Laboratory Analysis of HIV Infections in the Year 1 Unblinded Period of HPTN 083

Injectable Cabotegravir for PrEP in MSM and TGW

Marzinke MA, Grinsztejn B, Fogel JM, Piwowar-Manning E, Hanscom B, Weng Z, Petropoulos C, Halvas, EK, Mellors J, Anderson P, Sued O, Chariyalertsak S, Scott H, Mayer KH, Arduino R, Kofron R, Cohen MS, St Clair M, Rinehart AR, Rooney JF, Adeyeye A, McCauley M, Eshleman SH*, **Landovitz RJ***

Disclosures

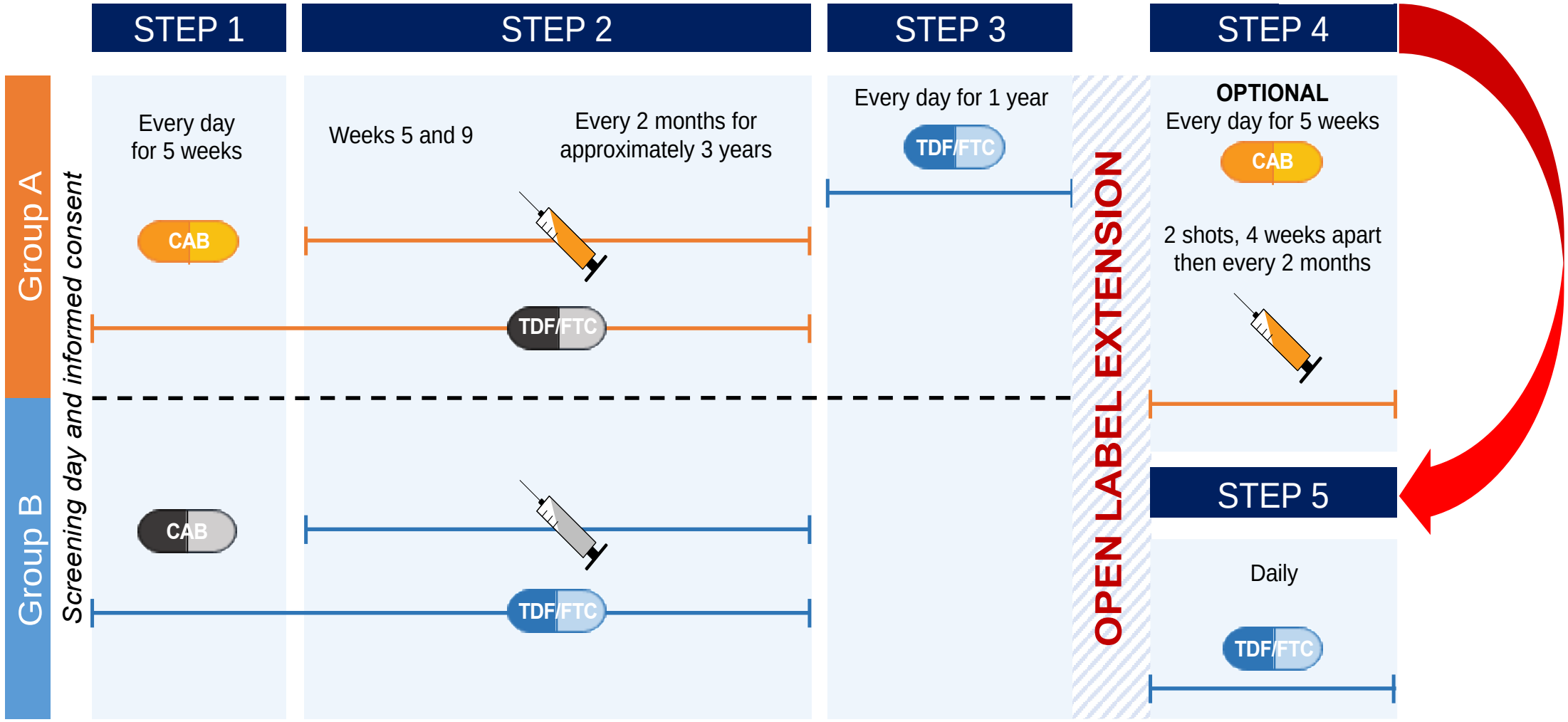
Raphael J. Landovitz has served on Scientific Advisory Boards for Gilead and Merck, and served as a consultant to Cepheid.

Background

- HPTN 083: Phase 2b/3 randomized controlled trial of increased-risk, HIV-uninfected MSM and TGW at 43 sites in 7 countries
- HPTN 083 consistently demonstrated a 66% reduction in HIV incidence in MSM/TGW assigned to cabotegravir injections vs. daily oral TDF/FTC for pre-exposure prophylaxis.[1]
- Virology and pharmacology of 58 HIV infections from the blinded study period were previously characterized[1-4]
- We now present virology and pharmacology findings for 52 additional cases that occurred up to one year after study unblinding

1. Landovitz, RJ et al, NEJM 2021.
2. Landovitz RJ et al, AIDS 2020, Abstract OAXLB0101
3. Marzinke M et al, CROI 2021, Abstract 153
4. Marzinke M et al, JID 2021.

HPTN 083 Study Design

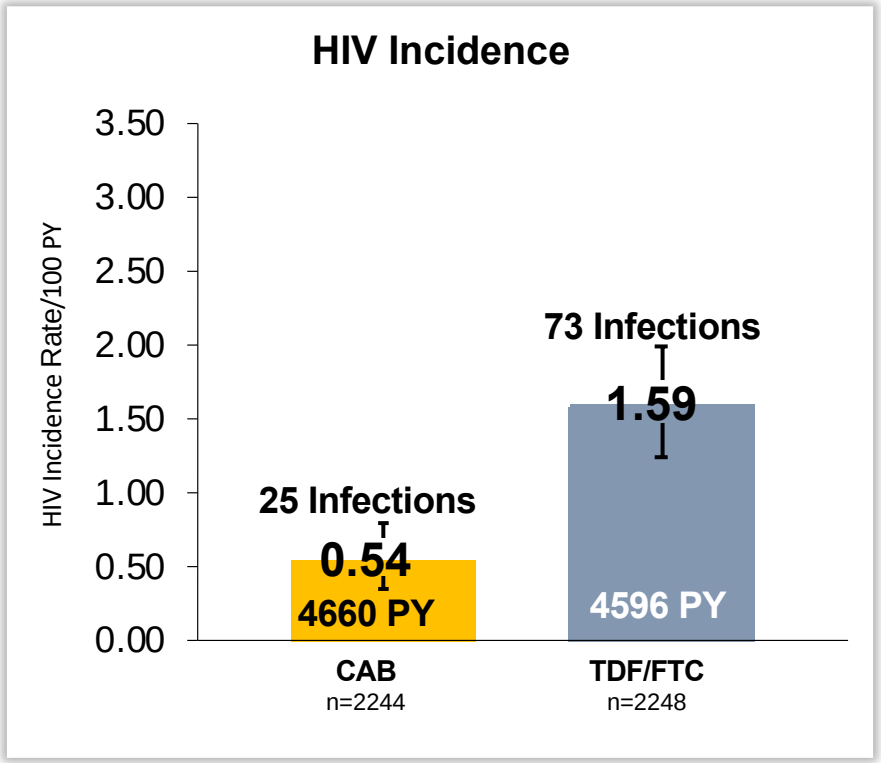


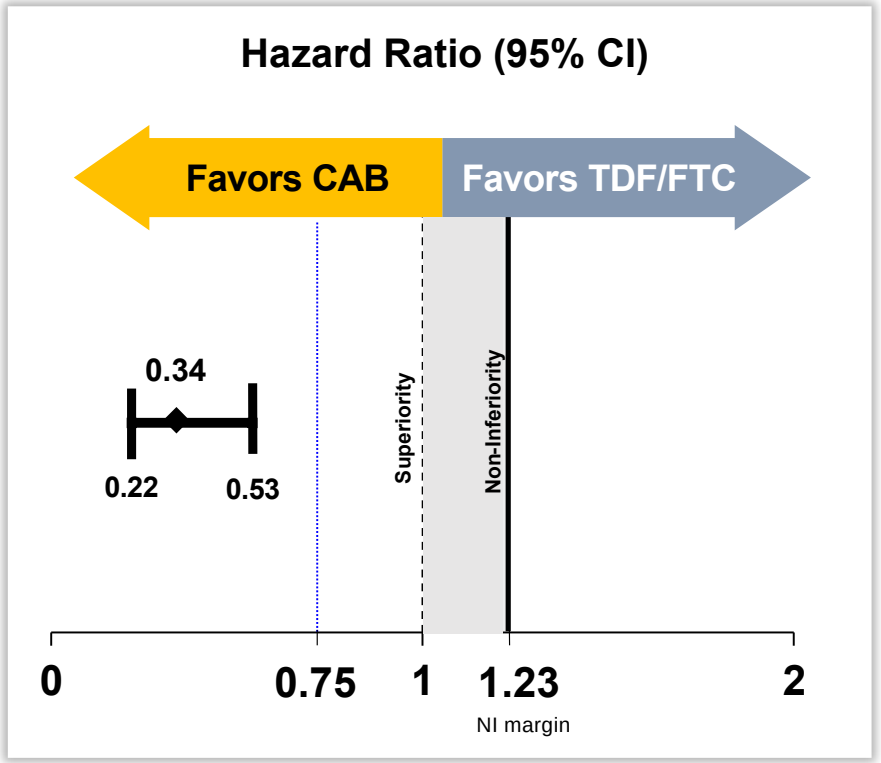
Methods

- New HIV infections detected at sites through November 15, 2021 for which first evidence of HIV infection was before May 15, 2021
- Concentrations of CAB and TFV in plasma and TFV-DP in DBS were quantified by LC-MS/MS
- Timing of HIV infection was assessed using an Ag/Ab test, a discriminatory test and RNA assays
- Drug resistance testing was performed using a commercial assay (viral load [VL] >500 c/mL) and a low VL integrase genotyping assay (VL <500 c/mL)[1]

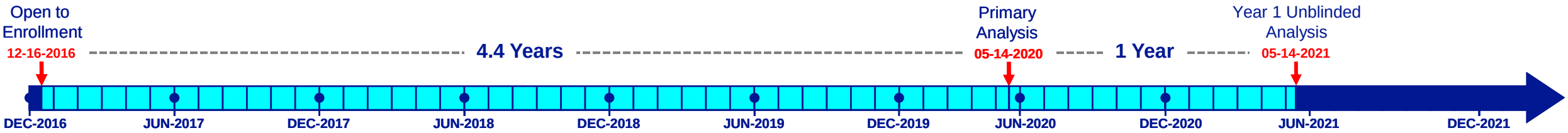
[1]Eshleman SE, JID 2022

HIV Incidence: CAB vs. TDF/FTC

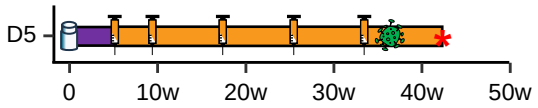




CI, confidence interval



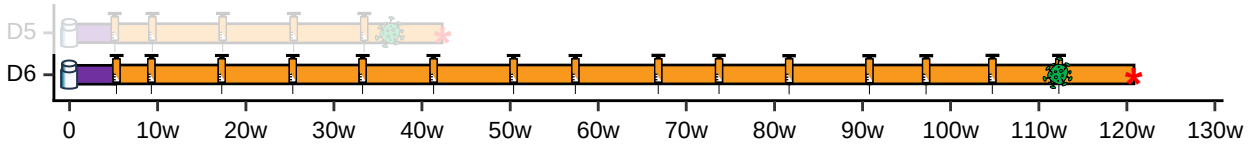
Cabotegravir Arm Infections



NEW
Blinded Period case

- Step 1: Oral CAB lead-in
- Step 1: Lapse in oral CAB coverage
- Step 2: CAB LA 600 mg IM
- Step 2: Lapse in CAB LA injection coverage
- Step 3: Open-label TDF/FTC
- Step 3: Overdue TDF/FTC dispensation
- Annual follow-up
- Oral lead-in
- CAB LA 600 mg IM
- Open-label TDF/FTC dispensed
- HIV-infection
- * First site positive HIV test

Cabotegravir Arm Infections



New Year 1 Cases (Unblinded)

<6m after last (D, Dx)

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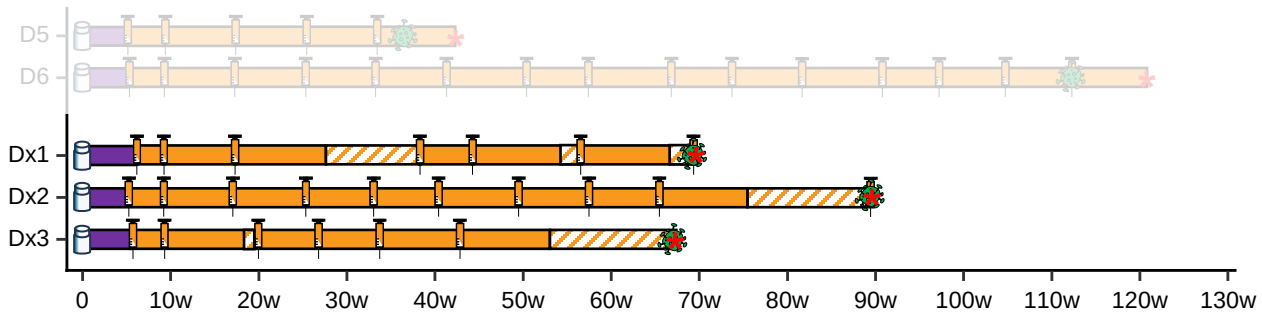

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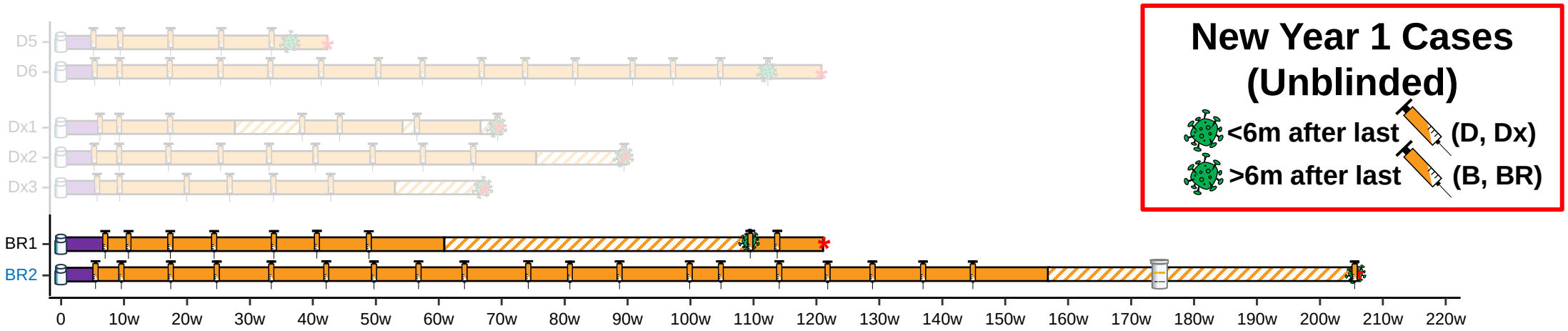

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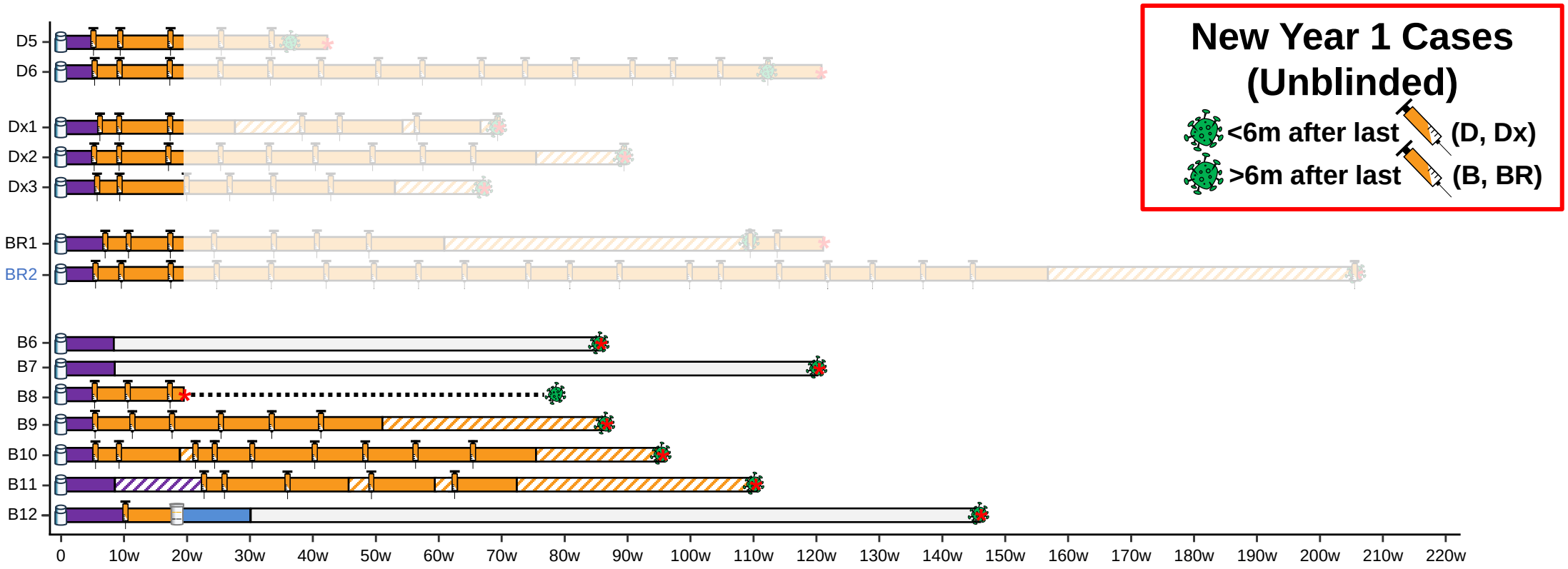
Cabotegravir Arm Infections



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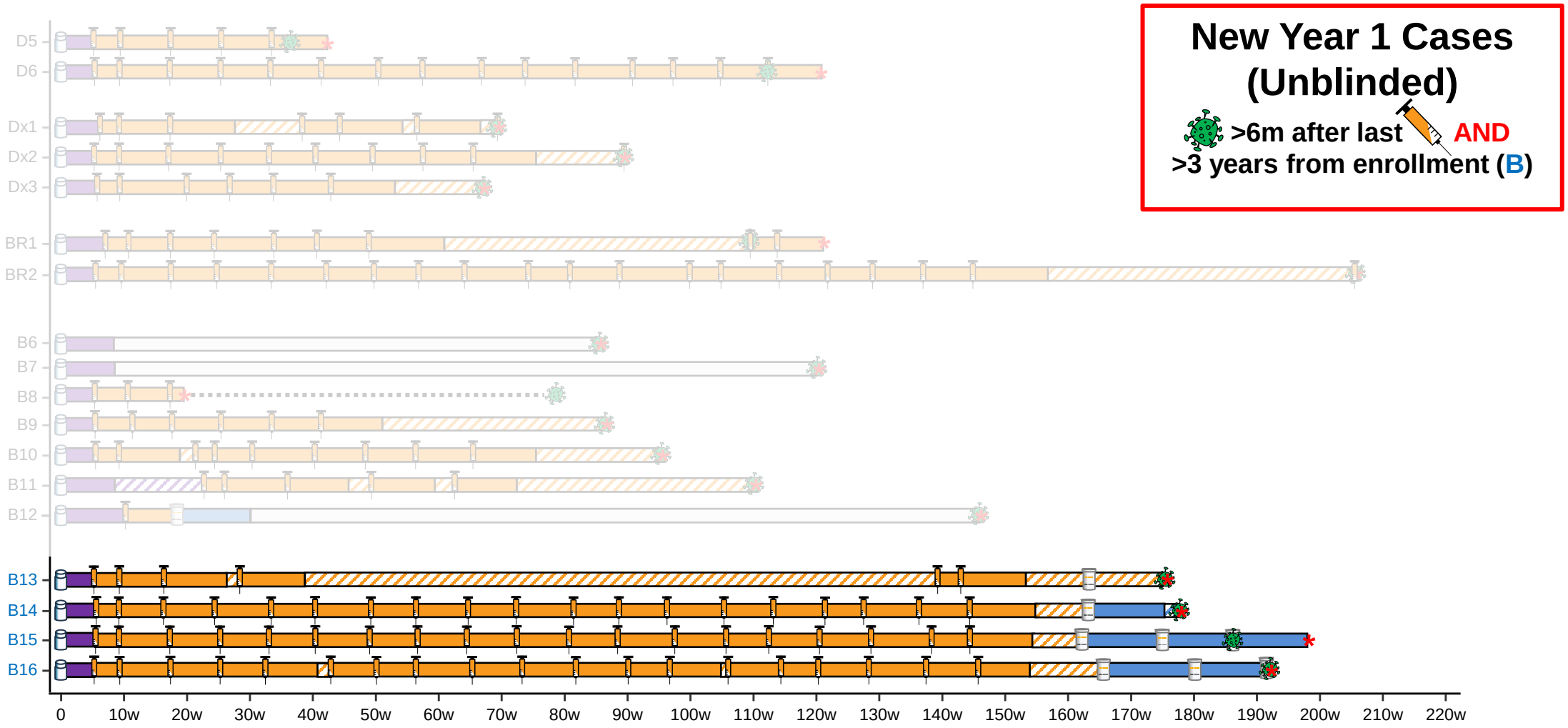
Cabotegravir Arm Infections

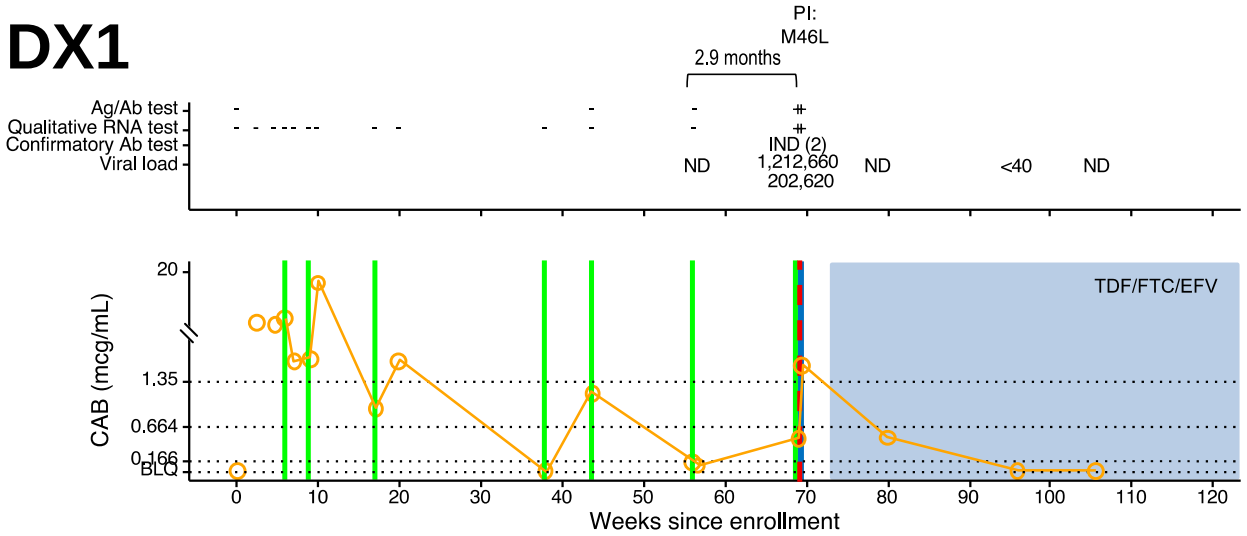


Cabotegravir Arm Infections

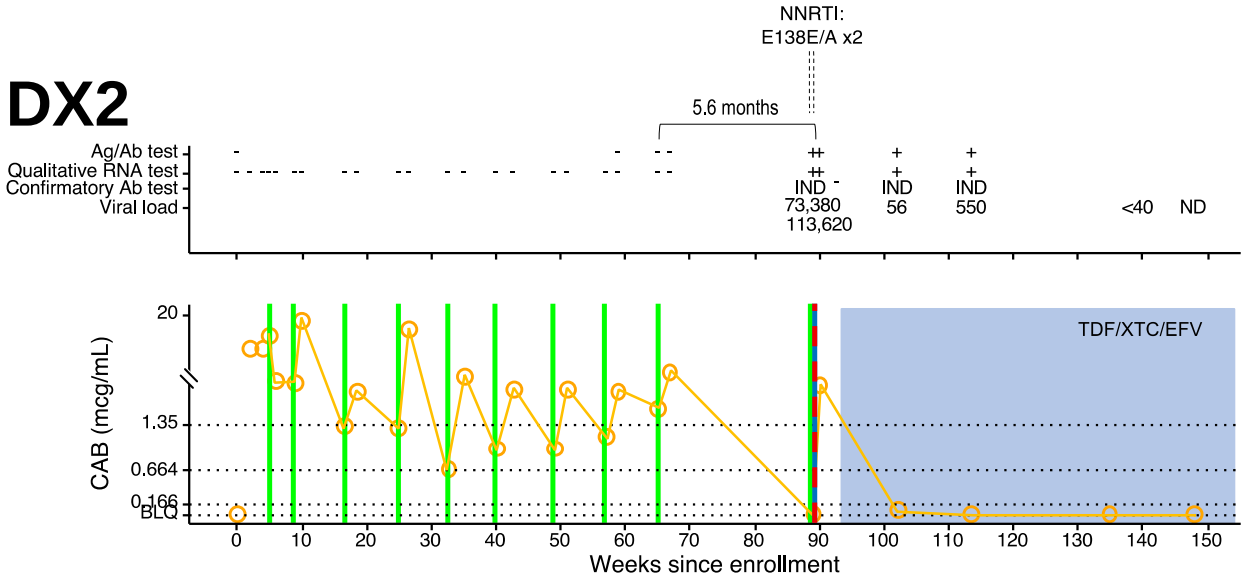
CAB concentration | CAB injection | First HIV positive visit | First site positive visit | First HIV positive visit and first site positive visit

Cabotegravir Arm Infections

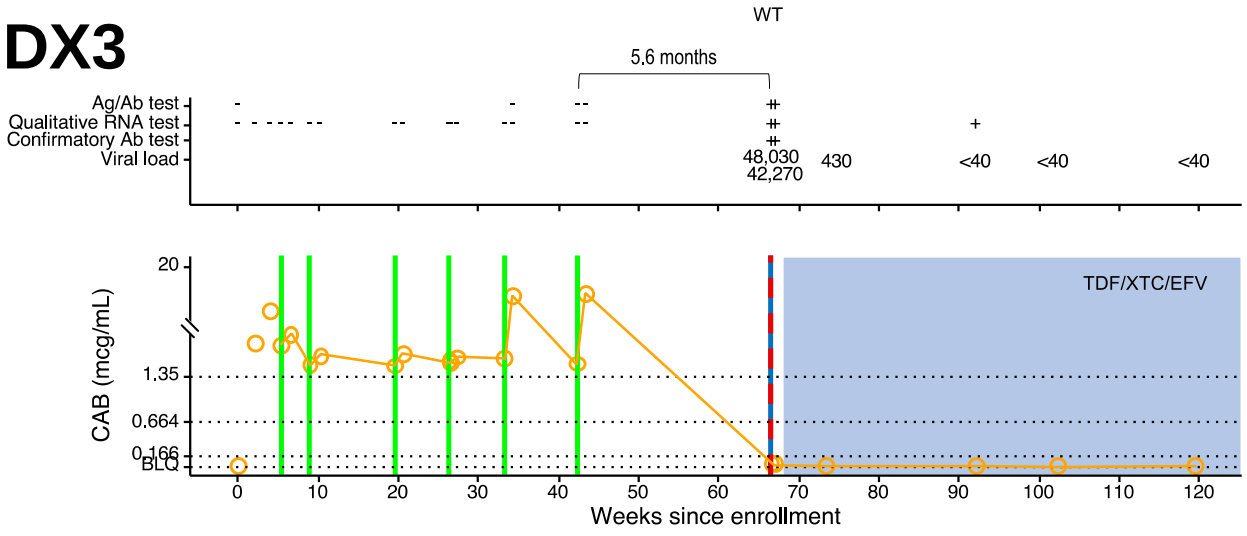
DX1

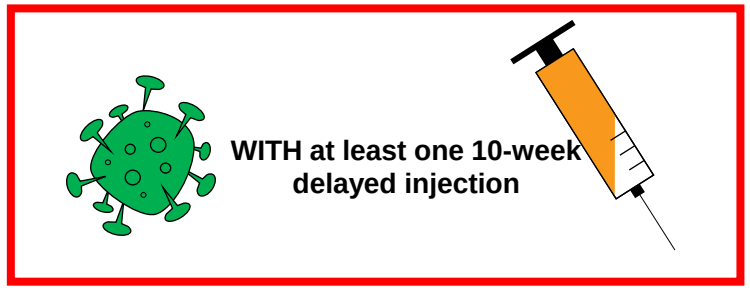


DX2



DX3





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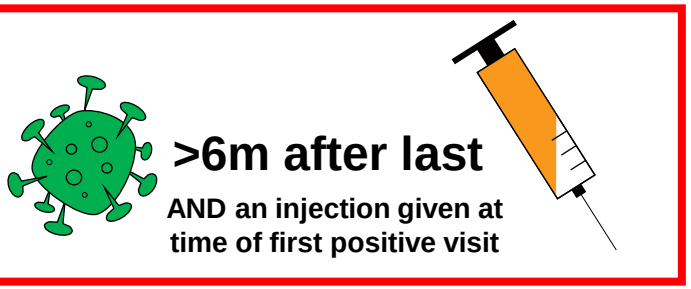
Cabotegravir Arm Infections



CAB concentration | CAB injection | First HIV positive visit | First site positive visit | First HIV positive visit and first site positive visit

Summary of HPTN 083 Major INSTI RAMs

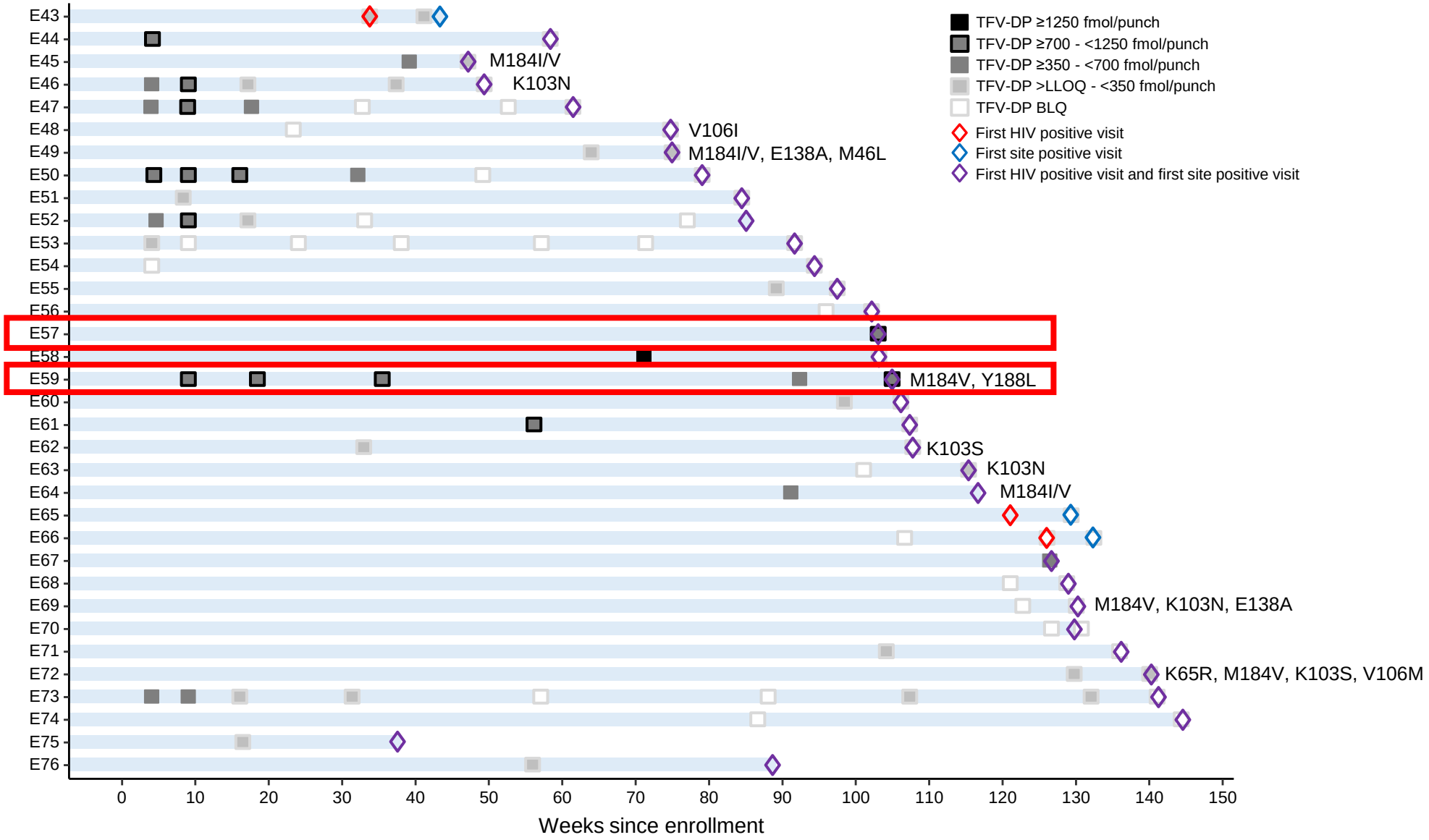
	N (%)	RAMs
CAB INITIATED OR RE-INITIATED WITH OCCULT HIV INFECTION		
A1-4	1 (25)	E138E/K, Q148K/R
BR1-2	1 (50)	Q148R
HIV ACQUISITION DURING OLI		
C1-3	2 (66)	E138E/A/K, G140G/S, Q148R
HIV BREAKTHROUGH INFECTION WITH ON-TIME INJECTIONS		
D1-6	6 (100)	E138K, G140A, Q148R, N155H, R263K
HIV BREAKTHROUGH INFECTION WITH AT LEAST ONE 10+ WEEK DELAY		
DX1-3	0 (0)	
HIV INFECTION 6+ MONTHS FROM LAST INJECTION		
B1-16*	0 (0)	

*No result for B4

GenoSure PRIme (Monogram Biosciences) | **Low VL INSTI Genotyping**

TDF/FTC Arm Infections in Year 1 Unblinded Phase

2 of 34 cases not explained by adherence



Conclusions

- **Plasma CAB concentrations were generally as expected**
  - **Cases of rapid CAB clearance require additional investigation**
- **INSTI mutations were observed in 3 new cases**
  - **All CAB arm infections with on-time injections to-date had INSTI RAMs**
  - **Initiation of CAB PrEP with undiagnosed infection can select for INSTI mutations**
- **HIV acquisition 6+ months after last CAB-LA did not have significant diagnostic delays nor INSTI resistance**
  - **The timeline may be different for individuals born female**
- **With additional experience, CAB efficacy advantage persisted; ongoing demonstration projects will further inform real-world implementation of CAB-LA PrEP**

Acknowledgements

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- Sue Eshleman
- Mark Marzinke
- Nirupama Sista
- Kathy Hinson
- Beth Farrell

Our Sites and Site Staff

HPTN HIV Prevention Trials Network 083

and

OUR PARTICIPANTS!

Questions? Email rlandovitz@mednet.ucla.edu or @doc_in_a_box