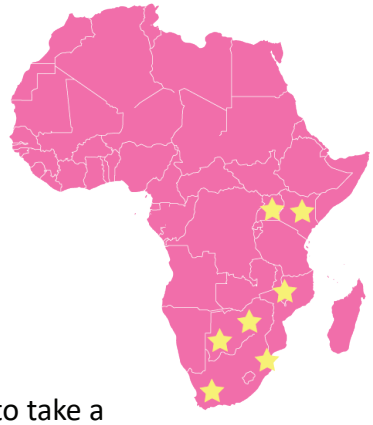
The HIV Prevention Trials Network

# HPTN 084 FAQ

HPTN 084
Long-acting Injectable For the Epidemic

**HPTN 084 Demonstrates Superiority of CAB LA to Oral FTC/TDF for the Prevention of HIV in cisgender women in sub-Saharan Africa**

## 1. What is HPTN 084 (LIFE - Long-acting Injectable For the Epidemic)?



HPTN 084 is the first study to compare the efficacy of a pre-exposure prophylaxis (PrEP) regimen consisting of an injection of long-acting cabotegravir (CAB LA) every eight weeks to daily oral tenofovir/emtricitabine (FTC/TDF) for HIV prevention among cisgender women. HPTN 084 enrolled 3,223 cisgender women at 20 sites in Botswana, Eswatini, Kenya, Malawi, South Africa, Uganda, and Zimbabwe.

## 2. Why was this study being done?

Taking a daily pill for PrEP is an effective tool for preventing HIV; however, remembering to take a daily pill can be hard for some people, others may prefer not to take daily pill, or some people may have medical reasons that prevent them from taking a daily pill. The development of safe and effective long-acting agents for HIV PrEP would increase HIV prevention choices and help those who find taking a daily pill challenging. Some people also may find periodic injections to be more discreet than daily pills. Having multiple HIV prevention methods available will give people more options to prevent HIV.

## 3. What organizations are involved in this study?

The HPTN 084 study is conducted by the HIV Prevention Trials Network (HPTN) and is jointly funded by the U.S. National Institute of Allergy and Infectious Diseases, part of the U. S. National Institutes of Health, Bill & Melinda Gates Foundation, and ViiV Healthcare. Study drugs are provided by ViiV Healthcare and Gilead Sciences, Inc.

## 4. What was the study design of HPTN 084?

Participants were assigned randomly (by chance) to either a regimen consisting of CAB LA or oral FTC/TDF. Neither the participants nor the study team knew who was in which group. Participants in each group received both injections and oral tablets – each participant received one active drug and one placebo (a placebo contains no active drug), in order to maintain the blinded nature of the study. Participants were randomized to one of two study arms that included three steps: Step 1 consisted of approximately one month of daily oral CAB and a FTC/TDF placebo or daily oral FTC/TDF and an oral CAB placebo; Step 2 consisted of up to 153 weeks of intramuscular CAB LA 600 mg every two months plus daily oral FTC/TDF placebo or daily oral FTC/TDF plus an intramuscular CAB LA placebo; and Step 3 consisted of open-label daily oral FTC/TDF for approximately one year after participants complete their last injection.

Cabotegravir Injection

Truvada Tablet

## 5. Why did the DSMB recommend stopping the blinded phase of the study?

On November 5, 2020, a Data and Safety Monitoring Board (DSMB) reviewed HPTN 084 study data and recommended that the blinded phase of the study be stopped early for successfully meeting its specified objectives. The HPTN 084 study found that a regimen containing CAB LA injected once every eight weeks was superior to daily oral FTC/TDF at preventing HIV acquisition in cisgender women. Among the 38 women in the trial who acquired HIV, four were receiving CAB LA and 34 were receiving daily oral FTC/TDF. This translated to an HIV incidence rate of 0.21% (95% confidence interval [CI] 0.06%-0.54%) in the cabotegravir group and 1.79% (95% CI 1.24%-2.51%) in the FTC/TDF group: in other words, approximately 9 times the number of incident HIV infections were in the FTC/TDF arm than in the CAB LA arm. The study sponsor, the U.S. National Institute of Allergy and Infectious Diseases (NIAID), approved the decision to stop the blinded part of the study.

## 6. Were the medications in the study deemed safe?

Both CAB LA and FTC/TDF were well-tolerated among the women enrolled in HPTN 084. The DSMB found no safety concerns. A small number of participants experienced pain or tenderness at the injection site, and this was slightly more common among women receiving CAB LA injections (32%) compared to those taking daily FTC/TDF (9%), who received placebo injections.

## 7. Did participants who acquired HIV while taking the regimen containing CAB LA have resistance identified in their HIV isolates?

Resistance testing for all participants who acquired HIV in either arm of HPTN 084 is ongoing. As soon as those data are available, they will be presented and/or published in peer-reviewed settings.

## 8. What will happen to the participants in HPTN 084 now?

Study participants will be informed of the study results and of which medication they were taking. Participants will be offered the opportunity to remain in the study, initially remaining on the active study medication that they were assigned to at the beginning of the study. Participants taking active FTC/TDF who wish to use CAB LA will be able to do so as soon as it is available. Participants who wish to may continue taking daily oral FTC/TDF.

## 9. What were the study demographics?

Among the women enrolled in HPTN 084, 57% were 18-25 years old, with an average age of 26 years old, 82% were not living with a partner, 55% reported two or more partners in the past month, with 34% having a primary partner who is reported to be living with HIV or having an unknown HIV status. Thirty-eight incident HIV infections were observed overall.

## 10. Will the oral lead-in for CAB before receiving the first injection of CAB LA continue to be required?

No, the oral lead-in will be optional in HPTN 084 for participants who choose to switch from FTC/TDF to CAB LA. The study will continue analyzing the safety data on the oral lead-in period of participants who switch from FTC/TDF to the regimen containing CAB LA.

## 11. Was more information learned about the need for oral PrEP to “cover the tail” of participants who wish to stop receiving CAB LA?

The study will continue collecting data on the specific case of participants who stop receiving injections of CAB LA. If a participant wants to stop receiving injections of CAB LA for PrEP and is still engaging in risk behaviors, she should transition to another HIV prevention modality - which may or may not include the use of a tenofovir-based PrEP product. In HPTN 084, participants will continue to be offered daily oral FTC/TDF for up to 48 weeks after their last CAB LA injection if they choose not to continue CAB LA.

## 12. What were the results from HPTN 083?

Results from HPTN 083 showed that a PrEP regimen containing CAB LA injected once every 8 weeks was superior to daily FTC/TDF for HIV prevention among cisgender men and transgender women who have sex with men. Overall, HPTN 083 enrolled 4,570 cisgender men and transgender women who have sex with men at research sites in Argentina, Brazil, Peru, South Africa, Thailand, the U.S., and Vietnam. Two-thirds of study participants were under 30 years of age, and 12% were transgender women. Half of the participants in the United States identified as Black or African American.

A total of 52 HIV infections occurred during follow-up, with 13 infections in the CAB arm (incidence rate 0.41%) and 39 infections in the FTC/TDF arm (incidence rate 1.22%). The hazard ratio in the CAB versus FTC/TDF arms was 0.34 (95% CI 0.18-0.62), corresponding to a 66% reduction in incident HIV infections in study participants given CAB compared to FTC/TDF. These results meet the statistical criteria for superiority of the regimen containing CAB compared to FTC/TDF in the HPTN 083 study population. The consistent adherence to FTC/TDF throughout the study and low incidence rate in both arms of the study clearly demonstrates both agents were effective at preventing HIV acquisition.

## 13. Is CAB LA also being tested in other populations?

Yes, two studies HPTN 083-01 and HPTN 084-01 are testing the safety, acceptability, and tolerability of CAB LA among adolescents.

## 14. Did COVID-19 play a role in the recommendation of the DSMB?

No. HPTN 084 continued throughout the COVID-19 pandemic in Africa. Plans were put in place to ensure participant and staff safety. The team also proactively established metrics of disruption and used these to assess whether an administrative censoring of data would be needed during potential periods of disruption. At no time during implementation did the study meet the pre-specified disruption threshold for censoring of data.

## 15. When will CAB LA be available for HIV PrEP?

It is too early to know when CAB LA may be available for individuals outside of the HPTN 084 study. The regulatory approval process for CAB LA requires several steps that need to occur first, including review and approval by the U.S. Food and Drug Administration and other regulatory agencies.

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