

HIV Prevention Trials Network

Summary of Changes Included in the Full Protocol Amendment of HPTN 084 DAIDS Document ID # 38070

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

**The Amended Protocol is identified as:
Version 4.0, dated 2 November 2022**

Information for Investigators

The modifications included in this protocol amendment and the associated rationale are summarized briefly below. HPTN 084 study investigators will submit this Summary of Changes and the corresponding protocol Version 4.0 and informed consents to all relevant regulatory authorities and Institutional Review Boards/Ethics Committees (IRBs/ECs) for approval. Upon receipt of all IRB/EC approvals, sites should begin implementation of the amended protocol immediately. The site will submit all required documents to DAIDS Protocol Registration Office (PRO) at the Regulatory Support Center.

This Amendment and all related IRB/EC correspondence must be retained in the site regulatory file in other pertinent files.

RATIONALE

The version 3.0 protocol of 12 August 2021 is being updated to provide instructions to extend CAB LA dosing by 48 weeks. Within the protocol, this extension is referred to 'OL 2.' This full amendment also incorporates three Letters of Amendment (LoAs) and two Clarification Memos (CMs).

Summary of Revisions and Rationale

- The protocol is being updated to incorporate LoA #1, LoA #2, LoA #3, CM #1, and CM #2 (please note that the revisions and rationales affiliated with all LoAs and CMs are not included in this summary, as they are outlined in each previously approved LoAs and CMs).
- The protocol is updated throughout for minor editorial changes and typographical errors.

Table of Contents

- Updated to match protocol sections/ pages.

Protocol Team Roster:

- Lydia Soto-Torres replaced Adeola Adeyeye as the Medical Officer in the protocol roster.
- Brett Hanscom replaced James Hughes as the Protocol Statistician in the protocol roster.
- Removed Priyanka Agarwal from the protocol roster.
- Updated phone numbers for Jennifer Farrior and Betsy Tolley in the protocol roster.

Throughout the V4.0 Protocol/ Appendix VIII: Procedures for Offering Open Label (OL) Cabotegravir-

- Clarified throughout that there are two OL phases: an initial 48-week OL (OL1, where participants are followed on Steps 4a, 4b, 4c, 4d or Step 5) followed by a second 48-week OL (OL2, where participants are followed on Step 4d, Step 5 or Step 6).
- Clarified the first open label period lasts 48 weeks and when it is completed there a second open label period which will last for another 48 weeks.

Section 2.1 (Duration)

- A proportion of participants will be followed up to 151 weeks.
- Pregnant participants may be enrolled in the study up to 200 weeks.

Section 2.2 (Study sites and population)

- Only participants who complete OL1 of HPTN 084 and who wish to continue taking CAB LA will be included in OL2.
- Pregnant women who were exposed to CAB LA during OL1 but elect to discontinue CAB LA, may continue to OL2 and be followed on Step 5.

Section 3 (Description of Steps 4, 5 and 6)

- Added more text around how pregnant participants will be followed in the different steps.
- Added a description of Step 6.
- Updated number of visits for Section 3.1, and Addendum to the Main SICF section *Important information.* Step 4c has seven visits and Step 6 has only 6 visits.

Step 4b, Appendix VIII: Schedule of Evaluations for Step 4b- Procedures for Participants Initiating or Re-starting CAB LA without the Optional Oral Lead-in; the Initial Dose Visit*

- Added an asterisk * Note that Step 4b may be used to provide a loading dose to participants where CAB LA injections have lapsed.

Appendix VIII SAMPLE QUALITATIVE ICF FOR MALE PARTNERS and section 5.16

- Updated to reflect that the qualitative substudy is being conducted in four of the HPTN 084 sites and will include a total of 120-158 women and 40-48 male partners.

Appendix VIII: Schedule of Evaluations for Step 6-Procedures for Participants on Maintenance Doses of CAB LA weeks 49-96

- Added the SOE for Step 6
- Clarified that pregnancy substudy participants may continue to take CAB LA through 48 weeks post-partum.
- updated to reflect acceptability assessments at Weeks 72 and 96.

Section A. Information in the Main Protocol that is Not Relevant to Protocol, V3.0 or Version 4.0

- In the section title and throughout this section made reference to the V4.0 protocol.

Section 4.0 (modified from the main protocol)

- Added text for Step 6- CAB-LA 600 mg administered as one 3 mL (600 mg) IM injection in the gluteal muscle every 8 weeks up to an additional (Week 56-96).

Clarified that CAB oral supply should come from Step 1 supply.

Section 5.0 (modified from the main protocol)

- Added injection visit windows for Step 6.
- Added text around acceptability assessments for the qualitative sub-study.

Section 7.0 (modified from the main protocol)

- Minor text changes to some of the OLE objectives to align with OLE 2.

Guidance on Toxicity Management for Specific Toxicities

- Added reference to Step 6.

Addendum to the Sample Informed Consent:

- Added text to differentiate the two open-label phases: OL 1 and OL 2.
- Added text around OL 2.

- Adjusted the verbiage to make sure that participants will know if they stop taking CAB LA “for any reason” that they will be offered Step 5 (48 weeks of TDF/FTC) to cover the PK tail.
- Updated language that pregnant substudy participants may take CAB LA all 48 weeks post-partum.
- Corrected the ICF to reflect vaginal swab collection at Weeks 72 and 96.
- Updated the ICF to remove mention of acceptability assessments at the “first visit” of Step 6 and updated blood storage requirements for this Step.
- Removed “taking pills” from the ICF.
- Removed incorrect language that CAB LA dosing would stop 24 weeks post-partum for those in pregnancy substudy.

APPENDIX VIII SAMPLE QUALITATIVE INFORMED CONSENT FORM FOR MALE PARTNERS AND
SAMPLE QUALITATIVE INFORMED CONSENT FORM FOR HEALTHCARE PROVIDERS

- Updated the number of participants.

REFERENCES

- Removed duplicated “Thomson” reference and re-numbered references in text.
- Updated the reference to the Investigator’s Brochure (IB). The current IB is dated 12 Jan 2022.