



Long acting injectable cabotegravir is safe and effective in preventing HIV infection in cisgender women: results from HPTN 084

*Sinead Delany-Moretlwe, MBBCh PhD
on behalf of the HPTN 084 study team*

Authors

S Delany-Moretlwe, JP Hughes, P Bock, S Gurrion, P Hunidzarira, D Kalonji, N Kayange, J Makhema, P Mandima, C Mathew, M Mokgoro, J Mpendo, P Mukwekwerere, N Mgodi, P Nahirya Ntege, G Nair, C Nakabiito, H Nuwagaba-Biribonwoha, R Panchia, N Singh, B Siziba, J Farrior, S Rose, R Berhanu, P Anderson, Y Agyei, SH Eshleman, M Marzinke, E Piwowar-Manning, A Asmelash, F Conradie, M Moorhouse, P Richardson, S Beigel-Orme, L Emel, K Bokoch, R White, S Hosek, B Tolley, N Sista, K Shin, A Adeyeye, J Rooney, A Rinehart, K Smith, B Hanscom, M Cohen, and M Hosseinipour

on behalf of the HPTN 084 study team



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LB1479

Disclosures

- I have served on MSD advisory boards
- I have received drug donations for research from Gilead Sciences

Background

- Antiretroviral-based pre-exposure prophylaxis can reduce HIV acquisition
- Women are disproportionately affected by HIV, esp. in sub-Saharan Africa where women experience individual and social barriers to consistent daily oral PrEP use
- Novel long-acting products e.g., CAB LA administered less frequently may simplify PrEP use and provide much needed HIV protection



Primary Objectives

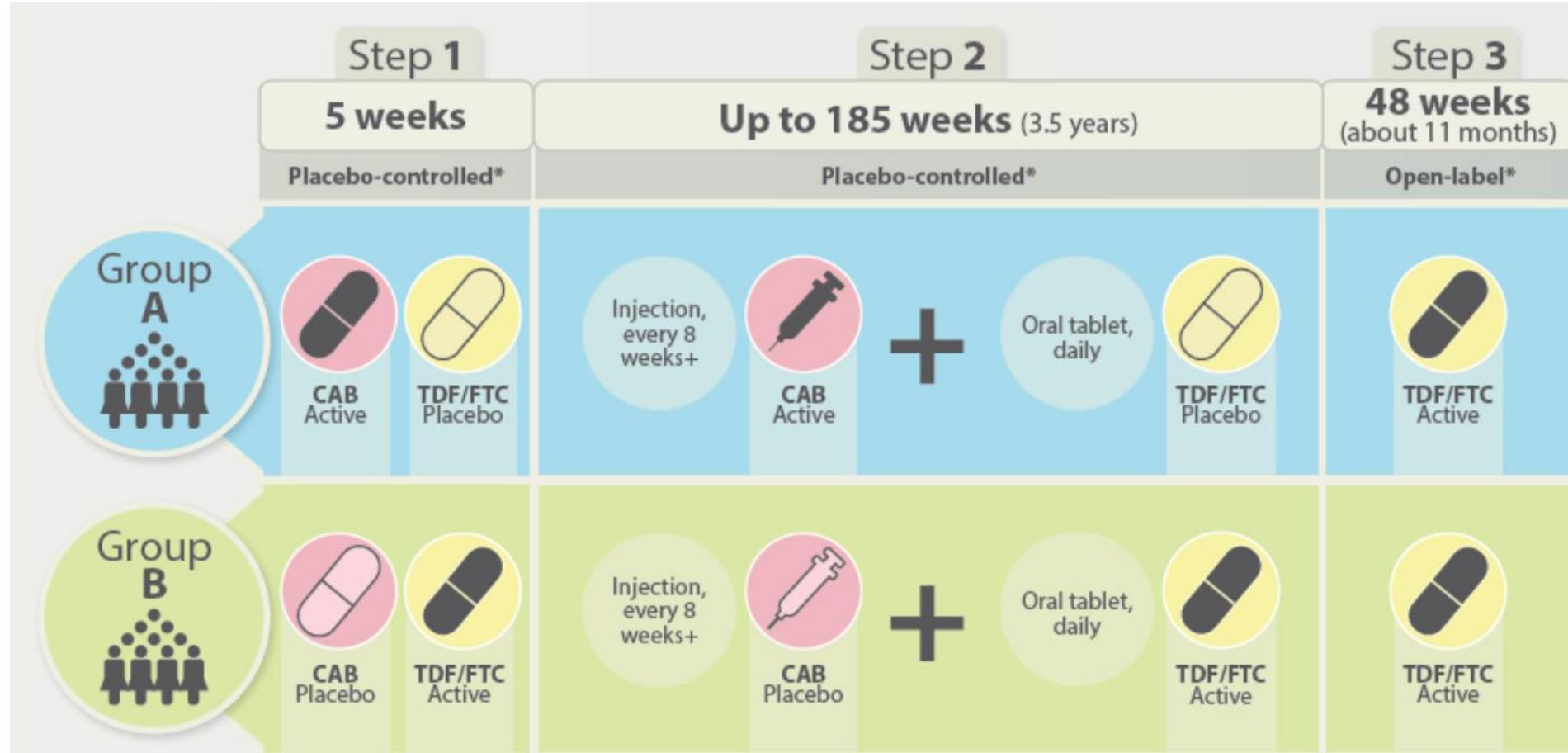
- To evaluate the relative efficacy of oral CAB/CAB LA vs. daily oral TDF/FTC for HIV prevention.
- To evaluate the relative safety of oral CAB/CAB LA vs. daily oral TDF/FTC for HIV prevention.

Study population

- Planned enrolment n=3200 at 20 sites
- Cisgender women aged 18-45 years
- HIV negative
- Sexually active
- Modified VOICE Risk Score $\geq 3^*$
 - Age, partner characteristics, alcohol use
 - Increased to ≥ 5
- No contraindications to either agent
 - No hepatic or renal insufficiency, seizures, allergy
- Not pregnant or breastfeeding
- Use reliable form of modern contraception
 - From May 2018, only LARC with <1% failure rate



Study design

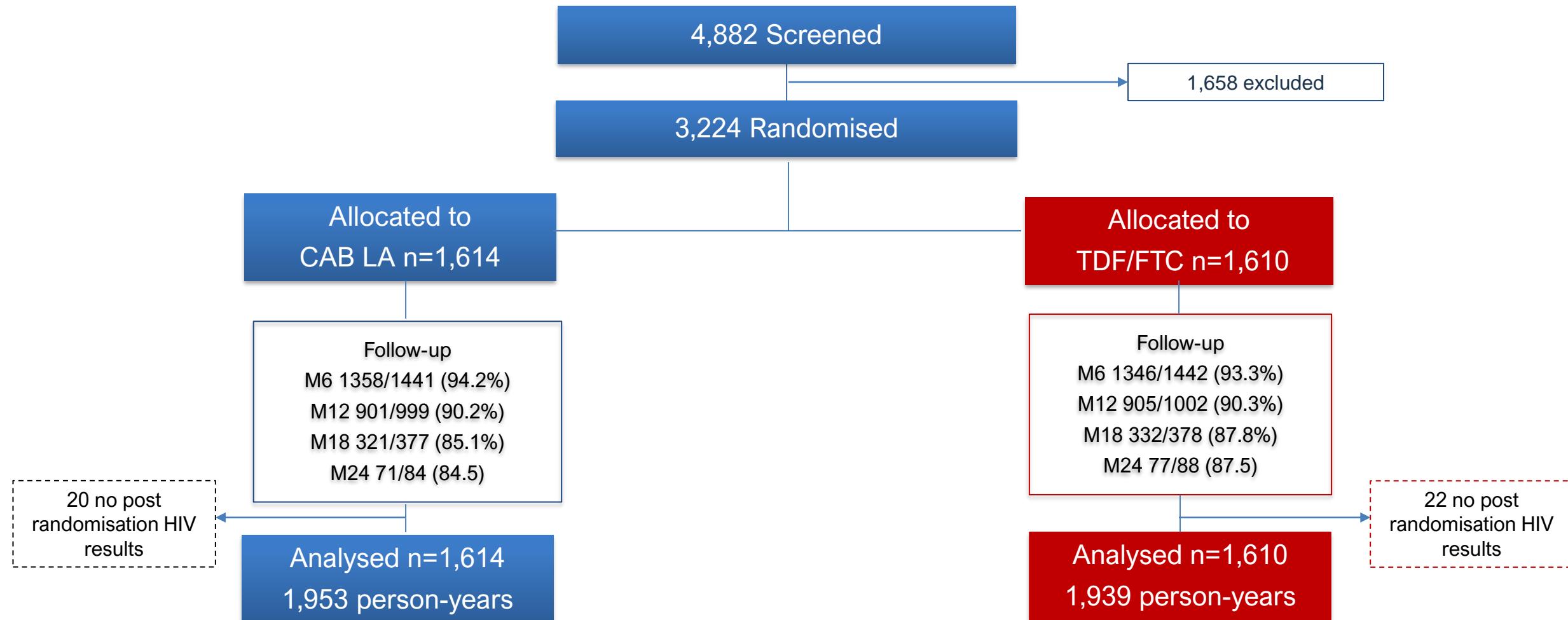


HIV, pregnancy testing and safety assessments at each product administration visit; additional post injection safety visits
Real-world adherence counselling support aligned with national guidelines

Statistical analysis

- Endpoint-driven trial (n=114)
 - Background HIV incidence in absence of PrEP 3.5% pa
 - CAB adherence 80-85%, TDF/FTC adherence 45-50%, LTFU 5% pa
 - 90% power, $\alpha = 0.05$ to detect RR 0.48-0.54
- Superiority analysis
 - HIV incidence during steps 1 and 2
 - Intent to treat, Cox proportional hazards model, stratified by site
- Interim reviews at 22%, 39%, 59%, 78% of information planned
 - Early stopping using an O'Brien-Fleming boundary for efficacy
 - Pre-specified stopping boundary crossed during planned interim review Nov 5, 2020

Screening, enrolment and follow-up



Participant baseline characteristics

	Total (n=3224) % or Median (IQR)	CAB (n=1614) n (%) or Median (IQR)	TDF/FTC (n=1610) n (%) or Median (IQR)
Median Age (years)	25 (22, 30)	25 (22, 30)	25 (22, 20)
≤ 25 years	57%	57%	57%
Not living with partner	82%	82%	82%
In the past month			
Partner HIV positive or unknown*	34%	34%	35%
≥ 2 sex partners*	54%	54%	55%
Transactional sex*	41%	41%	41%
Anal sex*	6%	5%	6%
Median VOICE risk score (IQR)	6 (5,7)	6 (5,7)	6 (5,7)
<i>C. trachomatis</i>	17%	17%	17%
<i>N. gonorrhoeae</i>	7%	7%	7%
BMI ≥ 25	55%	55%	56%

*Responses for 3210 participants, CAB n=1610 and TDF/FTC N=1600

Primary outcome: HIV incidence

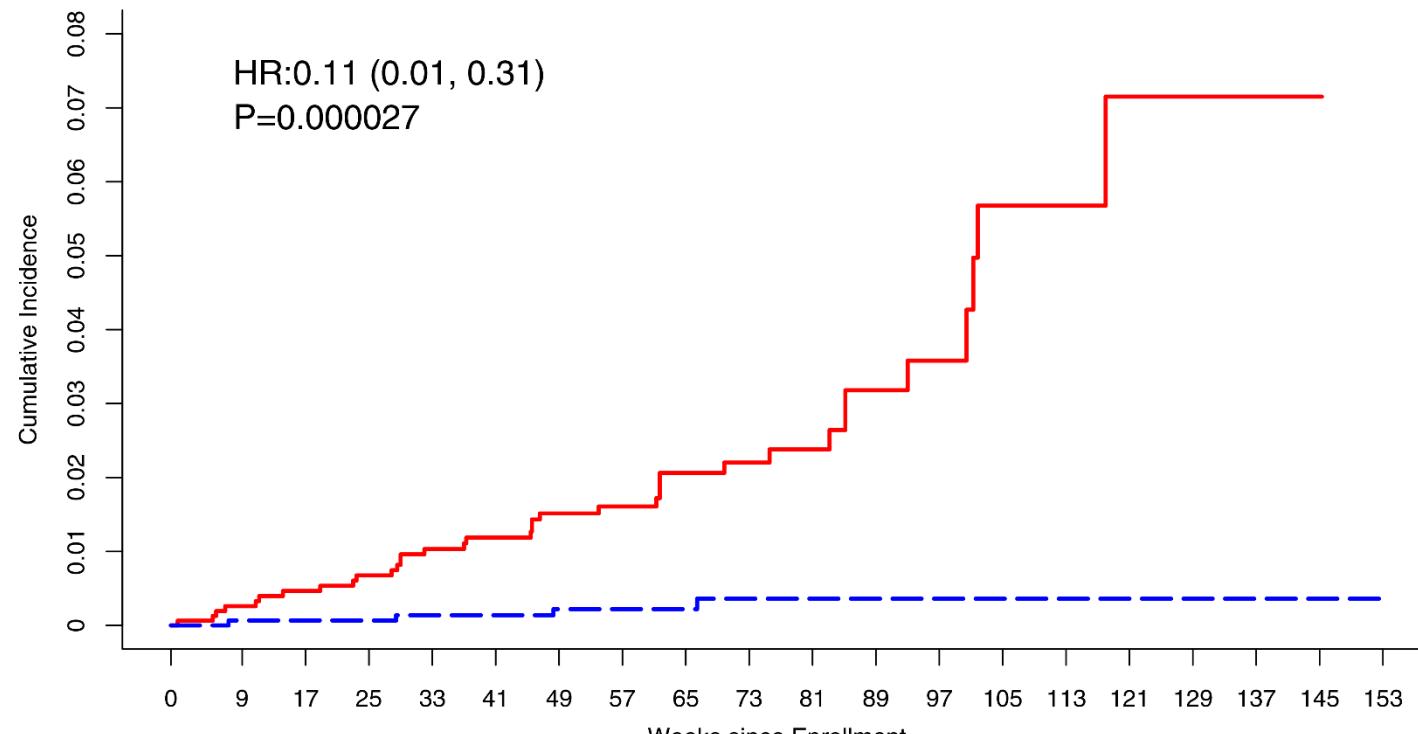
40 infections over 3892 person-years

Pooled HIV incidence 1.03 (0.73, 1.4) per 100 person-years

	CAB	TDF/FTC
HIV infections	4	36
Person-years	1,953	1,939
HIV incidence (95% CI)	0.2 (0.06, 0.52)	1.86 (1.3, 2.57)

Wald test z statistic – 4.20, efficacy stopping bound (z scale) – 3.61

Cumulative HIV incidence – ITT



HR:0.11 (0.01, 0.31)
P=0.000027

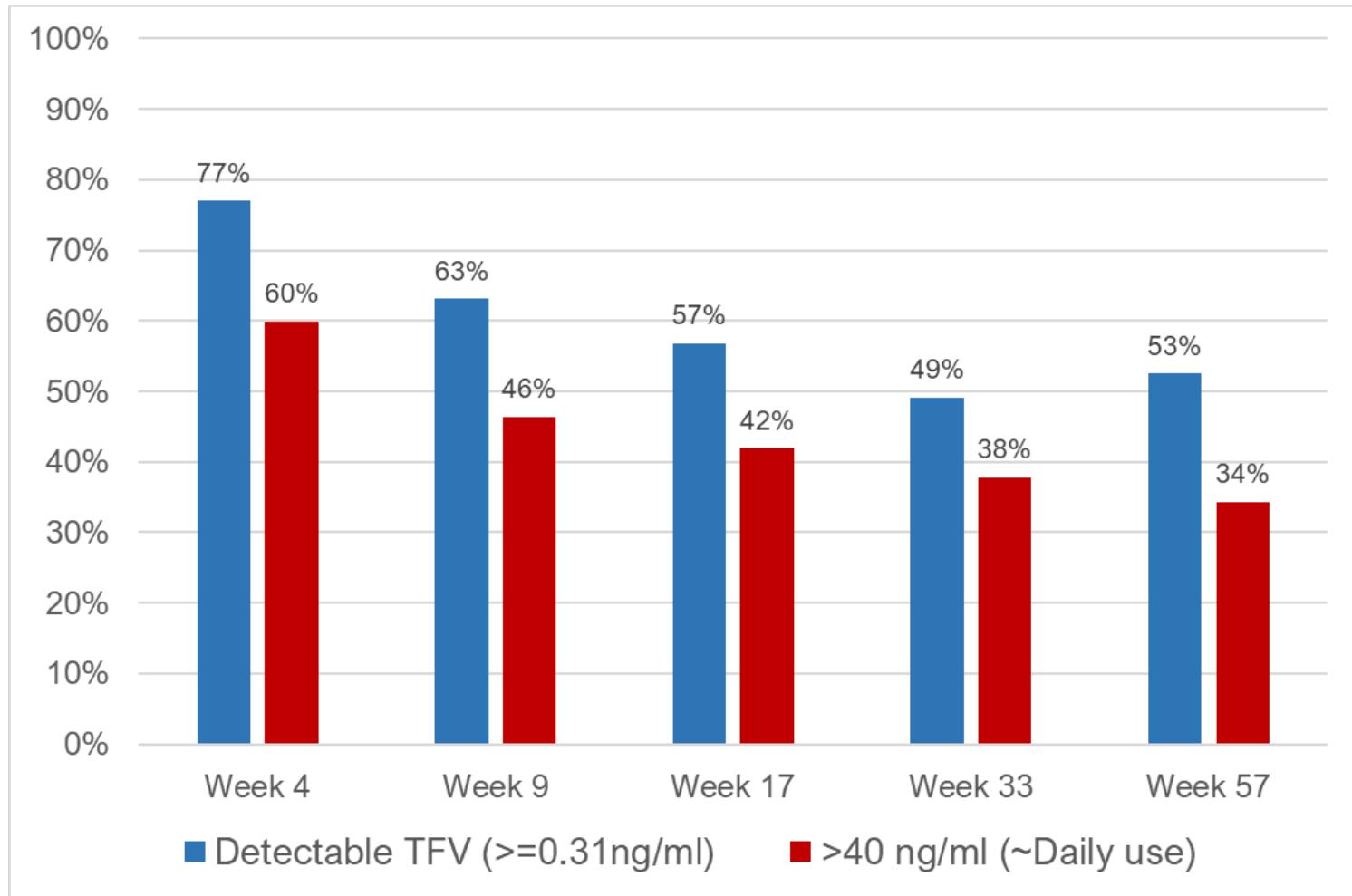
— TDF/FTC
- - Cabotegravir

*Women in the CAB group had an **89% lower risk of HIV infection**, compared to TDF/FTC group*

Number at Risk	
TDF/FTC	1609 1490 1429 1410 1351 1259 1158 982 799 655 482 306 201 113 70 63 52 22 3 0
Cabotegravir	1612 1485 1441 1429 1370 1279 1177 985 800 647 480 304 204 113 67 58 50 23 3 2

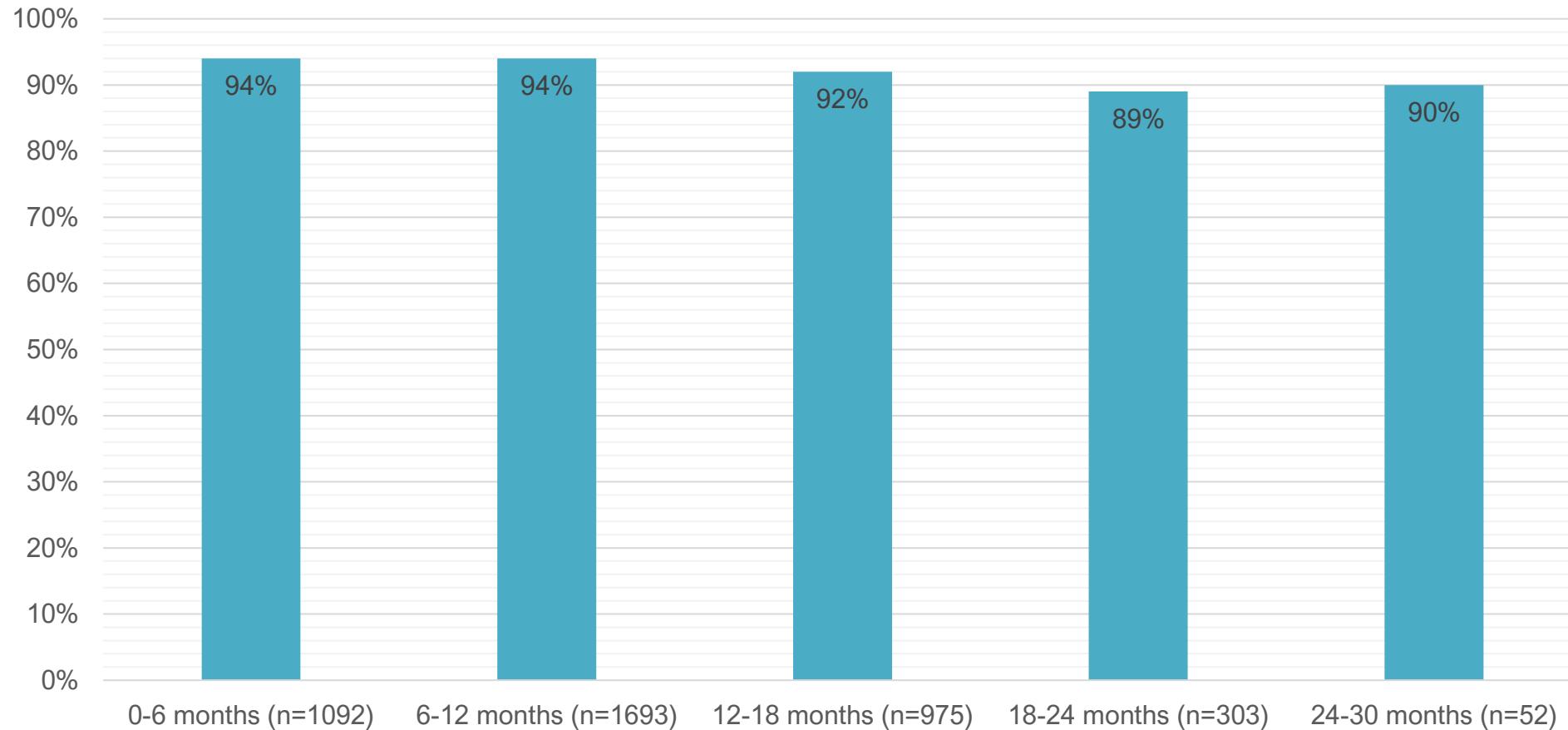
Cumulative Number of Events	
TDF/FTC	0 4 7 10 15 17 21 22 26 27 28 31 32 35 36 36 36 36 36
Cabotegravir	0 1 1 1 2 2 3 3 4 4 4 4 4 4 4 4 4 4 4

TDF plasma concentrations – adherence subset (n=375)



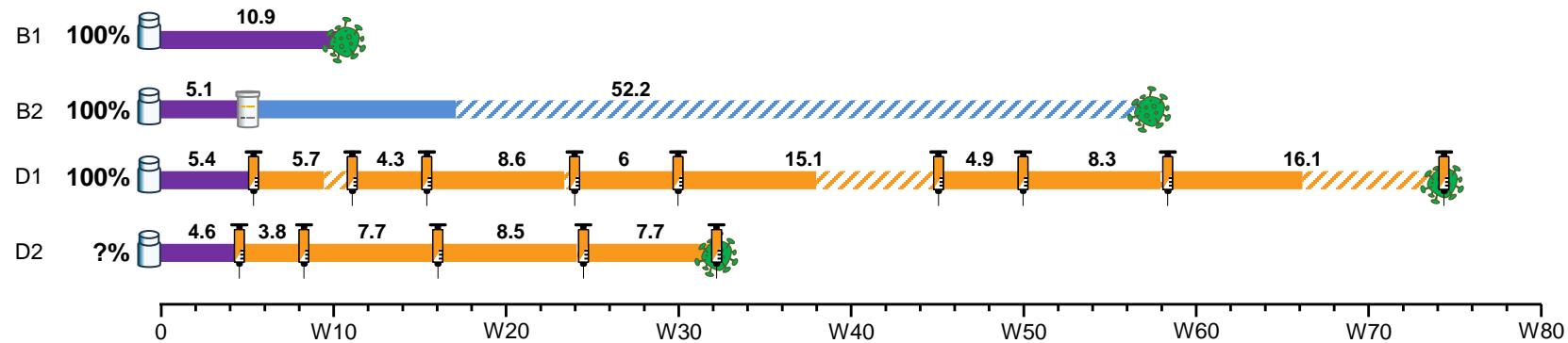
Overall,
62% detectable TFV
46% $>40\text{ng/ml}$

Injection coverage, 6-month intervals - all



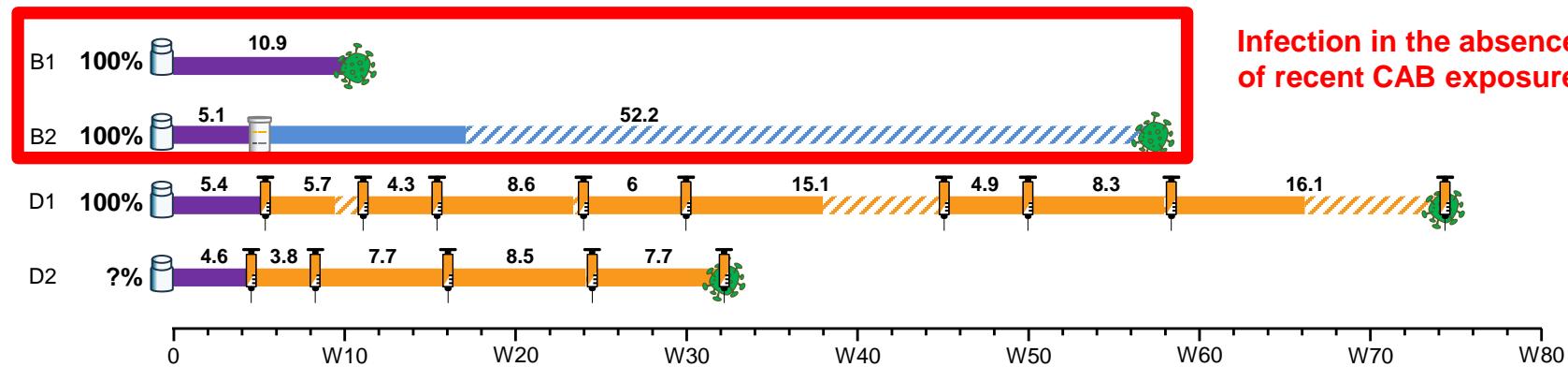
Injection coverage: injections administered as a proportion of total expected injection visits

Cabotegravir - 4 incident HIV Infections



- 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
- First site positive HIV test

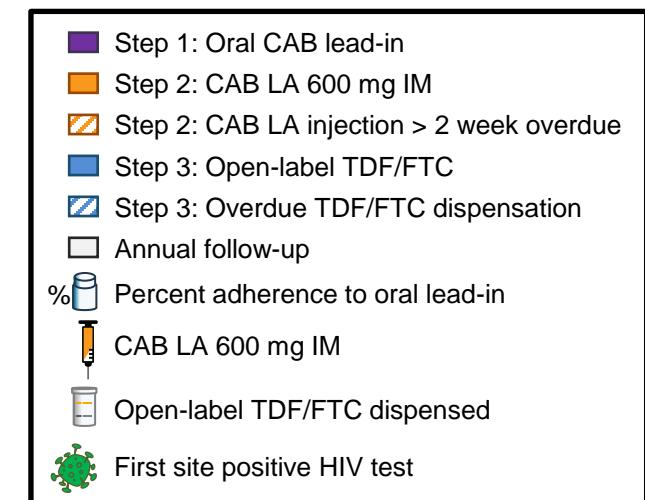
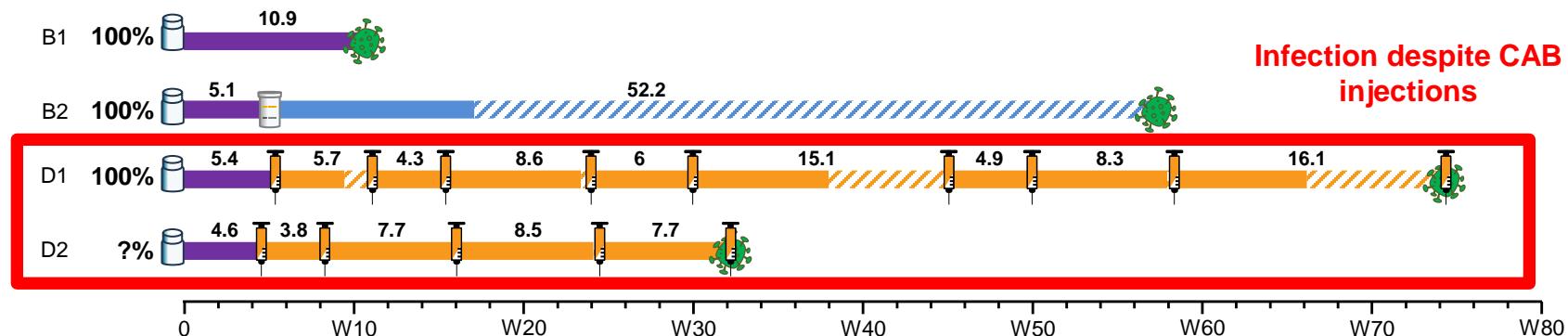
Cabotegravir - 4 incident HIV Infections



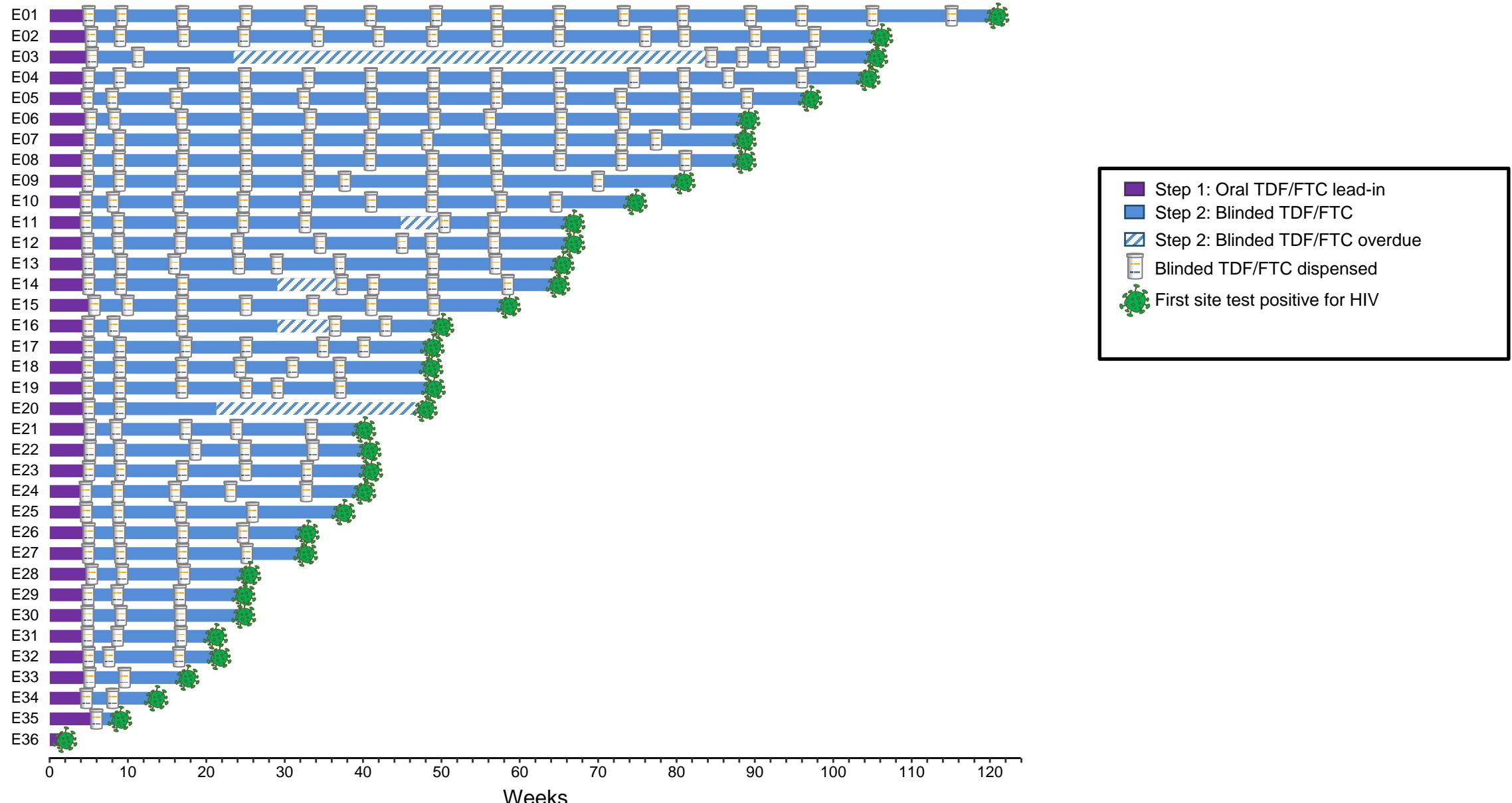
Infection in the absence
of recent CAB exposure

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

Cabotegravir - 4 incident HIV Infections



TDF/FTC - 36 Incident HIV Infections

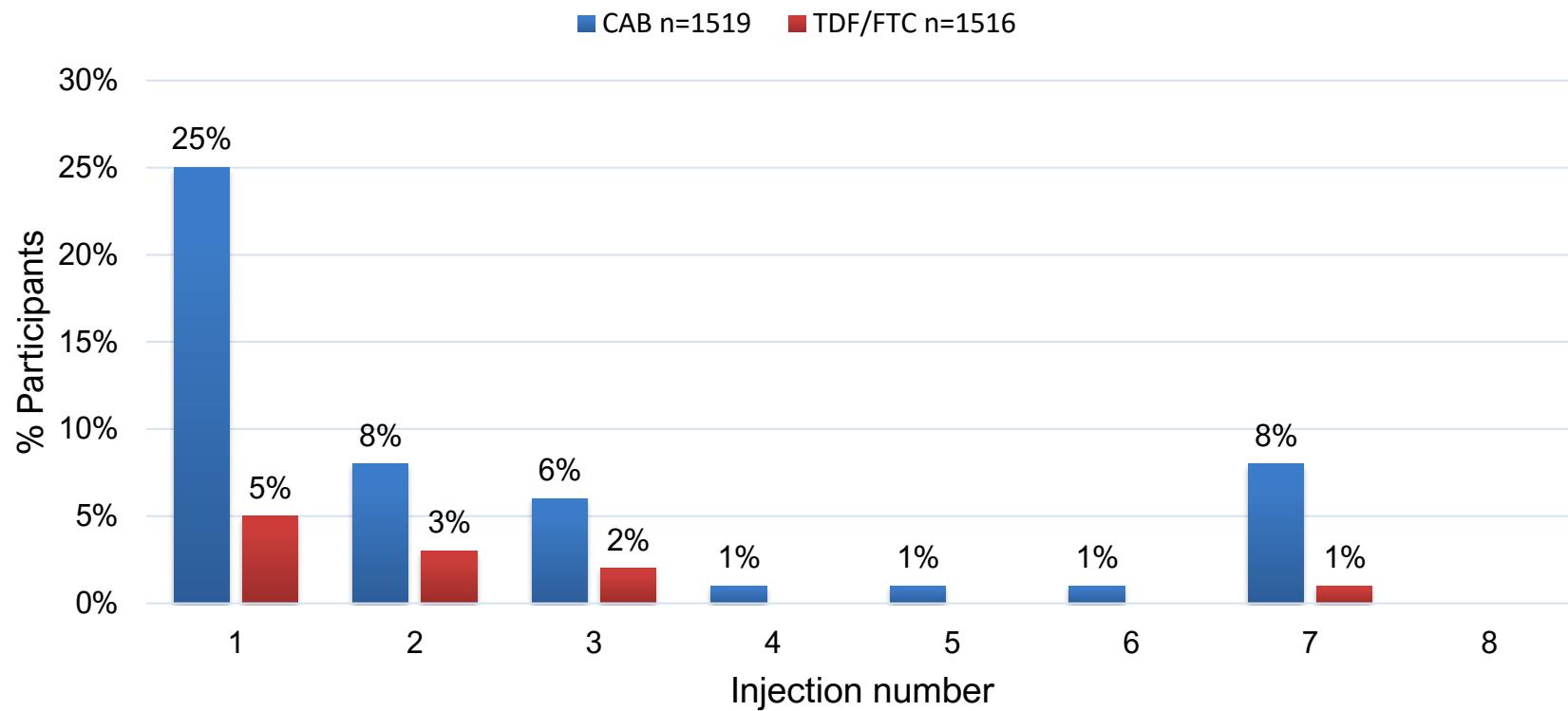


Additional testing among seroconverters, in progress

- HIV
 - Timing of first infection
- Drug concentrations
 - CAB all visits
 - TDF/FTC selected visits peri-infection
- Resistance profiles
 - HIV infection at time of first detection

Safety: Injection site reactions (ISR)

Any ISR, by injection number and arm

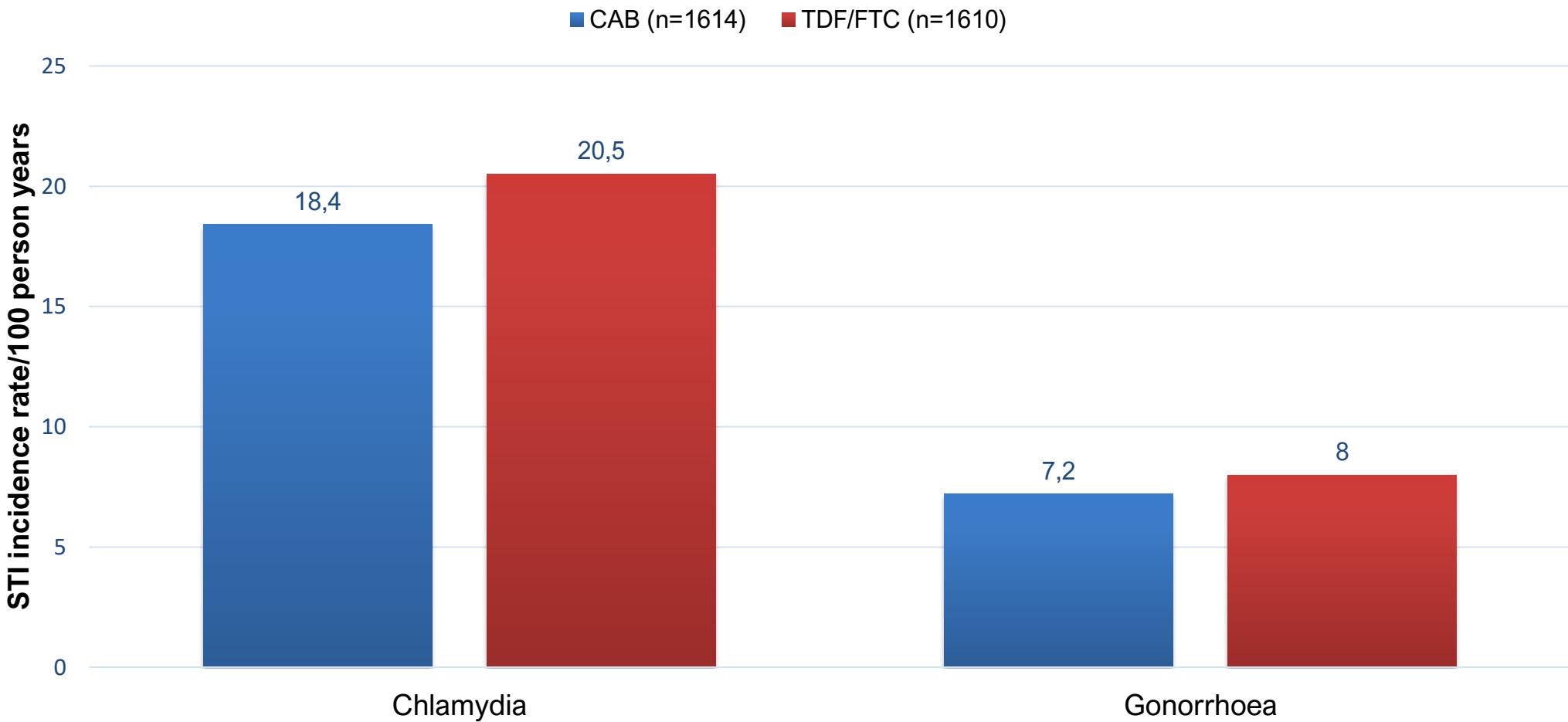


- 21% participants any ISR
 - 32% CAB vs. 9% TDF/FTC
- 4% participants Grade 2+ ISR
 - 7% CAB vs. 1% TDF/FTC
- Zero discontinuations d/t ISR

Safety: Grade 2+ adverse events - reported in $\geq 5\%$

Participants with \geq Grade 2 events	Total (n=3224)		CAB (n=1614)		TDF/FTC (n=1610)	
	n	%	n	%	n	%
Any Grade 2+ events	2956	92%	1477	92%	1479	92%
Creatinine clearance decreased	2359	73%	1166	72%	1193	74%
Creatinine increased	664	21%	337	21%	327	20%
Gastrointestinal disorders	650	20%	309	19%	341	21%
Chlamydia infection	528	16%	253	16%	275	17%
Upper respiratory tract infection	509	16%	236	15%	273	17%
Urinary tract infection	409	13%	210	13%	199	12%
Amylase increased	320	10%	172	11%	148	9%
Blood glucose decreased	292	9%	146	9%	146	9%
Vulvovaginal candidiasis	267	8%	145	9%	122	8%
Trichomoniasis	230	7%	123	8%	107	7%
Back pain	188	6%	89	6%	99	6%
Abnormal loss of weight	177	5%	76	5%	101	6%
Menorrhagia	166	5%	81	5%	85	5%
Nasopharyngitis	159	5%	86	5%	73	5%
Metrorrhagia	155	5%	79	5%	76	5%
Any SAE/EAE	73	2%	32	2%	39	2%
Deaths	3	0,1%	3	0,1%	0	0

CT/GC incidence - ITT (n=3,224)



Changes in weight, kg – ITT (n=3,224)



Initial immediate increase in weight on CAB

- +0.42 kg CAB, (95% CI 0.30,0.54)
- **p <0.001**

Overall, increase in weight in both arms

- CAB +2.4 (95% CI 2.1, 2.7)kg/year
- TDF/FTC +2.2 (95% CI 2.0, 2.4)) kg/year
- **p=0.12**

Pregnancy incidence and outcomes - ITT

	Total n=3224	CAB n=1614	TDF/FTC n=1610
No. confirmed pregnancies	50	29	21
Person-years	3829.7	1914.5	1915.2
Incidence rate (95% CI)	1.3 (1.0, 1.7)	1.5 (1.0, 2.2)	1.1 (0.7, 1.7)

Pregnancy outcomes - ITT

	Total n=50	CAB n=29	TDF/FTC n=21
Ongoing	23	15	8
Known pregnancy outcomes n=27			
Live births	20	10	10
Pregnancy loss			
>=37 weeks	0	0	0
20-36 weeks	3	1	2
<20 weeks*	4	3	1
Ectopic	0	0	0
Congenital anomalies n=27			
No	23	11	12
Unknown	4	3	1

*includes elective terminations

Conclusions

- Both agents highly effective in preventing HIV
 - Pooled incidence 1.03 (0.73, 1.4) per 100 py
- CAB was superior to daily oral TDF/FTC in preventing HIV in cisgender women
 - 89% lower risk of HIV infection in participants receiving CAB compared to TDF/FTC
 - CAB LA 8-weekly likely provided an adherence advantage over daily oral TDF/FTC
 - Ongoing testing to fully understand reasons for breakthrough infections
- Both products were safe and well tolerated with few differences in Grade 2+ adverse events by arm, apart from ISR
 - ISR were generally mild, associated with pain, and generally occurred at 1st injection
 - No discontinuations due to ISR
- Results complement data from HPTN 083, and confirm CAB as first safe and effective injectable PrEP agent for cisgender women

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HPTN Leadership & Operations (LOC)

Study Team

- Jennifer Farrior
- Scott Rose
- Jill Stanton
- Leah Schrumpf
- Barbara Long
- Nirupama Sista

Community Team

- Rhonda White
- Marcus Bryan
- Jonathan Lucas
- Abraham Johnson
- Nikkia Morrison

Communications Team

- Kevin Bokoch
- Laura Long
- Eric Miller

Finance Team

- Kathy Hinson
- Sarah Stone

HPTN Lab Center (LC)

- Estelle Piwowar-Manning
- Yaw Agyei
- Paul Richardson
- Mark Marzinke
- Sue Eshleman
- Pete Anderson

HPTN Statistical & Data Management Center (SDMC)

- Stephanie Biegel-Orme
- Jim Hughes
- Priyanka Agarwal
- Lynda Emel
- Gordon Chau
- Amber Guo

HPTN Leadership

- Myron Cohen
- Wafaa El-Sadr
- Deborah Donnell
- Sue Eshleman
- Nirupama Sista
- Kathy Hinson

Additional Protocol Team Members

- Kimberly Smith
- Alex Rinehart
- Lut Van Damme
- Craig Hendrix
- Sybil Hosek
- Betsy Tolley
- Anna Lawton
- Jim Rooney
- Adeola Adeyeye
- Mike Cohen
- Kimberly Scarsi
- Ribka Berhanu
- Katherine Shin

Our Community Working Group and CAB Members

CWG Protocol Representatives

- Elizabeth Magada
- Cissy Ssuuna

- Pumeza Mzizi
- Amanda Zindela
- Mathias Wambuzi
- Pamela Tshandu
- Godfrey Mbulelo Tabata
- Tereza Omoro
- Erick Okioma
- Vanessa Ntlombeni
- Mluleki Nompondwana
- Cynthia Nombeko Mpongo
- Sibusiso Nhleko
- Mduduzi Ngubane
- Siyabonga Ngqame
- Beauty Nerupfunde
- Gertrude Nanyonjo
- Daisy Namakula
- Teopista Nakyanzi
- Tarisal Murefu
- Nonkululeko Mtshali
- Tuelo Sylvia Mphele
- Ernest Mosimanegape Moseki
- Clifford Gcwensa
- Daniel Gondwe
- Gwynneth Hendricks
- Joanita Kawalya Muganga
- Doreen Kemigisha
- Edith Kibiribiri

- Macklean Mary Kyomya
- Jennie Makunganya
- Loreen Mangove
- Jabulile Mantantana
- Pearson Mmodzi
- Neetha Morar
- Livona Chitibura
- Nelecy Chome
- Wandile Dube
- Lindelwa Dyabenai

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HIV alias team members

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- Michelle Moorhouse

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