

HIV Prevention Trials Network

Clarification Memo # 2 to:

HPTN 084: A Phase 3 Double Blind Safety and Efficacy Study of Long-Acting Injectable Cabotegravir Compared to Daily Oral TDF/FTC for Pre-Exposure Prophylaxis in HIV-Uninfected Women Protocol Version 2.0, dated 6 November 2019

FINAL Clarification Memo (CM) Version: 1.0, dated 16 October 2020

The items clarified in this Clarification Memorandum (CM) have been approved by the DAIDS Medical Officer and are to be implemented immediately upon issuance. Institutional Review Boards/Ethics Committees (IRBs/ECs) approval of this CM is not required by the sponsor; however, investigators may submit the CM to the IRB/EC overseeing the study at their site for information. This CM is official HPTN 084 documentation and is effective immediately.

This CM and all related IRB/EC correspondence must be retained in the site regulatory file and in other pertinent files. Protocol registration approval is not required by DAIDS for CMs.

If the full HPTN 084 protocol is amended in the future, the changes in this CM will be incorporated into the next version.

Summary of Revisions and Rationale

1. Deleted text was removed (updated information) from the Introduction and Appendix IV “track changes” version of the protocol but not noted having been deleted from Appendix IV in the actual LoA 2 document dated 10 September 2020.

Deletions to the protocol text are indicated by ~~strikethrough~~; additions are indicated in **bold**.

Revision 1: Appendix IV: Sample Screening and Enrollment Informed Consent Form

PREGNANCY

We do not know if CAB can cause birth defects in babies. Birth defects have not been found in any animal studies of CAB so far. We have information from a different study conducted in Botswana with dolutegravir (DTG), a medicine that is similar to but not the same as cabotegravir (CAB), the medicine being studied in HPTN 084. In that study, some women living with HIV were taking DTG for treatment of HIV infection around the time of conception. That study,

known as the Tsepamo study, collected information on 153,899 deliveries at government hospitals throughout ~~public health facilities~~ Botswana from August 2014 to April 2020 and reported on babies that had birth defects of the spinal cord and brain (neural tube defects). These defects occur early on in the development of the pregnancy.

~~Overall, among 1683 deliveries in women who became pregnant while they were taking dolutegravir, 5 neural tube defects were found, that is a rate of 3 per 1000 babies born. This is compared to 15 neural tube defects in 14,792 babies born to women taking non-dolutegravir antiretroviral therapy for HIV at the time of conception or one in 1000 babies born.~~

BENEFITS

There may be no direct benefit for you if you participate in the study.

TDF/FTC is known to protect people from getting HIV if taken daily as directed. The recent results from the HPTN 083 study comparing CAB to TDF/FTC conducted in men who have sex with men and transgender women at 43 sites globally showed that participants given daily TDF/FTC pills had about three times the number of HIV infections compared to participants getting long-acting CAB. CAB has not yet been shown to protect against ~~getting HIV~~ HIV infection in cisgender women, which is the reason we are doing this study.