The HIV Prevention Trials Network

HPTN 084 FAQ

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

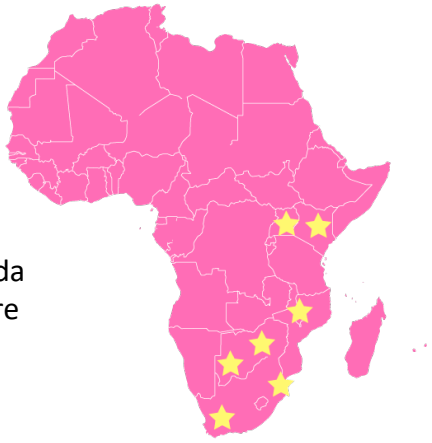
HPTN 084 (LIFE) is the first study to test if an injection of cabotegravir (CAB) given once every two months works better than a Truvada pill taken every day for HIV prevention in women.

Cabotegravir Injection

Truvada Tablet

2. When and where will this study be done?

The study is taking place in Botswana, Kenya, Malawi, South Africa, Eswatini, Uganda and Zimbabwe. HPTN 084 (LIFE) started in late 2017.



3. What organizations are involved in this study?

The HPTN 084 (LIFE) study 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. Why is this study being done?

Women in sub-Saharan Africa are at risk for HIV and new effective methods of HIV prevention are needed. A Truvada pill taken every day containing two drugs, TDF and FTC (TDF/FTC), is currently recommended by the World Health Organization (WHO) for use as PrEP (the use of medication to prevent infection) for people at risk for HIV infection. Several countries have approved TDF/FTC for use as PrEP.

Taking a daily pill for PrEP could be an effective tool for preventing HIV, but remembering to take a pill every day can be hard for some people. Newer, safer products that do not need to be taken every day are needed for people who may not want to take a daily pill or who may find it difficult to take a pill every day. As with contraception (birth control), we believe that more prevention options may lead to better use of HIV prevention products by people at risk for HIV infection. If shown to work and be safe, PrEP given as an injection has the potential to prevent HIV without relying on a daily behavior like pill-taking. An injection will be discrete and may protect the privacy of the person receiving the medication.

5. How many people will be in this study and who can join?

The study will enroll about 3,200 women who are HIV uninfected. Women who join the study must be 18-45 years old and on a highly effective, long acting method of contraception including an injectable, implant or IUD/IUC. Women who have received a tubal ligation procedure (sterilization) are also eligible for the study. Women who want to become pregnant should not join this study.

6. What will happen during the study?

Women who enroll in the study will be assigned at random (like flipping a coin) to either Group A or Group B. Each woman in each group will get an injection in the buttock every two months and a daily pill.

Women in both groups will get the same number of pills and the same number of injections. Group A will get cabotegravir (CAB) pills and CAB injections plus placebo Truvada pills (pills that look like Truvada pills, but have no active drug). Group B will get Truvada pills and placebo CAB pills (pills that look like CAB pills, but have no active drug) and placebo CAB injections (injections that look like CAB injections, but have no active drug). Both groups go through three steps in the study and some participants could be in the study for up to 4.5 years.

Group A

This group gets CAB pills and CAB injections plus Truvada placebo pills.

Step 1: CAB pill plus a placebo Truvada pill every day for five weeks

Step 2: One singular CAB injection initially, then another injection a month later, and then every two months after that up to three and half years plus a Truvada placebo pill every day

Step 3: Truvada pill every day for about a year, then referred to local HIV prevention services, which may include PrEP.

Group B

This group gets Truvada pills plus placebo CAB pills and placebo CAB injections.

Step 1: Truvada pill plus a placebo CAB pill every day for five weeks

Step 2: Truvada pill every day plus one singular placebo CAB injection initially, then another placebo injection a month later, and then every two months after that up to three and a half years

Step 3: Truvada pill every day for about a year, then referred to local HIV prevention services, which may include PrEP.

7. Will injectable cabotegravir be tested for HIV prevention in men also?

Yes. A study known as HPTN 083 is testing cabotegravir for HIV prevention in cisgender (identifies with their sex at birth) men who have sex with men and transgender (does not identify with their sex at birth) women who have sex with men. HPTN 083 is taking place in Argentina, Brazil, Peru, South Africa, Thailand, United States and Vietnam.

8. Is injectable cabotegravir safe?

Studies so far in HIV-infected (treatment studies) and HIV-uninfected (prevention studies) people have shown injections of cabotegravir (CAB) to be safe and acceptable. The most common side effects in another HPTN study using injectable CAB, HPTN 077, were headache and injection site reaction. Safety will continue to be looked at in HPTN 083 and 084.

9. How is the HPTN ensuring the safety of HPTN 084 study participants?

Multiple people and groups will carefully look at the safety of women in HPTN 084. This study has been reviewed by regulatory authorities and research ethics committees in the U.S. and in each of the countries where the study will be conducted. The study investigators will review safety including side effects regularly. In addition, a Clinical Management Committee will help principal investigators if unexpected safety concerns arise.

An independent (has no other involvement in the study) Data and Safety Monitoring Board (DSMB) will conduct reviews of participants' safety. A DSMB is composed of clinical research experts, statisticians, ethicists, and community representatives who meet periodically during a study to review safety and efficacy data as it is gathered. A statistician who is not part of the study team presents mid-study data to the DSMB. The DSMB will tell the study team if there are new safety concerns for study participants, if there is a sign that the study is working, or if the study cannot answer one of the questions it was made to answer. If it is thought to be needed by the DSMB, the DSMB can advise that the study be ended early. Regular safety reports will also be given to regulatory and research ethics committees in each country to ensure participant safety.

In 2018, the HPTN 084 DSMB was asked to review the safety data emerging from a study of a similar drug called dolutegravir. HPTN 084 implemented additional safety measures at that time and additional data were released about dolutegravir in July of 2019.

10. What is dolutegravir?

Dolutegravir (DTG) is an anti-HIV treatment drug (ARV) that belongs to a group of drugs called integrase inhibitors. Integrase inhibitors prevent HIV from making copies of itself and can reduce the amount of HIV in the body. DTG comes in a pill form. Dolutegravir is only used for the treatment of HIV.

11. Is DTG being used in HPTN 084 (LIFE)?

No, DTG is not being used in HPTN 084 (LIFE). CAB is used in HPTN 084. CAB and DTG are both integrase inhibitors. They are different drugs, but work in a similar way. CAB is being evaluated for both treatment (people living with HIV) and prevention (PrEP) of HIV, while DTG is only used for treatment of HIV.

12. Why were people talking about dolutegravir (DTG)?

In 2018, information from a study in Botswana using DTG to treat HIV infection was released. The information showed an increase in a specific type of birth defect called a "neural tube defect" (NTD) in some babies born to

mothers living with HIV while taking DTG for treatment before and during early pregnancy. The possible association between DTG and NTDs was concerning; data from more pregnancies was needed. Newer information from two large studies in Africa have shown the risks of NTDs to be much lower than what the initial information from the study in Botswana suggested in 2018.

The newer information prompted the World Health Organization (WHO) to update antiretroviral treatment (ART) recommendations in July of 2019. The WHO recommends DTG as the preferred HIV treatment option for all populations, including pregnant women and those of childbearing potential.

An NTD happens during the first four weeks of a pregnancy when the baby's spine or head do not form properly. NTDs are not common but they do occur; they usually happen when the mother has a specific vitamin deficiency (folate), has taken certain medications or there is a family history of NTDs. There is no cure for NTDs and babies who survive usually have lifelong health complications.

13. What is HPTN 084 doing for women who become pregnant in the study?

The updated recommendations from WHO regarding the use of DTG will not change HPTN 084. HPTN 084 will continue with the additional safety measures that were implemented in 2018:

- Oral contraceptives are no longer permitted; women who participate in the study must be on an injectable contraceptive, implant or use an IUD/IUC
- Pregnancy prevention counseling efforts will be strengthened
- If a woman accidently becomes pregnant during HPTN 084 she will stop receiving study products, she will be offered Truvada (TDF/FTC) and referred for prenatal care including an ultrasound to look at the baby's head and spine

14. Can injectable cabotegravir protect participants from getting infected with HIV?

We do not know if cabotegravir (CAB) given as an injection can protect people from getting HIV. Based on data from other studies, we think that CAB given as an injection may work for preventing HIV. We are conducting HPTN 083 and HPTN 084 to find out if CAB given as an injection works for preventing HIV infection.

15. What is Descovy®?

Descovy is a daily oral pill for PrEP that was recently approved by the U.S. Food and Drug Administration (FDA) for use among men who have sex with men and transgender women. Descovy is similar to Truvada but uses a newer form of tenofovir (TDF) called tenofovir alefenamide (TAF) instead of TDF. The FDA approval is based on the DISCOVER study. This study was done in over 5,000 gay men and transgender women in the U.S. and Europe. The results showed that Descovy was "non-inferior" to Truvada. Non-inferior is a term that means Descovy prevented about as many HIV infections as Truvada but was not worse than Truvada at HIV prevention. In the U.S. Descovy may be used for HIV prevention by all methods except for vaginal sex.

16. Is Descovy® being used in HPTN 084?

No, Descovy for PrEP is not being used in HPTN 084. Truvada for PrEP is being used in HPTN 084. Although Descovy is similar to Truvada, there has not been a study to test how well Descovy prevents HIV infections for cisgender women who have vaginal sex. Truvada is the only approved drug for PrEP to prevent HIV infections for vaginal sex. For this reason, the protocol team does not plan to make changes to the trial design at this time.

17. What will happen to study participants who become infected with HIV during the trial?

Study participants who become infected with HIV during the study will stop receiving study drugs and will be referred to local medical providers for HIV care and treatment.

18. What HIV preventive care will study participants receive?

Study participants will be offered condoms, treatment for sexually transmitted infections (STIs), open-label PrEP (study participants, regardless of study arm, will be given open-label Truvada in Step 3), and HIV risk reduction counselling.

19. How will participants be supported to take their study medication?

Study participants will receive support from clinic staff at each visit. Staff will discuss with the study participant why it might be easy or difficult for them to take a pill every day and/or attend study visits.

20. When did HPTN 084 begin and when are results expected?

HPTN 084 began near the end of 2017. The study will last about four and a half years, with participants active in the study between one and a half and three and a half years. Results are expected in 2023.

21. Where can I find out more information?

More information can be found at www.hptn.org/research/studies/hptn084