Long acting injectable cabotegravir: updated efficacy and safety results from HPTN 084

S Delany-Moretlwe, JP Hughes, P Bock, S Dadabhai, D Gadama, P Hunidzarira, S Innes, D Kalonji, J Makhema, P Mandima, C Mathew, J Mpendo, P Mukwekwerere, N Mgodi, P Nahirya Ntege, C Nakabiito, H Nuwagaba-Biribonwoha, R Panchia, F Angira, N Singh, B Siziba, E Spooner, J Farrior, S Rose, R Berhanu, Y Agyei, SH Eshleman, M Marzinke, E Piwowar-Manning, S Beigel-Orme, S Hosek, A Adeyeye, J Rooney, A Rinehart, B Hanscom, M Cohen, M Hosseinipour

on behalf of the HPTN 084 study team

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HPTN 084
Long-acting Injectable For the Epidemic

Background

- HPTN 084 is an ongoing Phase 3 randomized, controlled trial that demonstrated the superiority of long-acting injectable cabotegravir (CAB) compared to daily oral TDF/FTC for HIV prevention in individuals assigned female at birth.
  - HIV incidence CAB 0.20 vs TDF/FTC 1.85 per 100 py, HR 0.12; 95% CI 0.05 - 0.31

- The blinded portion of the trial was stopped at a planned interim review in November 2020.

- Participants were subsequently unblinded and continued on their original randomised study regimen pending a protocol amendment to offer open-label CAB.

Methods

- We report on HIV infections detected in the 12-month period following trial unblinding
  - 5/11/20-5/11/21, detected through 31/12/21
  - based on site and HPTN Laboratory Center testing.

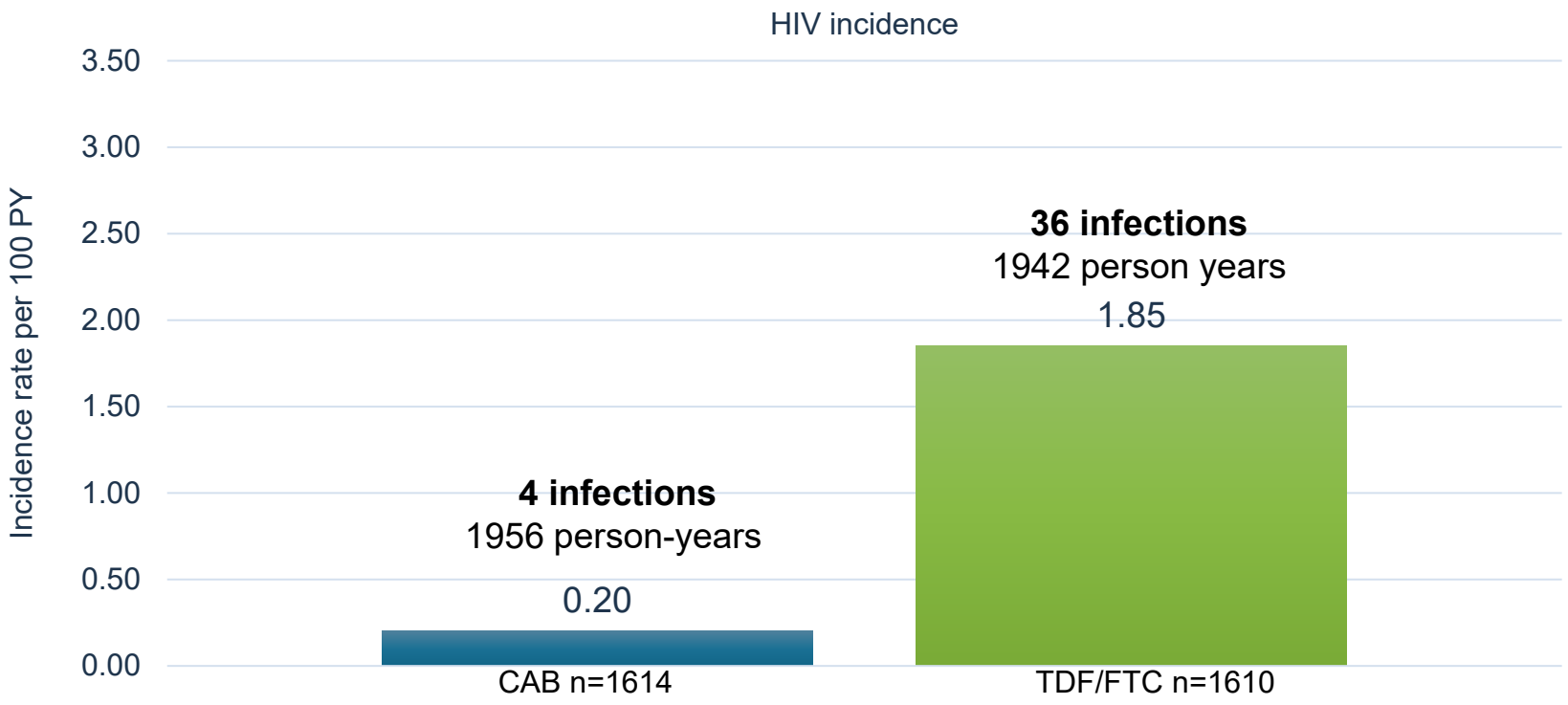
- We estimated cumulative HIV incidence for the combined primary blinded and 12-month unblinded follow-up period, by study group.

- We report grade 2+ adverse events, injection site reactions , pregnancy incidence and outcomes for the 12-month post-unblinding period only.

HIV incidence: CAB vs TDF/FTC

Blinded period, through Nov 2020

HR 0.12; 95% CI 0.05 - 0.31



Delany-Moretlwe, Lancet 2022

HIV incidence: CAB vs TDF/FTC

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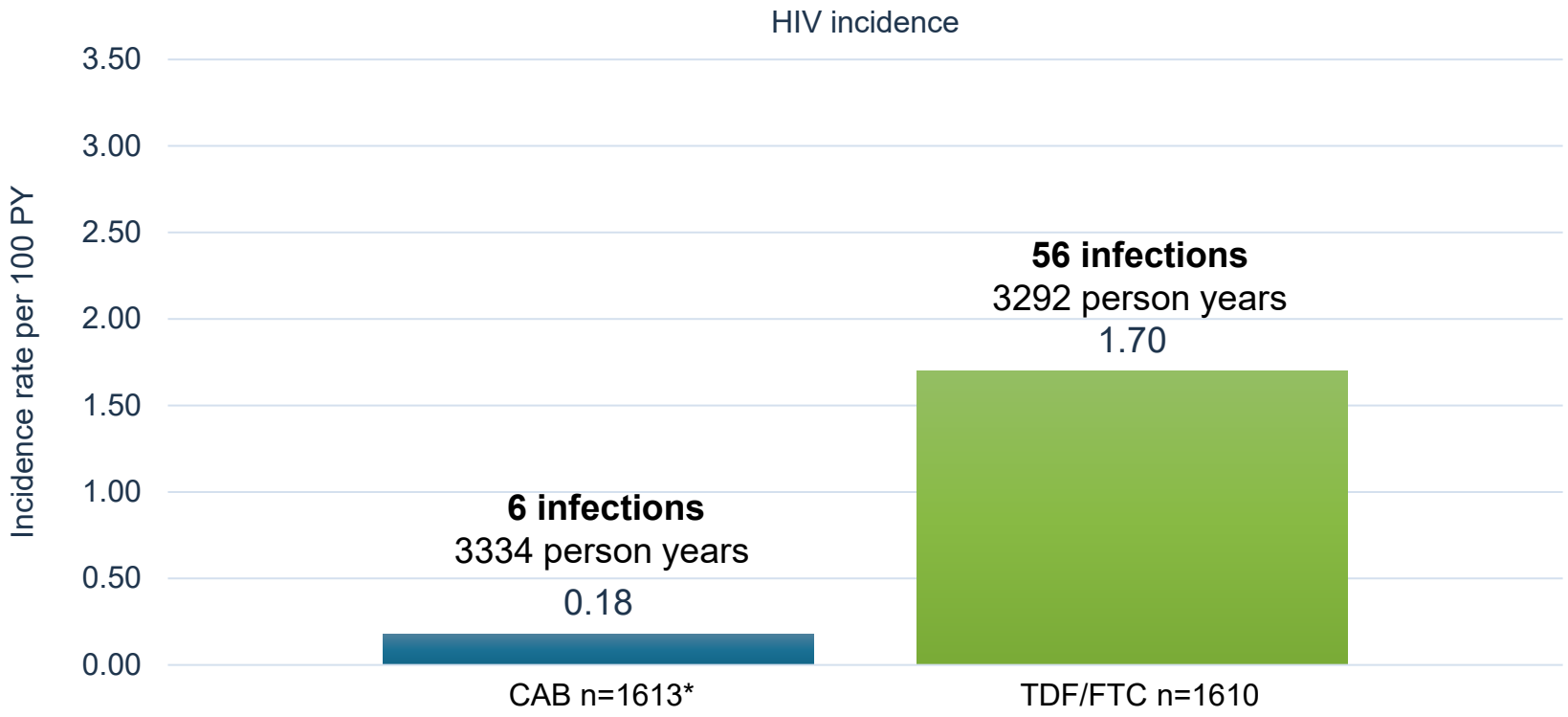
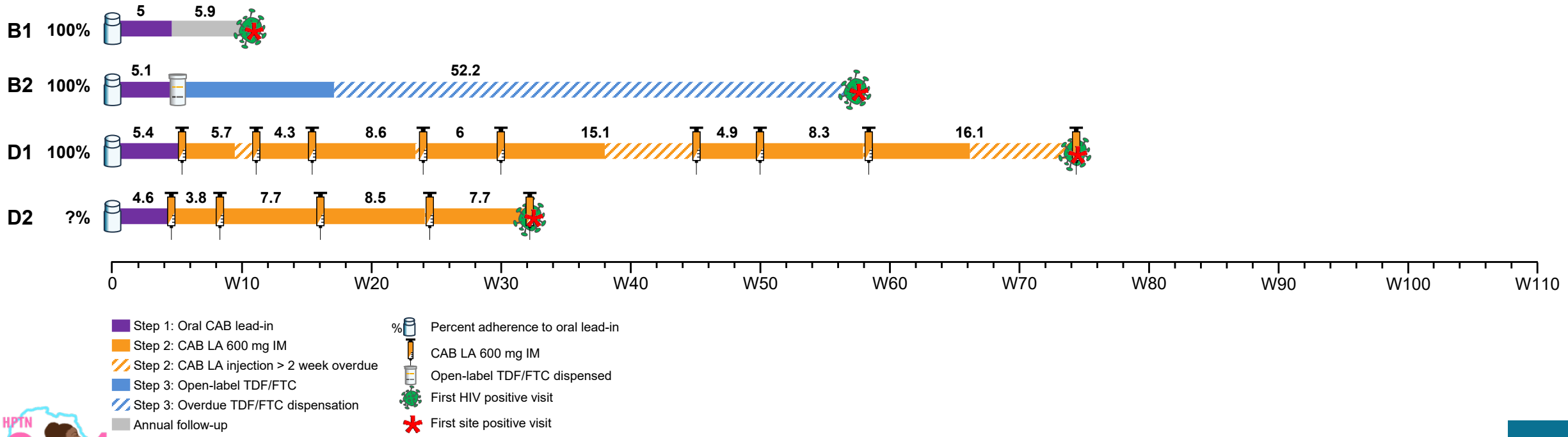
Combined blinded and unblinded period, through Dec 2021

HR 0.11; 95% CI 0.05 - 0.24

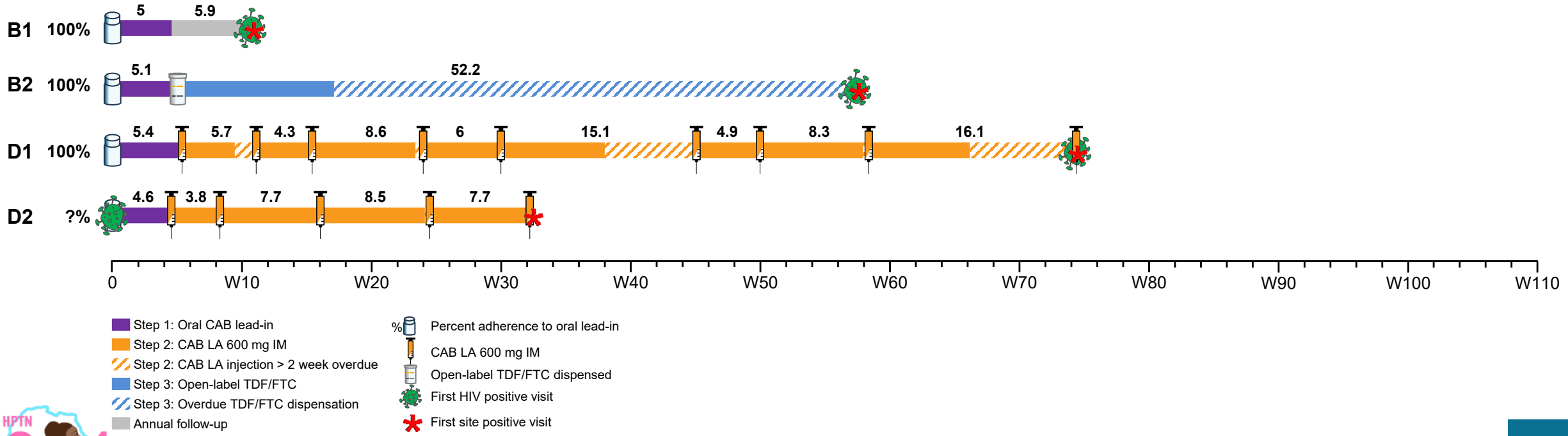


*Excludes 1 baseline infection from the blinded period

Cabotegravir infections: blinded period



Cabotegravir infections: blinded period



Cabotegravir infections: blinded period

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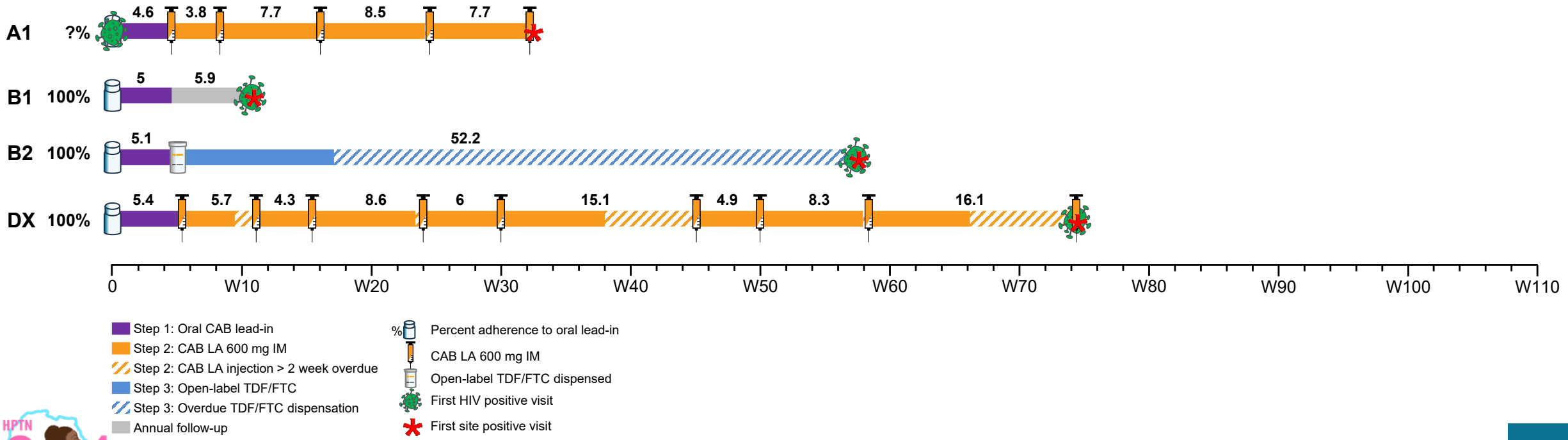

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Cabotegravir infections: cumulative

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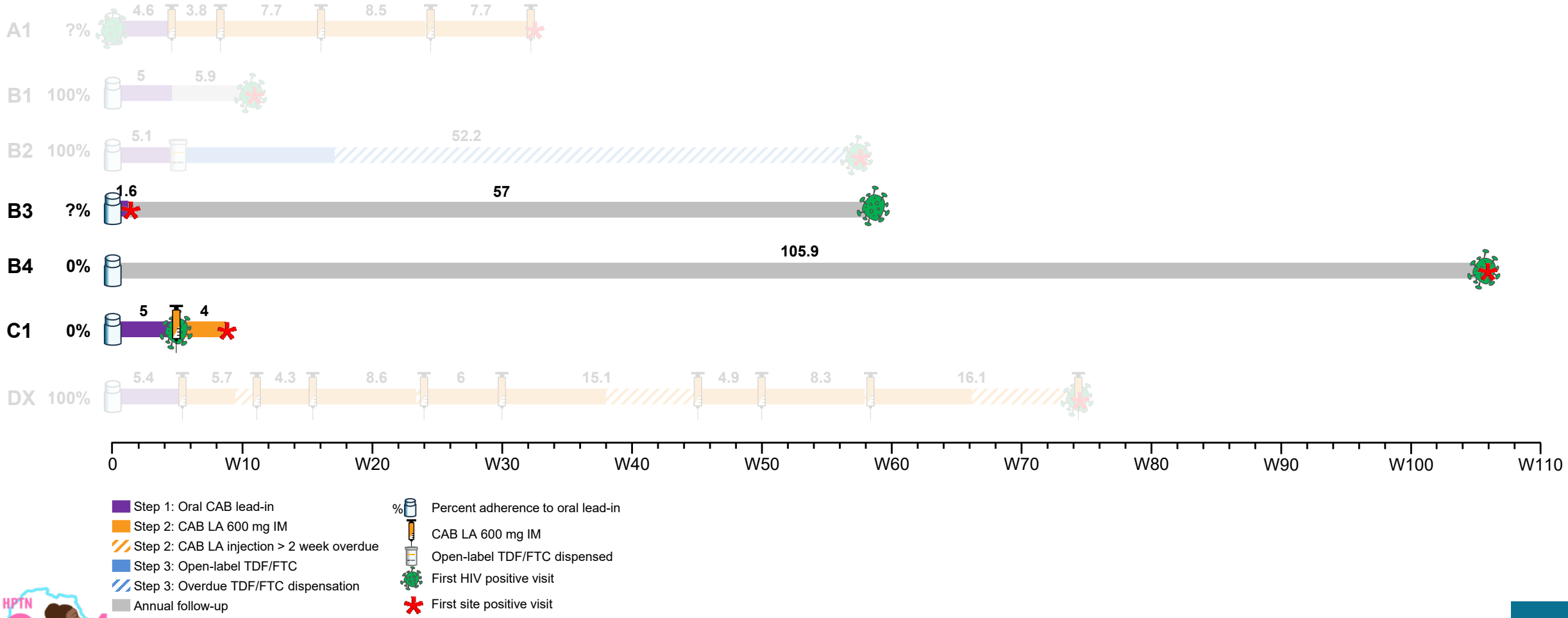

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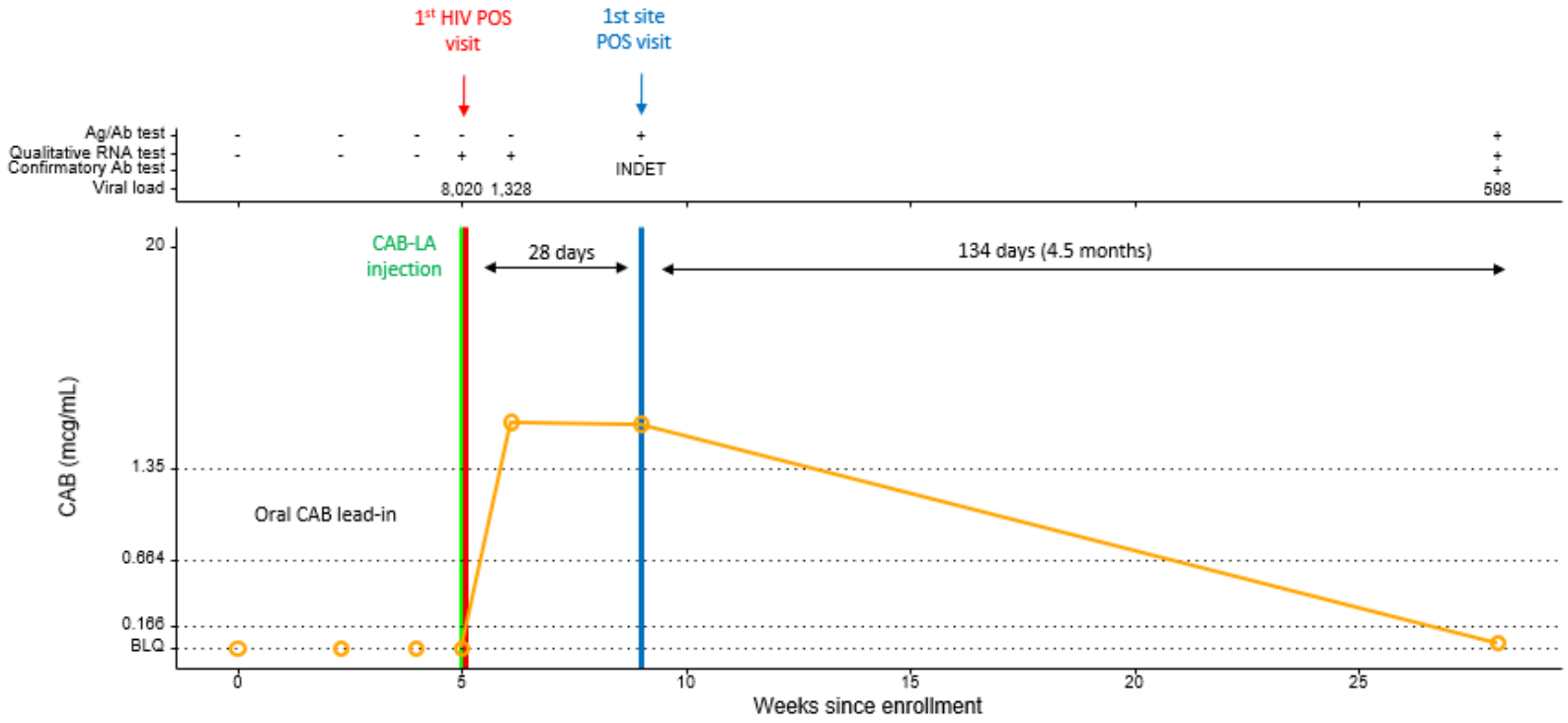
Cabotegravir group infections: C1

- No detectable CAB during the oral lead-in
- Participant received first injection at first HIV positive visit
- Site-based testing did not detect infection at that visit
- Site detected infection 28 days later, when product was held



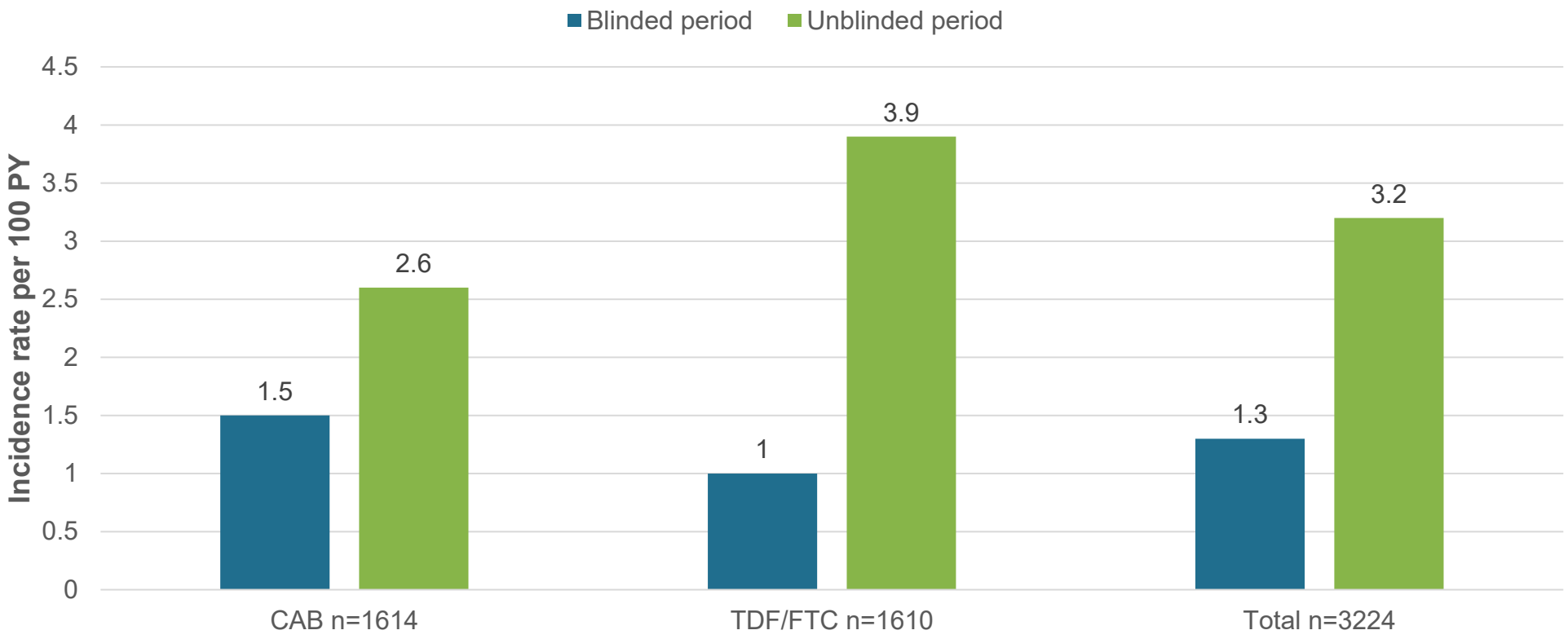
Safety: Grade 2+ events, unblinded period

Participants with ≥ Grade 2 events	Total (n=2865)		CAB (n=1440)		TDF/FTC (n=1425)	
	n	%	n	%	n	%
Any Grade 2+ events	2391	83%	1194	83%	1197	84%
Creatinine clearance decreased	1146	40%	562	39%	584	41%
Chlamydia infection	453	16%	225	16%	228	16%
Gastrointestinal disorders	385	13%	211	15%	174	12%
Creatinine increased	338	12%	168	12%	170	12%
Urinary tract infection	258	9%	140	7%	118	8%
Gonorrhoea	213	7%	115	7%	98	7%
Upper respiratory tract infection	184	6%	89	7%	95	7%
Trichomoniasis	165	6%	94	7%	71	5%
Headache	164	6%	91	7%	73	5%
Vulvovaginal candidiasis	157	5%	78	7%	79	6%
Back pain	154	5%	75	7%	79	6%
Blood glucose decreased	140	5%	71	7%	69	5%
Abnormal uterine bleeding	123	4%	59	7%	64	4%
Any SAE/EAE	48	2%	26	2%	22	2%
Deaths	2	0,1%	2	0,1%	0	0%
ISR - Grade 2+ (n=1318)			32	2%		

Events reported at frequency ≥ 5%

*80% of Grade 2+ adverse events considered **unrelated** to study products, both arms*

Pregnancy incidence: CAB vs TDF/FTC



	CAB n=1614	TDF/FTC n=1610	Total n=3224
Cumulative confirmed pregnancies	63	69	132
Cumulative person-years	3239.1	3238.3	6477.3

Cumulative pregnancy outcomes

	Total n=132	CAB n=63	TDF/FTC n=69
Ongoing	57	23	34
Known pregnancy outcomes*			
Live births	60	31	30
Pregnancy loss			
>=37 weeks	2	1	1
20-36 weeks	3	1	2
<20 weeks**	12	9	4
Congenital anomalies	0	0	0

*includes multiple births
**includes ectopic pregnancy, elective and spontaneous abortion

Conclusions

- CAB continues to be superior to TDF/FTC in preventing HIV infection in individuals assigned female at birth
  - 89% lower risk of HIV in CAB vs. TDF/FTC group
  - No new safety concerns identified

- Three additional CAB group infections were identified
  - All associated with poor/absent product use
  - no on-injection breakthrough infections observed

- Pregnancy incidence increased in the unblinded period
  - Confirms importance of CAB safety and pharmacology in pregnancy during the open-label extension

Acknowledgments

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HIV Prevention Trials Network

- Leadership and Operations Centre, FHI360
- Laboratory Centre (Johns Hopkins)
- Statistical Center for HIV/AIDS Research and Prevention, Fred Hutchison Cancer Research Center
- HPTN Leadership

HPTN 084 Study team

- 20 sites in 7 countries in sub-Saharan Africa
- Community advisory boards and partners

… and our study participants!

UM1AI068619-15 (HPTN Leadership and Operations Center), UM1AI068617-15 (HPTN Statistical and Data Management Center), and UM1AI068613-15 (HPTN Laboratory Center).

Extra slides

Figure S1.

TDF/FTC adherence subset