Utilizzo di Cabotegravir iniettivo nella PrEP

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QUID EST HOMO?

COIs

Il sottoscritto **NOZZA SILVIA**
in qualità di relatore

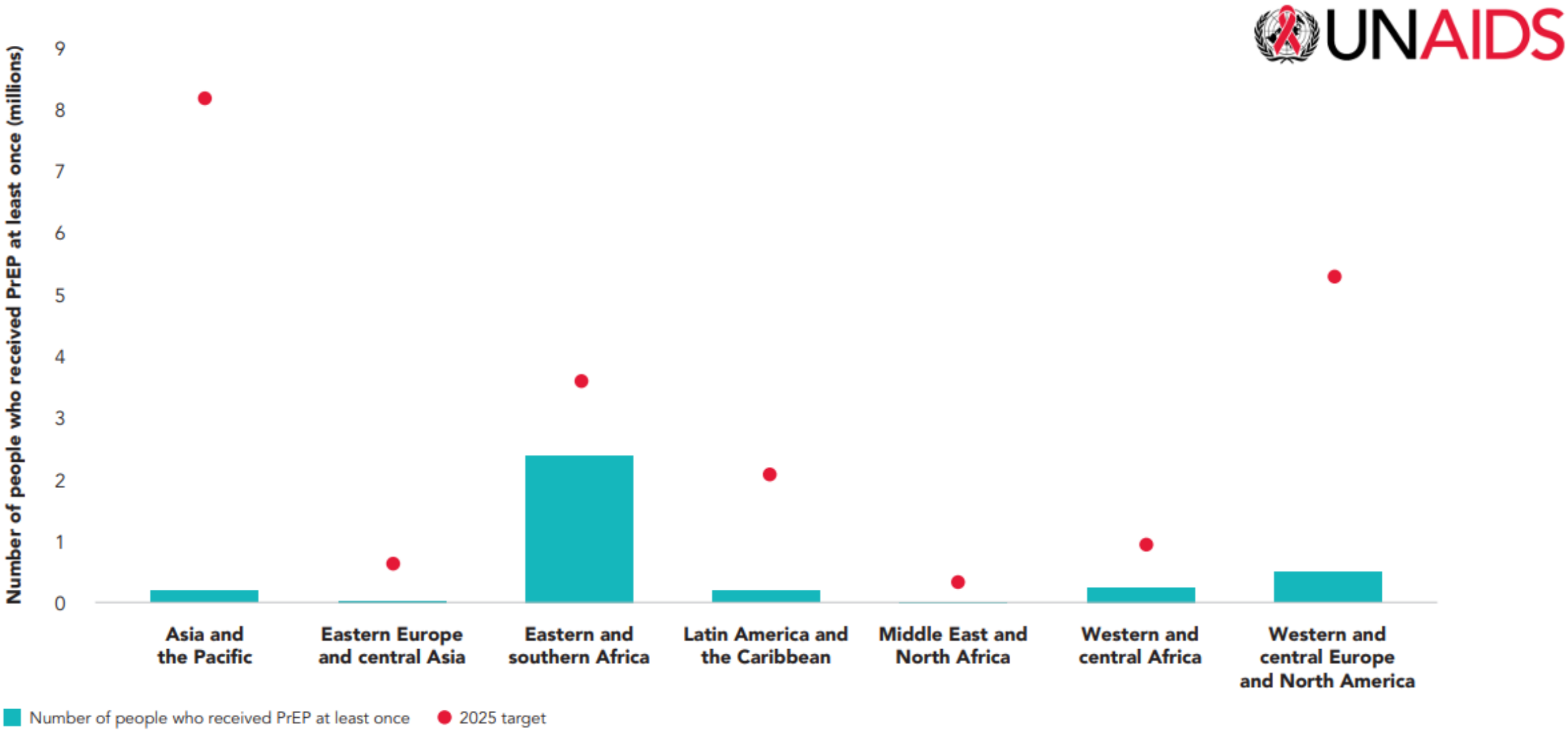
ai sensi dell'art. 76, comma 4 dell'Accordo Stato-Regioni del 2 febbraio 2017 e del paragrafo 4.5. del Manuale nazionale di accreditamento per l'erogazione di eventi ECM

dichiara
che negli ultimi due anni ha avuto i seguenti rapporti anche di finanziamento con soggetti portatori di interessi commerciali in campo sanitario:
ViiV Healthcare
Gilead Sciences
MSD

PrEP BARRIERS

- ✓Adherence.
- ✓Persistence.
- ✓PrEP failures and mutations.
- ✓Toxicity: bone.
- ✓Toxicity: kidney. Poor studies in TDF/FTC with creatinine clearance < 80 mL/min.

Figure 0.4 Number of people who used pre-exposure prophylaxis (PrEP) at least once in 2023, by region, and 2025 target



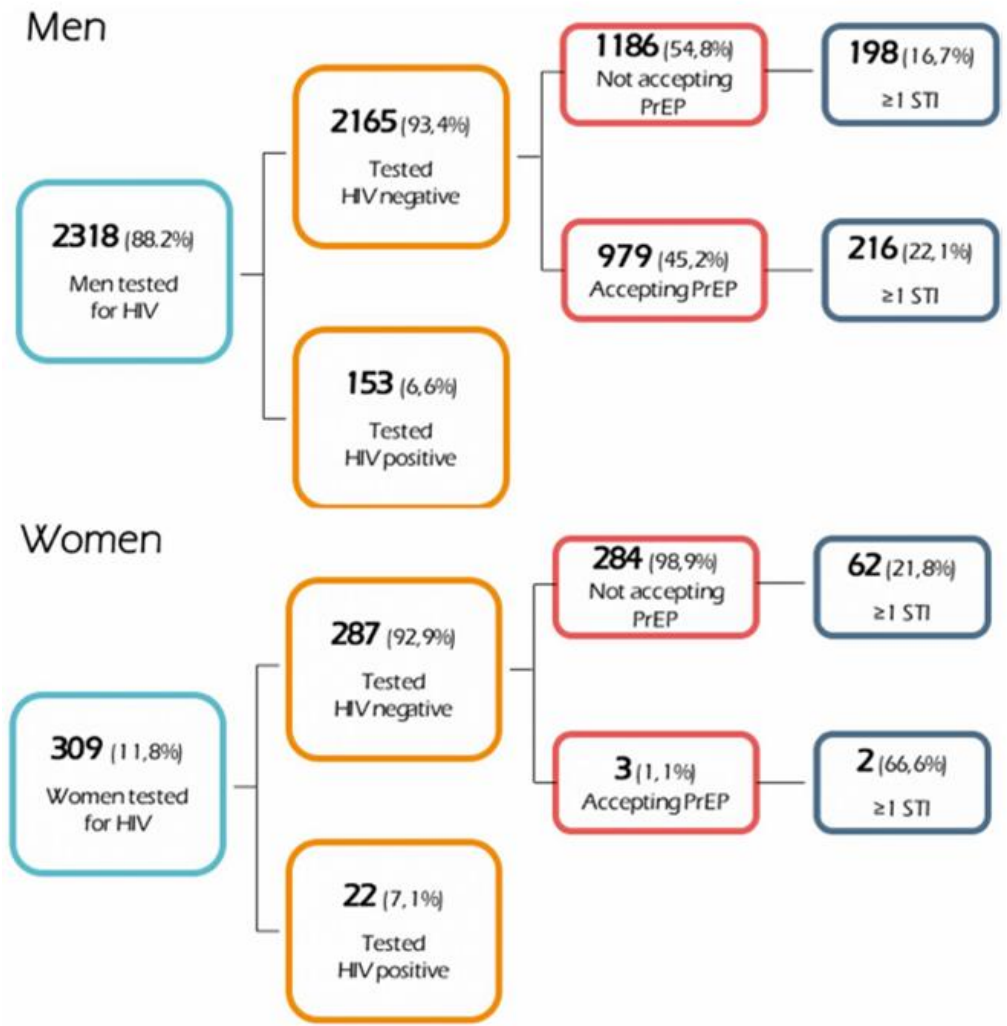
KEY POPULATIONS

- ✓Gay, bisex and others men who have sex with men **(MSM).**
- ✓People who use intravenous drug **(PWID).**
- ✓**Sex workers.**
- ✓Transgender people **(TG).**
- ✓Young people, in particular women.
- ✓Prisoners.

TABLE 1. Characteristics of Individuals With Negative HIV Test Result at Time of HIV Testing According to PrEP Acceptance

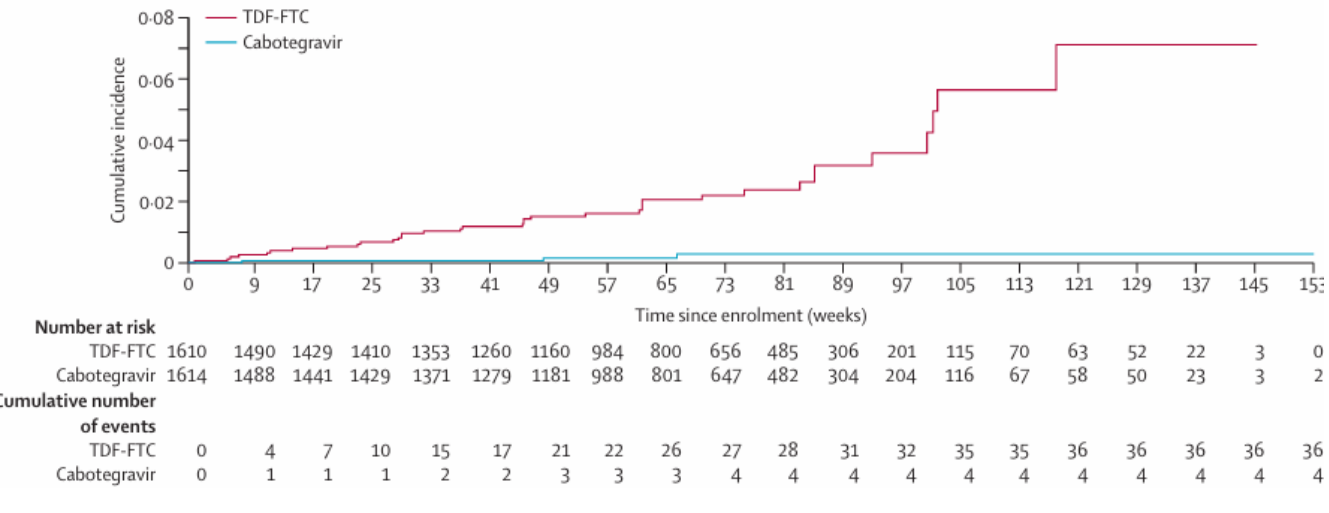
	Overall N = 2452	Not Started PrEP N = 1470	Started PrEP N = 982	*P*
Gender identity (%)				**<0.001**
Female	287 (11.7)	284 (19.3)	3 (0.31)	
Male	2165 (88.3)	1186 (80.7)	979 (99.7)	
Transgender	3 (0.1)	1 (0.1)	2 (0.2)	0.568
Ethnicity (%)				**<0.001**
White	2275 (92.8)	1340 (91.2)	935 (95.2)	
Asian	32 (1.3)	23 (1.6)	9 (0.9)	
Black	57 (3.2)	50 (3.4)	7 (0.7)	
Hispanic	84 (3.4)	53 (3.6)	31 (3.2)	
Age (yr)	34.3 (28.7–42.4)	34.6 (27.9–44.8)	34.1 (29.7–40.2)	0.312
Concurrent gonorrhea (%)*	206 (8.4)	93 (6.3)	113 (11.5)	**<0.001**
Rectal	98 (8.4)	46 (3.1)	52 (5.3)	
Urethral	51 (2.1)	35 (2.4)	16 (1.6)	
Pharyngeal	64 (2.6)	19 (1.3)	45 (4.6)	
Concurrent chlamydia (%)*	182 (7.4)	92 (6.3)	90 (9.2)	**0.009**
Rectal	138 (5.6)	65 (4.4)	73 (7.4)	
Urethral	61 (2.5)	44 (3.0)	17 (1.7)	
Concurrent syphilis (%)*	82 (3.3)	42 (2.9)	40 (4.1)	0.127
At least 1 concurrent STI (%)*	478 (19.5)	260 (17.7)	218 (22.2)	**0.007**
At least 1 previous STI (%)†	897 (36.6)	312 (21.2)	585 (59.6)	**<0.001**
Positive HbsAg (%)	16 (1.3)	16 (1.3)	0 (0)	**0.005**
Positive hepatitis C virus-Ab (%)	41 (1.9)	38 (3)	3 (0.3)	**<0.001**

Bold values are significant to $P < 0.05$.
*At time of the HIV test (baseline).
†In medical history.

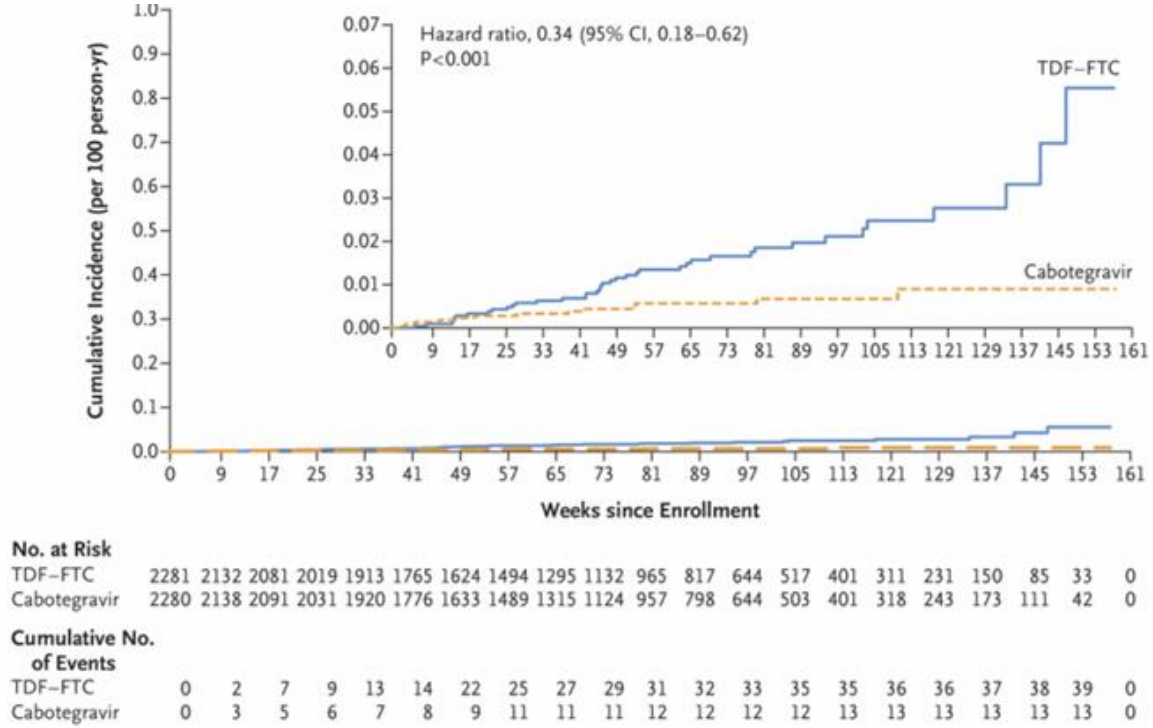


Raccagni A.R. et al., *JAIDS* 2025

CABOTEGRAVIR



HPTN 084
Delaney-Moretlwe S. et al, Lancet 2022



HPTN 083
Landovitz RJ et al., NEJMN Engl J Med 2021

LONG ACTING PrEP OPTIONS: SUMMARY

	CISGENDER WOMEN		MSM/TGW	
	PURPOSE 1 N=2134[1]	**HPTN 084 N=1614[2]**	**PURPOSE 2 N=2180[3]**	**HPTN 083 N=2282[4]**
Age	21 (16-25)	25 (22-30)	28 (17-74)	26 (22-32)
Enrollement in clinical trials	0,84 years	1,24 years	0,75 years	1,4 years
HIV infections	0	0	2	4
HIV incidence in TDF/FTC arm	16 1,69 (per 100p-year)	36 1,85 (per 100p-year)	9 0,93 (per 100p-year)	39 1,22 (per 100p-year)
Total injections (median per partecioant)	10.184	12.901	15.239	20.286
Approval	NO	YES	NO	YES

1. Bekker, L.G. et al, NEJM,; 391:1179-1192, 2024.
2. Delaney-Moretlwe, S. et al, Lancet, 2022; 399 (10337), P1779-1789.
3. Landovitz RJ et al., NEJMN Engl J Med 2021;385:595-608.
4. Kelley CF et al., NEJM 2024

LONG ACTING PrEP OPTIONS: ADVERSE EVENTS

	CISGENDER WOMEN		MSM/TGW	
	PURPOSE 1 N=2134[1]	**HPTN 084 N=1614[2]**	**PURPOSE 2 N=2180[3]**	**HPTN 083 N=2282[4]**
Discontinuations (any reason)	227 (10,6%)	85 (5,2%)	UK	185 (12,5%)
Discontinuations due to ISRs	4	0	26	50
% experiencing ISRs	68,8%	38%	83,2%	81,2%
Nodules	63,8%	5%	63,4%	12%
Induration	NR	12%	UNK	15%
Swelling	44%	12%	UNK	12%
Median duration ISRs (days)	NR	8 days	183 days	4 days

1. Bekker, L.G. et al, NEJM; 391:1179-1192, 2024.
2. Delaney-Moretlwe, S. et al, Lancet, 2022; 399 (10337), P1779-1789.
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DDIs PROFILES: CABOTEGRAVIR

- ✓Anticonvulsivants
- ✓Mycobacterials
- ✓Not DDIs with CHEMS

CABOTEGRAVIR IN GUIDELINES

- Significant renal disease.
- Difficulty with adherent use of oral PrEP
- Users who prefer injections every 2 months to an oral PrEP dosing schedule.

600 mg of cabotegravir injected into gluteal muscle every 2 months is recommended for PrEP in adults at risk of acquiring HIV. 30 mg daily oral cabotegravir is optional for a 4-week lead-in prior to injections.

EACS Guidelines

MONITORING

Table 7 Timing of CAB PrEP-associated Laboratory Tests

Test	Initiation Visit	1 month visit	Q2 months	Q4 months	Q6 months	Q12 months	When Stopping CAB
HIV*	X	X	X	X	X	X	X
Syphilis	X			MSM^/TGW~ only	Heterosexually active women and men only	X	MSM/TGW only
Gonorrhea	X			MSM/TGW only	Heterosexually active women and men only	X	MSM/TGW only
Chlamydia	X			MSM/TGW only	MSM/TGW only	Heterosexually active women and men only	MSM/TGW only

* HIV-1 RNA assay
X all PrEP patients
^ men who have sex with men
~ persons assigned male sex at birth whose gender identification is female

CDC Guidelines

MONITORING

- ✓Efficacy after one week (10-15% after two days)
- ✓Monitoring every 3 months after discontinuation (one year)

CDC Guidelines

FAILURES IN PrEP IN OSR

- 12 failures/1814 first PrEP prescriptions
- 4/12 mutations

	HIVRNA	MUTATIONS	DRUGS
NUMBER 1	46.300	M184V	NRTIs
NUMBER 2	9.960	M184V	NRTIs
NUMBER 3	20.100	M184MV, L210W	NRTIs
NUMBER 4	244.000	M46MI, G48GA, I54IATV, V82VA	PIs

CABOTEGRAVIR IN REAL LIFE N=2345

	IDWeek 2024		HIVR4P 2024		CROI 2024	
	OPERA[1]	TRIO[2]	MHS SAN FRANCISCO[3]	UC SAN DIEGO[4]	HOWARD BROWN[5]	SEARCH[6]
Participants	N=764	N=526	N=111	N=187	N=270	N=487‡
Population	Black: 29% Hispanic: 29%	Black: 32%	NR	Black: 3% Hispanic: 40%	Black: 25% Hispanic: 24%	NR
Location	 US (Multicenter)	 US (Multicenter)	 CA, US (Multicenter)	 CA, US (Single center)	 IL, US (Single center)	 Kenya, Uganda (Multicenter)
Injections received	Median (IQR): 5 (3–7)*	NA	NA	≥1 injection	Median (range): 4 (1–12)	NA
Time on CAB LA	Median (IQR): 10 months (7–13)*	Median (IQR): 7 months (3–14)†	Mean (95% CI): 221 days (181, 260)	NA	NA	48 weeks
Effectiveness	**99.7%**	**100%**	**100%**	**100%**	**99.6%**	**100%**

*Complete initiators only; †Individuals who received ≥2 injections of CAB LA; ‡Primary outcome ascertained in 485
CA, California; **IL,** Illinois; **NA,** not available; **NR,** not reported

1. Hsu RK, et al. IDWeek 2024. Oral 508; **2.** Ramgopal M, et al. IDWeek 2024. Oral 505
3. Heise MJ, et al. HIVR4P 2024. Oral OA0503; **4.** Turner C, et al. HIVR4P 2024. Poster 01725
5. Hazra A, et al. CROI 2024. Poster 1241; **6.** Kamya M, et al. CROI 2024. Oral 172

TRIO Health COHORT: LA CAB PrEP in the Real World

- TRIO cohort: from 12 geographically distributed health clinics in US
- Current study: retrospective analysis of EHR to evaluate persistence, adherence, efficacy, and safety with LA CAB for PrEP in TRIO cohort over first 2 yr of use
  - People without HIV who weigh ≥35 kg, with LA CAB prescription and data on injections received, who have never participated in clinical trial for LA CAB

Characteristic, n (%)	All Patients (N = 526)
Median age, yr (IQR)	32 (25-41)
Race	
▪ Black	167 (32)
▪ Other (Asian, American Indian, Alaska Native, Native Hawaiian, and other)	69 (13)
Gender	
▪ Female	72 (14)
▪ Transgender	45 (9)

70% of participants were previously prescribed PrEP in the past year—high baseline level of engagement in PrEP

Ramgopal. IDWeek 2024. Abstr 505.

Slide credit: clinicaloptions.com

TRIO Health Cohort: Persistence and Adherence

- Median follow-up: 7 mo (IQR: 3-14 mo)
- 85 (18%) met discontinuation criteria
- No seroconversions ≤12 mo after discontinuation of LA CAB for PrEP

PrEP After Discontinuation	Discontinued (n = 85)
Remained in care, n (%) ▪ Switched to oral PrEP, n ▪ No PrEP, n	48 (56) 27 21
Reinitiated LA CAB, n (%)	13 (15)
Lost to follow-up, n (%)	24 (28)

- Of 16% with delayed second injection:
  - Median delay: 22 days
- Of 33% with delayed third or later injection:
  - Median delayed injections: 1
  - Median delay: 12 days

Ramgopal. IDWeek 2024. Abstr 505.

TRIO Health Cohort: Efficacy, Testing, and Safety

- CDC guidelines recommend **both** HIV Ag/Ab and HIV RNA screening before **each** injection
  - 97% had HIV screening within 30 days prior to first injection or at initiation

HIV Test Frequency in All Patients (N = 526)	HIV Ag/Ab	HIV-1 RNA	Both HIV Ag/Ab and HIV-1 RNA	Either HIV Ab/Ag or HIV-1 RNA	No HIV Test
n (%)	292 (56)	199 (38)	**177 (34)**	**333 (63)**	8 (2)

- Injection-site reactions: 3 of 526 (0.5%); all individuals discontinued treatment
- **No HIV seroconversion episodes,** but testing was inconsistent and not in accordance with CDC guidelines

Ramgopal. IDWeek 2024. Abstr 505. CDC. Clinical Guidance for PrEP. 2024.

Slide credit: clinicaloptions.com

OPERA: Initiation and Follow-up Injection Outcomes

- **Complete initiators** (second injection ≤60 days of first injection): 646 participants (85%)
  - Median injections/person: 5 injections (IQR: 3-7 injections)
  - Median follow-up: 10 mo (IQR: 7-13 mo)
- **Incomplete initiators** (second injection >60 days of first injection): 118 participants (15%)
  - 66 participants (56%) received an additional injection a median of 11 wk later (IQR: 9-14 wk)

Parameter, n (%)	LA CAB Users With Complete Initiation (n = 646)
All injections on time	443 (69)
Any delayed injection	203 (31)
Delayed second injection in initiation phase (38-60 days since first injection) Median time after target, days (IQR)	 68 (11) 7 (3-19)
Delayed injection in continuation phase (68-90 days since last injection) Median time after target, days (IQR)	 155 (24) 3 (2-10)
Required reinitiation (≥91 days without injection) ▪ Received additional injection ▪ Median time after target, days (IQR)	205 (32) 87 (42) 53 (42-58)
Missed ≥2 target windows (≥128 days without injection) ▪ Received additional injection ▪ Median time after target, days (IQR)	124 (19) 18 (14) 100 (73-143)

Mills. IDWeek 2024. Abstr 508.

Slide credit: clinicaloptions.com

OPERA: HIV Testing and Seroconversions

- 65% received HIV testing at initiation (only 17% received any RNA test); 50% received HIV testing at all subsequent injections
  - Like TRIO, HIV testing was inconsistent and not in accordance with CDC guidelines
- 2 HIV seroconversions (0.3%) among 764 participants receiving LA CAB PrEP
- **Case 1:** FTC/TAF for 70 days, then received 3 LA CAB injections (Days 0, 32, 92)
  - No HIV testing at time of LA CAB initiation, until Day 92 of CAB
  - Day 92: HIV Ab/Ag positive; HIV-1 RNA <20 c/mL; no genotyping performed
- **Case 2:** FTC/TAF for 65 days, then received 4 LA CAB injections (Days 0, 93, 212, 272)
  - Tested and remained HIV negative over course of LA CAB PrEP
  - **No PrEP for 130 days after LA CAB**, then restarted on FTC/TAF after negative HIV Ag/Ab test
  - HIV-1 RNA >100,000 c/mL at after 9 days of FTC/TAF; retained susceptibility to all ARVs

Mills. IDWeek 2024. Abstr 508.

LA CAB PrEP in a Community Pharmacy Setting: Acceptability at Baseline and Feasibility at Wk 26

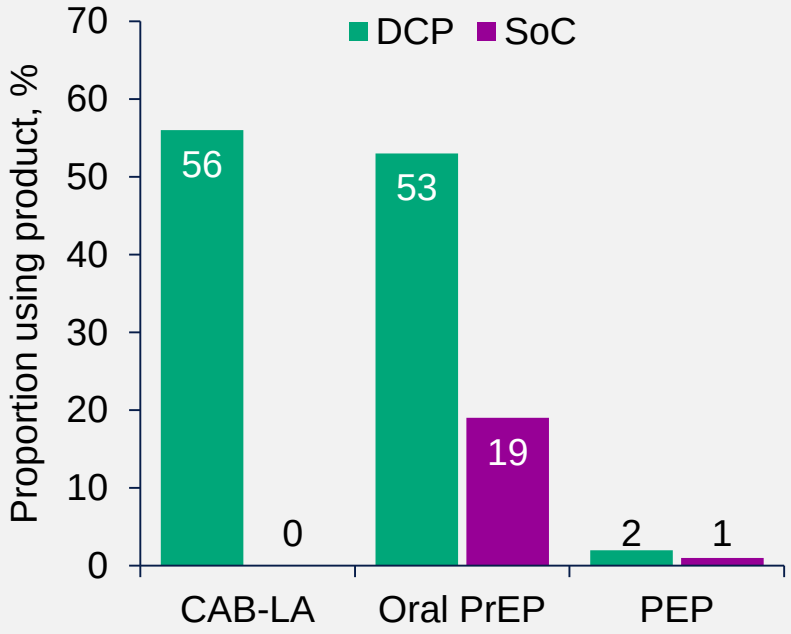
Acceptability at Baseline (N = 49), n (%)	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
Overall, I am feeling comfortable with receiving PrEP injections every 2 mo	32 (65)	15 (31)	2 (4)	0	0
I feel informed about injectable LA CAB PrEP	36 (73)	12 (24)	1 (2)	0	0
I am motivated to start injectable LA CAB PrEP	34 (69)	13 (27)	2 (4)	0	0
I would be ashamed if people knew I received LA CAB PrEP	0	0	0	10 (20)	39 (80)

Feasibility Outcome at Wk 26	LA CAB PrEP (N = 50)
Participated in baseline survey, n/n (%)	49/50 (98)
Retention: still on LA CAB PrEP, n/n (%)	35/43 (81)
Adherence: on-time injections, no.	115/122 (94)

Tung. IDWeek 2024. Abstr 506.

Reduced HIV Incidence Rates Were Observed Among Participants Given a Choice of Treatment

Summary of Product Use, Extension Phase



Among participants who initiated CAB-LA at baseline, **42% were not using a prevention product** in the prior month

28% of participants in the DCP arm used at least **2 different products** vs <1% of participants in the SoC arm

DCP Arm

487 participants → 400 PY → 0 Incident HIV diagnoses → IR → 0%

SoC Arm

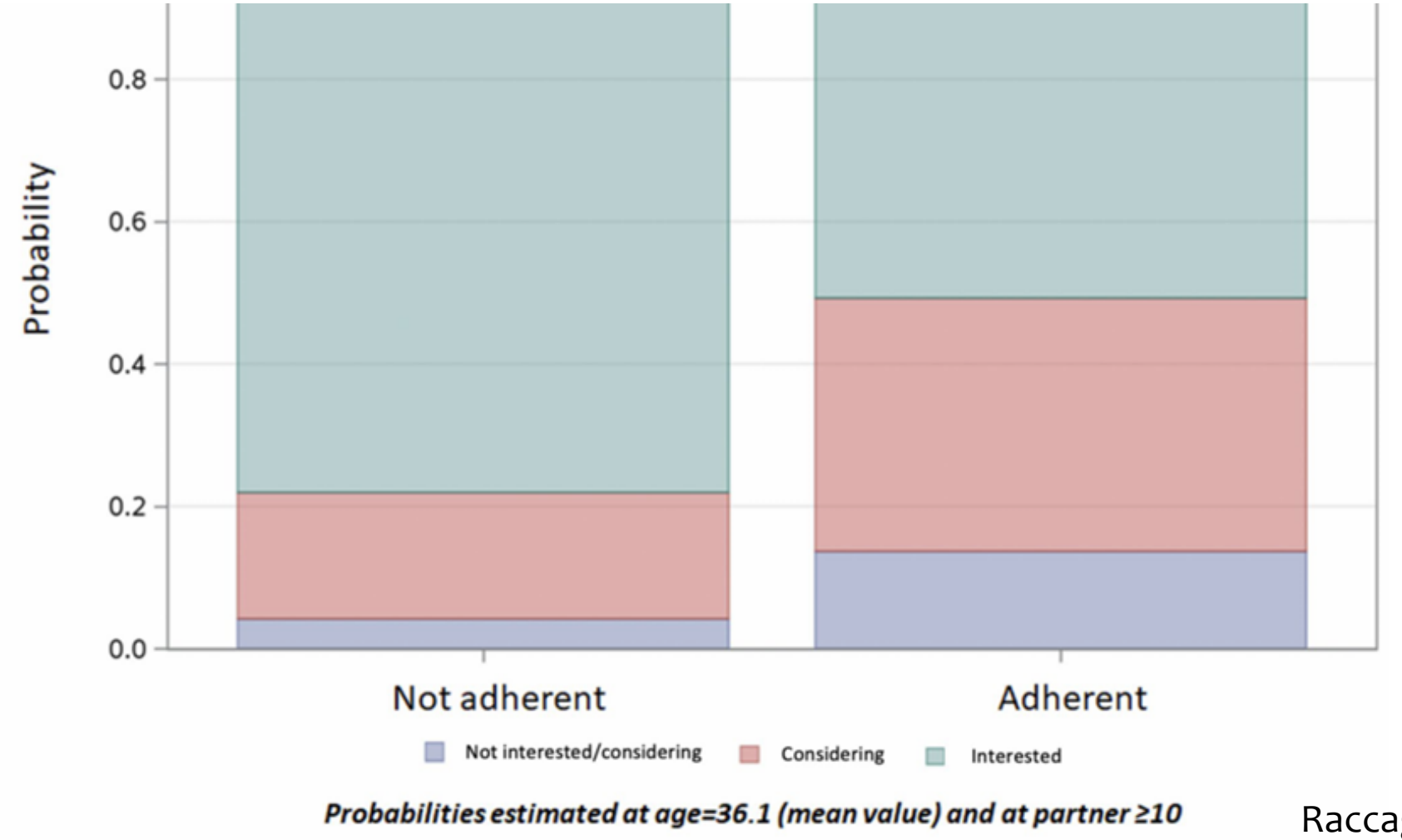
497 participants → 390 PY → 7 Incident HIV diagnoses* → IR → 1.8%

- In the DCP intervention arm, 56% of participants used CAB-LA and no incident HIV diagnoses were observed compared with no CAB-LA use in the SoC arm and an HIV incidence rate of 1.8% (p=0.01)

*One infant born to a participant in the SoC arm acquired HIV perinatally but was not included in the IR calculation.

Kamya et al. CROI 2024; Denver, CO. Oral presentation 172.

OSR: PROPENSITY TO SWITCH TO CABOTEGRAVIR



Raccagnu AR et al., AIDS and Behavior (2024) 28:907–911

PrEP CON CABOTEGRAVIR IN OSR

CAB PrEP users	N=70
MSM	69/70 (98.5%)
Women	1/70
Italian	67/70 (95.7%)
Oral PrEP experienced	68/70 (97.1%)
Chemsex / Adherence issues	46/70 (65.7%)
Kidney issues	15/70 (21.4%)
Bone issues	4/70 (5.7%)
Intolerance to FTC/TDF	20/70 (28.6%)

Nozza S., unpublished data

TAKE HOME MESSAGES

- ✓Cabotegravir efficacy is confirmed in clinical trials and real world data.
- ✓Testing is crucial.
- ✓The TRIO cohort study and OPERA study showed that LA CAB PrEP was well-tolerated, with rare instances of seroconversion, although further follow-up is needed due to suboptimal HIV testing compared with CDC guidelines.
- ✓Strategies to retain individuals on PrEP are needed.
- ✓Is it right to offer cabotegravir in limited settings?

GRAZIE