HIV Prevention Trials Network

Letter of Amendment #4 to:

HPTN 084-01

Safety, Tolerability and Acceptability of Long-Acting Cabotegravir (CAB LA) for the Prevention of HIV among Adolescent Females – A sub-study of HPTN 084

DAIDS Study ID: 38655

Protocol Version 1.0, dated 14 October 2019

Date of Letter of Amendment: 15 August 2022

LETTER OF AMENDMENT SIGNATURE PAGE

I will conduct the study in accordance with the provisions of this protocol and all applicable protocol-related documents. I agree to conduct this study in compliance with United States (US) Health and Human Service regulations (45 CFR 46); applicable U.S. Food and Drug Administration regulations; standards of the International Conference on Harmonization Guideline for Good Clinical Practice (E6); Institutional Review Board/Ethics Committee determinations; all applicable in-country, state, and local laws and regulations; and other applicable requirements (e.g., US National Institutes of Health, Division of AIDS) and institutional policies.

I have read and understand the information in this protocol and will ensure that all associates, colleagues, and employees assisting in the conduct of the study are informed about the obligations incurred by their contribution to the study.

Signature of Investigator of Record

Date

Name of Investigator of Record
(printed)

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The following information impacts the HPTN 084-01 study and must be forwarded to all responsible Institutional Review Boards/Ethics Committees (IRBs/ECs) as soon as possible for their information and review. This Letter of Amendment (LoA) must be approved by all responsible IRBs/ECs before implementation.

The IRB/EC will determine if trial participants need to be informed of the new information provided in this LoA, after considering HPTN 084-01 study status, participant roll over onto HPTN 084 OLE (Open Label Extension), and participants remaining on HPTN 084-01.

The information contained in this LoA does not impact the informed consent forms (ICFs).

Upon receiving final IRB/EC approval for this LoA, sites should implement the LoA immediately. Sites are required to submit an LoA registration packet to the DAIDS Protocol Registration Office (PRO) at the Regulatory Support Center (RSC). As part of the registration package, sites must submit the Letter of Amendment Investigatory Signature Page, signed and dated by the Investigator of Record. Sites will receive a registration notification for the LoA once the DAIDS PRO verifies that all the required LoA registration documents have been received and are complete. A LoA registration notification from the DAIDS PRO is not required prior to implementing the LoA. A copy of the LoA registration notification along with the LoA and any IRB correspondence should be retained in the site's regulatory files.

If the full HPTN 084-01 protocol is amended in the future, the changes in this LoA will be incorporated into the next version.

Summary of Revisions and Rationale

1. On 3 May 2022, the NIAID DAIDS Multinational Data and Safety Monitoring Board (DSMB) met to review the open and closed reports for HPTN 084-01. Given that the parent trials had been unblinded, efficacy data are now known, and CAB LA was recently FDA approved, the DSMB agreed to discontinue its reviews of the HPTN 084-01 protocol.

2. Relatedly, the HPTN 084-01 Study Monitoring Committee (SMC) met approximately one month prior to DSMB meetings for this trial and had – at last meeting – decided to discontinue its reviews of HPTN 084-01, should the DSMB come to a similar decision.

3. Changes with respect to discontinuation of DSMB and SMC reviews have now been made within the HPTN 084-01 protocol.

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

Revision 1: Section 6.4 Clinical Data Review

~~This study will be monitored by a NIAID Data and Safety Monitoring Board (DSMB), along with the parent protocols, which will meet at least annually to review safety and efficacy data. More frequent or ad hoc reviews of safety data may be conducted by the DSMB as needed.~~

Revision 2: Section 7.6.1 Study Monitoring Committee

~~NIAID DSMB oversight is planned for this study.~~ Monitoring guidance will be detailed in a separate Interim Monitoring Plan. ~~In addition, approximately every six months the HPTN SMC will conduct interim reviews of study progress, including rates of participant accrual, visit retention, and completion of primary and main secondary endpoint collection. The frequency and content of SMC reviews will be determined prior to the start of the study as outlined in the HPTN Manual of Procedures (MOP).~~

Revision 3: Section 10.3 Study Coordination

Close coordination between protocol team members will be necessary to track study progress, respond to queries about proper study implementation, and address other issues in a timely manner. Rates of accrual, adherence, follow-up, and AE incidence will be monitored closely by the team ~~as well as the HPTN SMC~~. The protocol team's CMC will address issues related to study eligibility and AE management and reporting as needed to assure consistent case management, documentation, and information-sharing across sites.