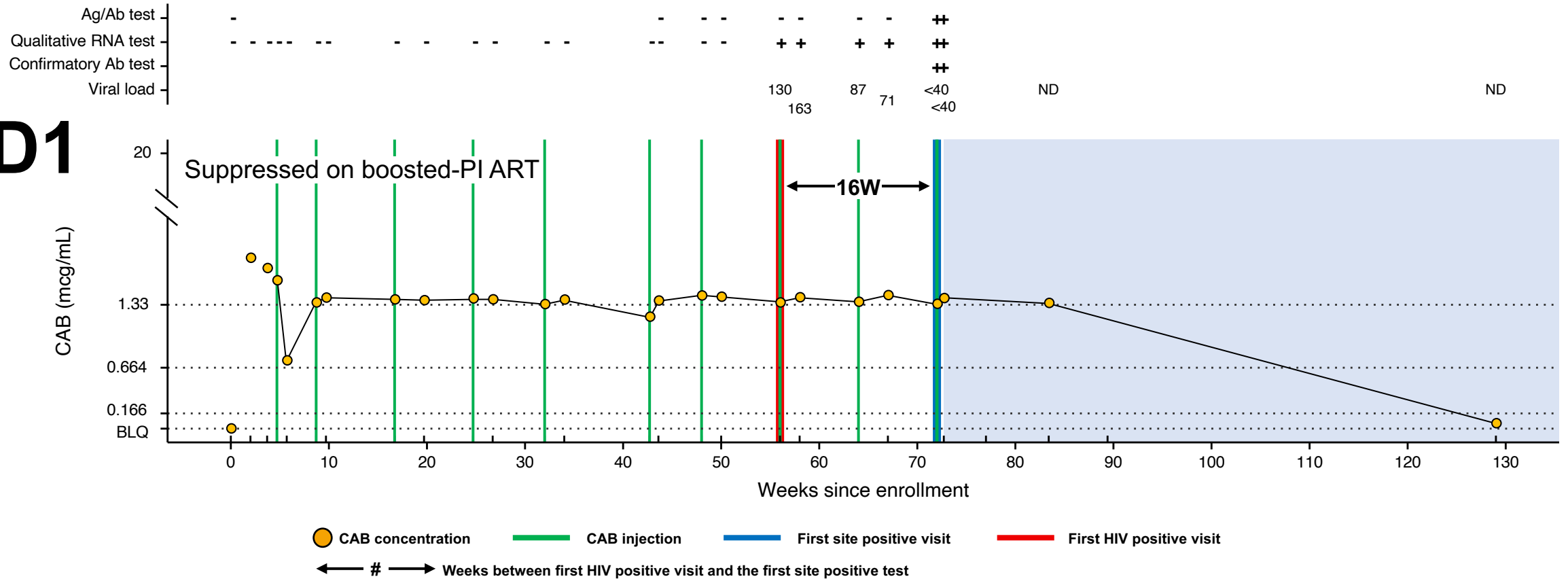


- CAB concentration
- CAB injection
- First HIV positive visit
- First site positive visit
- First HIV positive visit and first site positive visit
- ← # → Weeks between first HIV positive visit and the first site positive test

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

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

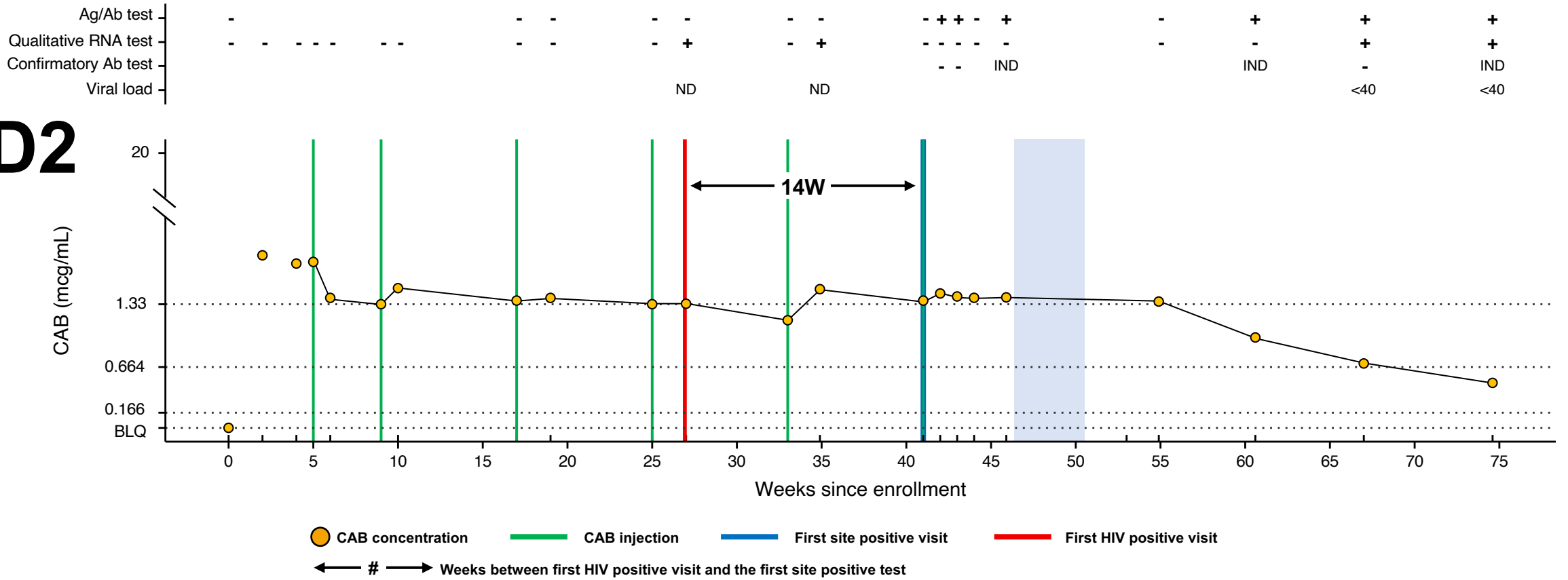
# D1



The shaded area represents time on ART.



# D2



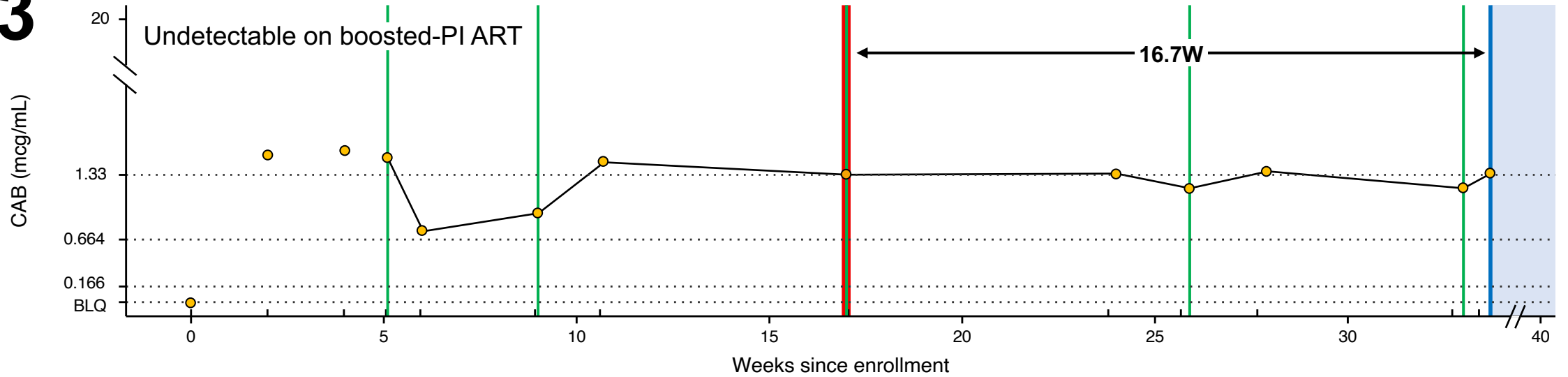
The shaded area represents time on ART.

Ag/Ab test	-	-	-	-	-	-	-	-	-	+	+				
Qualitative RNA test	-	-	-	-	-	-	-	-	-	+	+				
Confirmatory Ab test										-	IND				
Viral load										860	ND	<40	112	7,160	5,510

NNRTI:  
K103N

NNRTI:  
K103N  
INSTI:  
R263K

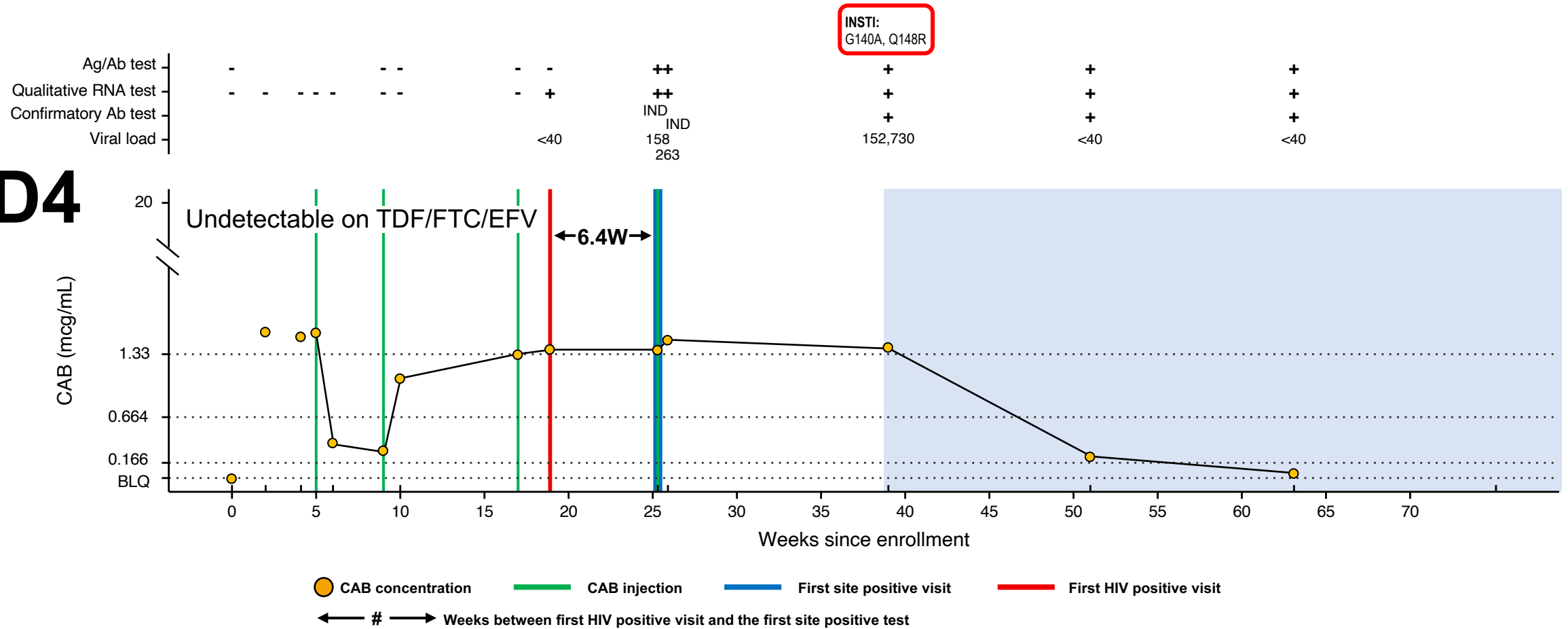
# D3



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

The shaded area represents time on ART.

# A Cautionary Tale



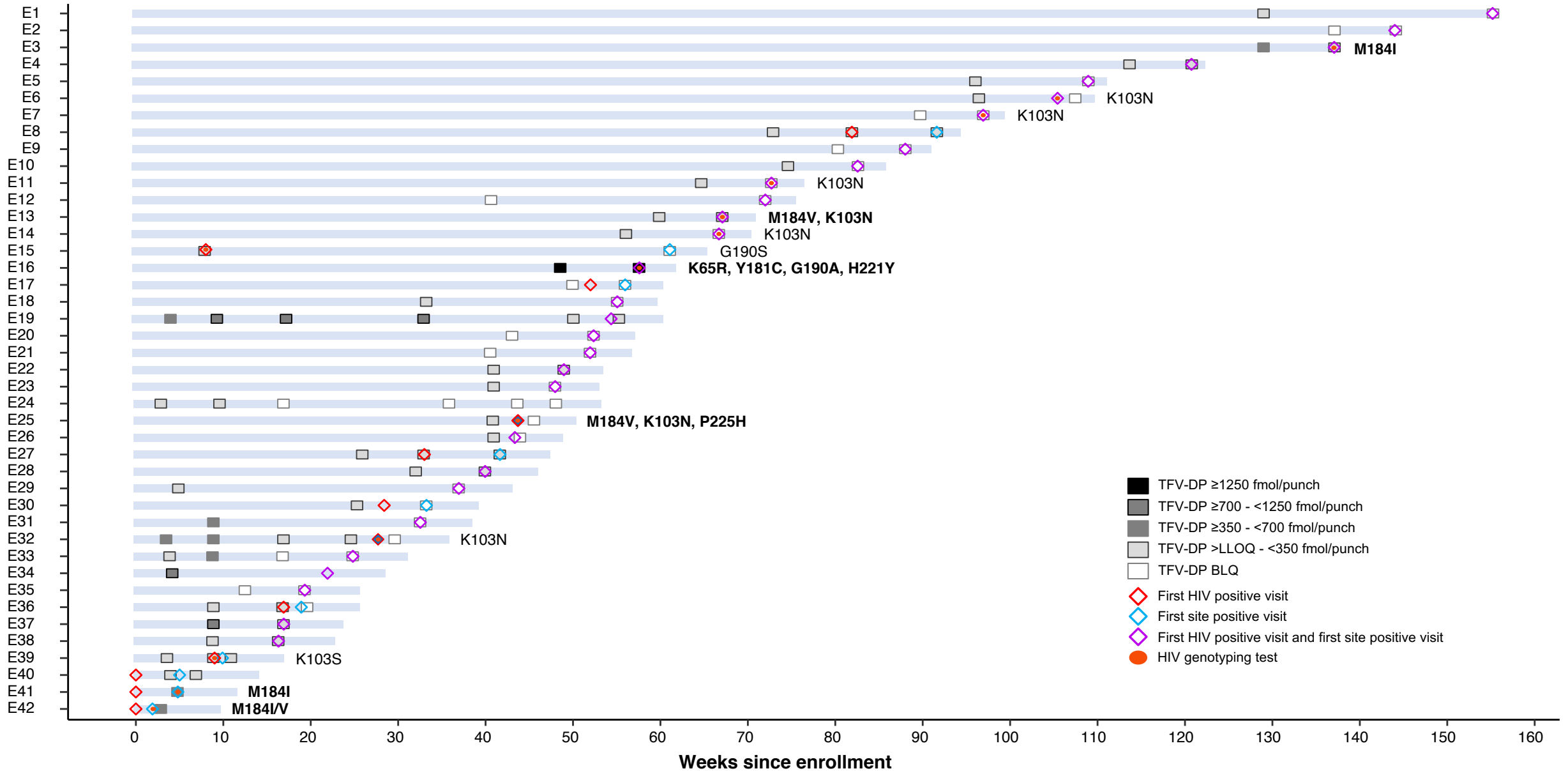
The shaded area represents time on ART.

# **Key virology findings - CAB arm**

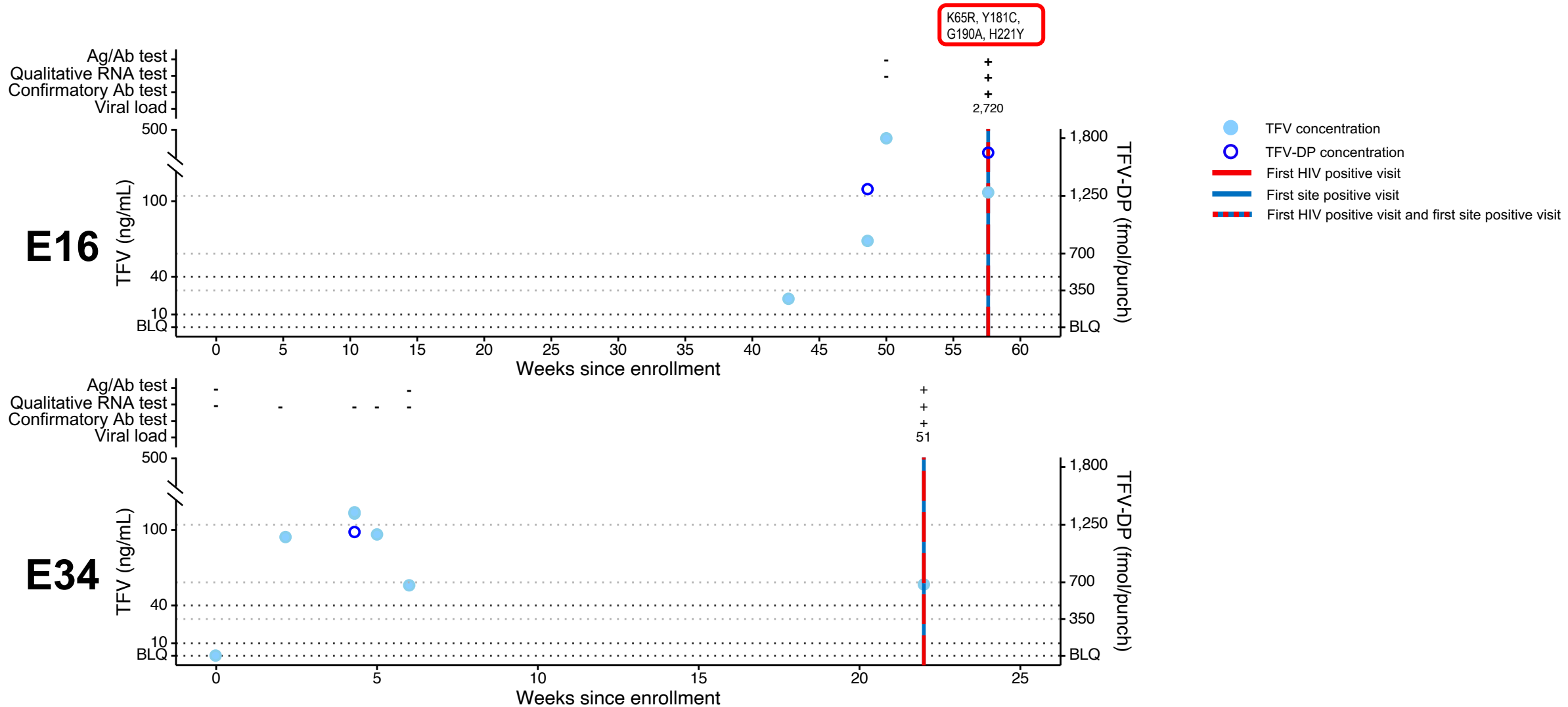
- **Extended testing identified earlier infection dates in many cases**
- **Virus loads were often low at the first HIV positive visit**
- **There was often a prolonged period of viral suppression after infection**
- **Antibody expression was diminished / delayed in many cases**
- **In some cases, RNA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

**TDF/FTC arm**

# 39 Incident, 3 Baseline Infections: TDF/FTC



# TDF/FTC arm – infected despite good adherence





# 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 avoid resistance**

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



# 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



@doc\_in\_a\_box

