Use of Long-acting Cabotegravir for Pre-Exposure Prophylaxis to Prevent Infection with HIV

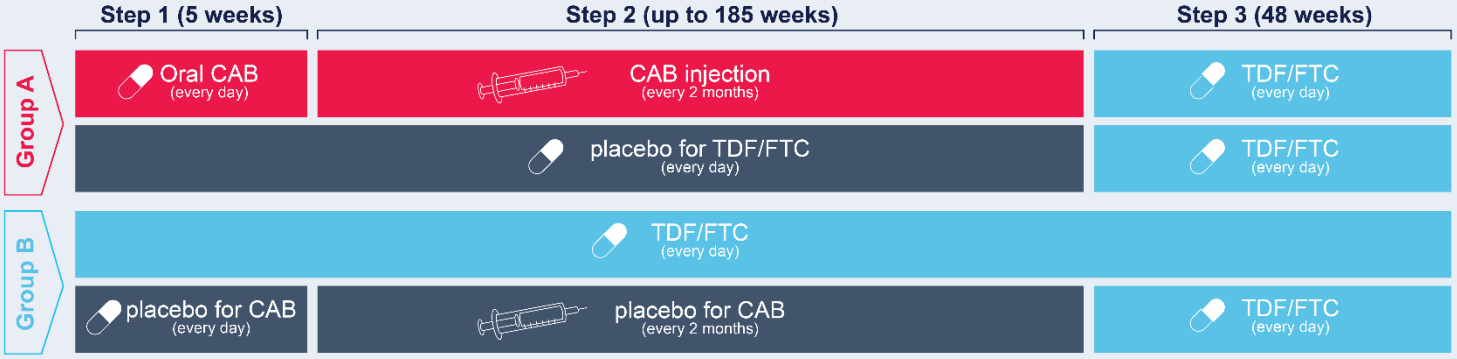
Animal data, human genital tract/rectal PK data, and phase 2 clinical data supported the progression of CAB LA into Phase 3 trials

HPTN 083 and HPTN 084: Study Design

HPTN 083 and HPTN 084 are two randomized, double-blind, double-dummy, phase 2b/3 studies designed to assess the safety and efficacy of CAB LA compared to daily oral tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) for pre-exposure prophylaxis (PrEP) in HIV-uninfected cisgender men and transgender women (TGW) who have sex with men (MSM), and cisgender women, respectively.[1,2]

HPTN 083 enrolled 4566 participants including 87% MSM and 13% TGW. The median (IQR) age was 26 (22-32) and 68% were <30. In the United States, a high percentage of participants were Black (50%).[1]

HPTN 084 included 3,224 cisgender women with a median age of 25 years, 57% of study participants were ≤ 25 years of age.[2]



HPTN 083: Study Results

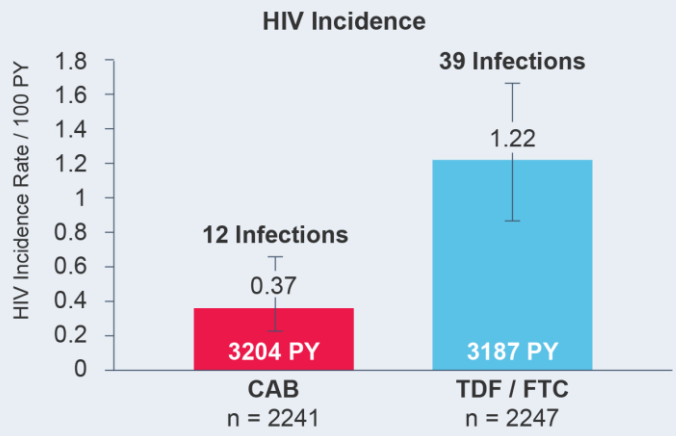
Initial Analysis

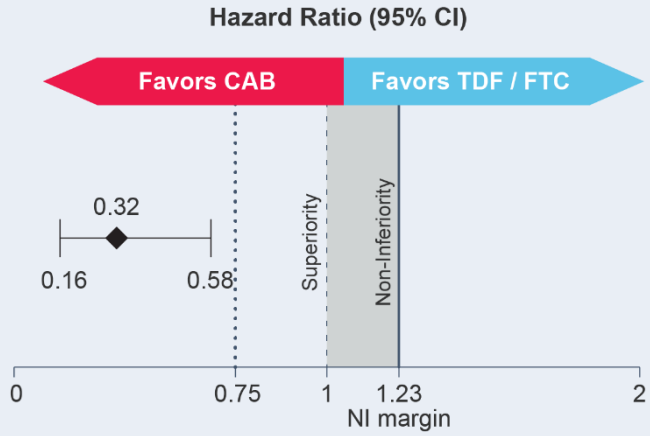
There were a total of 52 HIV infections were reported; 13 among participants who were randomized to CAB LA and 39 among participants randomized to TDF/FTC.[1] CAB LA was 66% more effective than TDF/FTC at preventing HIV acquisition (HR=0.34, 95% CI 0.18-0.62, *P*<0.001). Among key subgroups, there were numerically fewer new HIV infections in subjects receiving CAB LA than those receiving TDF/FTC.

Post-Hoc Assessment of Virology and Efficacy

Following the initial report of the results of HPTN 083, a laboratory assessment of the subjects who seroconverted was undertaken.[3] This post-hoc testing resulted in the re-adjudication of the time of the first positive HIV test in 2 cases. This resulted in a net decrease in the number of incident infections in the CAB LA arm from 13 to 12.

Updated HIV Incidence in HPTN 083[3]





For additional details about the results of HPTN 083 please click here.

Use of Long-acting Cabotegravir for Pre-Exposure Prophylaxis to Prevent Infection with HIV

Summary of Re-adjudicated Results[3]

Of the 16 infections (12 incident/4 baseline) among subjects randomized to CAB LA, 5 involved the development of integrase strand-transfer inhibitor (INSTI) resistance.[3] In all 5 cases, INSTI resistance developed after a period of oral cabotegravir and/or CAB LA monotherapy due to a delay in the detection of HIV infection at the study sites.

There was no INSTI resistance reported among the 4 subjects who seroconverted during the pharmacokinetic tail of CAB LA.[3]

The most common adverse events reported in the CAB LA arm were injection site reactions (ISRs).[1]

There were 51 incident infections overall: 12 in the CAB LA arm and 39 in the TDF/FTC arm[1]

CAB LA was 68% more effective than TDF/FTC at preventing HIV acquisition in men and transgender women who have sex with men (HR = 0.32 [95% CI 0.16, 0.58])[1]

Relationship of HIV Infection to CAB LA Administration in HPTN 083[1,3]

	Number of Infections (n=16)
Group A: Infection prior to administration of any study product	4
Group B: Infection after prolonged hiatus from CAB LA	5
Group C: Infection during oral lead-in (OLI) phase	3
Group D: Infection despite continuous, on-time CAB LA injections	4

Among key subgroups, there were numerically fewer new HIV infections in subjects receiving CAB LA than those receiving TDF/FTC[1]

HIV Incidence in Populations Most at Risk in HPTN 083[1]

	CAB LA (N=2282) Events/PY (IR%)	TDF/FTC (N=2284) Events/PY (IR%)	HR (95% CI)
Age			
≤30	11/2189 (0.50)	33/2116 (1.56)	0.33 (0.17, 0.65)
TGW	2/370 (0.54)	7/388 (1.80)	0.34 (0.08, 1.56)
MSM	11/2831 (0.39)	32/2797 (1.14)	0.35 (0.18, 0.68)
Race (US only)			
Black/African American	4/688 (0.58)	15/715 (2.10)	0.28 (0.10, 0.84)

Safety[1]

Overall, 81% of subjects who received at least 1 dose of CAB LA experienced an ISR event. The most common ISR reported was pain (61%). Fifty (2.4%) CAB LA recipients permanently discontinued treatment as a result of an injection-related adverse event.

Approximately 31% of subjects who received at least 1 dose of placebo CAB LA (Intralipid 20% fat emulsion) experienced an ISR.

ISRs were generally mild to moderate in severity and the incidence and severity of them decreased over time.

Adherence: 91.5% of person-years were considered "covered" by injectable CAB LA or placebo whereas 72% of participants in the TDF/FTC arm has tenofovir concentrations in dried blood spots indicative of receipt of at least 4 doses per week over the previous 1-2 months.[1]

Use of Long-acting Cabotegravir for Pre-Exposure Prophylaxis to Prevent Infection with HIV

HPTN 084: Study Results

This study evaluated the Safety and Efficacy of Long-Acting Injectable Cabotegravir Compared to Daily Oral TDF/FTC for Pre-Exposure Prophylaxis in HIV-Uninfected Women.[2]

Initial Analysis

There were a total of 40 HIV infections; 4 in the CAB LA arm and 36 in the TDF/FTC arm. CAB LA was 92% more effective than TDF/FTC at preventing HIV acquisition (HR=0.12, 95% CI 0.05-0.31, *P*<0.0001).[2]

Post-Hoc Assessment of Virology and Efficacy[4]

Following the initial report of the results of HPTN 084, a laboratory assessment of the subjects who seroconverted was undertaken. This post-hoc testing resulted in the re-adjudication of the time of the first positive HIV test in 2 cases. This resulted in a net decrease in the number of incident infections in the CAB LA arm from 4 to 3. CAB LA was statistically superior to TDF/FTC at preventing HIV acquisition (HR=0.08, 95% CI 0.03-0.27).

There were 39 infections overall: 3 in the CAB LA arm and 36 in the TDF/FTC arm[2]

CAB LA was 92% more effective than TDF/FTC at preventing HIV acquisition in cisgender women (HR = 0.08 [95% CI 0.03, 0.27])[2]

Relationship of Incident HIV Infection to CAB LA Administration[4]

Of the 3 infections in participants randomized to CAB LA, only 1 occurred in a participant who had received CAB LA. This participant experienced 3 delayed injection over the course of 70+ weeks. There was no resistance development in any participant who received CAB LA.

Adherence[2]

Adherence to CAB LA was approximately 93%; adherence to TDF/FTC decreased over the course of the study (35 of the 36 infections occurred in women with poor or inadequate adherence). TDF/FTC adherence was assessed by tenofovir PK measurements. CAB LA adherence was assessed by office visits (no PK).

Injection site reactions[2]

ISRs were reported in 38% of participants who received CAB LA versus 11% of participants who received TDF/FTC plus CAB LA placebo. Most ISRs occurred in the CAB LA arm after the injections at Week 1. There were no discontinuations due to ISRs in either arm.

Safety[2]

Most common (>15%) non-ISR adverse events regardless of relation to study drug.

	CAB LA	TDF/FTC
Creatinine clearance (CrCl) decreased	72%	74%
Gastrointestinal disorders	21%	23%
Increased serum creatinine	21%	21%
Abnormal uterine bleeding	19%	19%
Headache	17%	17%
Upper respiratory tract infection	17%	19%
Chlamydia infection	16%	18%

For additional details about the results of HPTN 084 please click here.

Abbreviations: AA, African American; LA, long-acting; CI, confidence interval; HPTN, HIV Prevention Trials Network; HR, hazard ratio; IR, incidence rate; ISR, injection site reaction; ITT, intention-to-treat; MSM, men who have sex with men; NI, non-inferiority; OLI, oral lead in; PrEP, pre-exposure prophylaxis; PY, patient-years; TGW, transgender women.

Some information contained in this response is outside the approved Prescribing Information. This product is not approved for the use described. This response is not intended to offer recommendations for administering this product in a manner inconsistent with its approved labeling. In order for ViiV Healthcare to monitor the safety of our products, we encourage healthcare professionals to report adverse events or suspected overdoses to the company at 877–844–8872. Please consult the attached Prescribing Information. This response was developed according to the principles of evidence-based medicine and, therefore, references may not be all-inclusive.

References: 1. Landovitz RJ, et al. N Engl J Med 2021;385:595-608. **2.** Delany-Moretlwe S, et al. Lancet 2022;399:1779-89. **3.** Marzinke MA, et al. J Infect Dis 2021;224:1581-92. **4.** Marzinke M. IAS 2021. #PECLB25