HIV Prevention Trials Network

Letter of Amendment # 1 to:

HPTN 083-01

HPTN 083-01: Safety, Tolerability and Acceptability of Long-Acting Cabotegravir (CAB LA) for the Prevention of HIV among Adolescent Males – A Sub-study of HPTN 083

DAIDS Study ID: 38654

Version 3.0, dated 2 July 2021

Date of Letter of Amendment: 14 January 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)

HIV Prevention Trials Network

Letter of Amendment # 1 to:

HPTN 083-01

HPTN 083-01: Safety, Tolerability and Acceptability of Long-Acting Cabotegravir (CAB LA) for the Prevention of HIV among Adolescent Males – A Sub-study of HPTN 083

DAIDS Study ID: 38654

Version 3.0, dated 2 July 2021

Date of Letter of Amendment: 14 January 2022

The following information impacts the HPTN 083-01 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 information contained in this LoA does 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 083-01 protocol is amended in the future, the changes in this LoA will be incorporated into the next version.

Summary of Revisions and Rationale

1. **SCHEMA:** specific analysis details have been added to the follow-up safety objective (3rd bullet) under Secondary Objectives for clarity.

2. **Section 2.2:** added details on evaluation and analysis plans to third bullet of section for clarity.

3. **Section 2.3:** clarification is made to indicate that an adverse event (AE) due to study product would result in discontinuation of study product during Step 2 "due to AE occurrence".

4. **Section 5 (Procedures):**

a. **Section 5.8:** information on loading dose visit for injectable cabotegravir for participants restarting CAB injections after a lengthy pause has been included to provide dosing guidance in the rare event that scenario arises.
b. **Section 5.10:** clarified that the target window for injection visits is not always +/- 3 days.

5. **Section 7 (Statistical Considerations):**
   a. **Section 7.2.2:** added intent to treat (ITT) analysis for primary safety endpoint.
   b. **Section 7.7.1:** clarification in analysis, to allow for injections in Step 3.
   c. **Section 7.8.2:** clarification in analysis, to allow for injections in Step 3.

6. **Section 8.2:** input language regarding how informed consent/assent will be obtained, per previous request of DAIDS and to be consistent with HPTN 084-01.

7. **Section 10.3:** clarification added to refer to DAIDS SCORE Manual (and not DAIDS SOPs which were superseded by the manual upon its release).

8. **Appendix III (Step 3 – Oral PrEP):**
   a. HIV testing (inclusive of HIV RNA) is, under V3.0, required at every visit, including the Week +8 and early discontinuation visits to avoid missing very early incident HIV infection not identified by rapid HIV testing.
   b. This change will be made and, therefore, medical history and evaluation of concomitant medications will be added to Week +8 and early discontinuation visits.
   c. Also due to the addition of HIV testing, blood collection will be added to the early discontinuation visit.
   d. Provision of TDF/FTC will be deleted from the early discontinuation visit because participants will be transitioned to local care (see below).
   e. Associated to this, adherence counseling will be added to all visits except the Week +8 visit, with a footnote (see new footnote 3) for Week +48 and early discontinuation that adherence counseling should consist of transition to local care and/or publicly available product at those visits.
   f. Chemistry and Liver Function Tests will be removed from Weeks +12 and +36 so the 6-monthly assessment frequency aligns with standard care.
   g. HIV viral load RNA testing details have been added to footnote 4.

9. **Appendix IV (Step 3 – Injection):**
   a. As mentioned above, HIV testing (inclusive of HIV RNA) is required at every visit under V3.0.
   b. Therefore, medical history and evaluation of concomitant medications should be taken at Week +8 and early discontinuation visits.
   c. Also due to the addition of HIV testing, blood collection will be added to the early discontinuation visit.
   d. Injections will not be given at any early discontinuation visits and ISR evaluation does not need to be completed at Week +8, since it was done at Week 34, so ISR at Week +8 will be removed.
   e. Footnote 3 has been added to describe Adherence Counseling at Week +48 and any early discontinuation visits as consisting of transition to local care and/or publicly available product.
   f. CBC with differential will be added to the early discontinuation visit, in line with Step 3 – Oral.

g. Chemistry and Liver Function Testing are currently listed at the Week +8 visit. These tests are not required at the Week +8 visit and, so, will be removed.
h. Urinalysis will be added to Weeks +24 and +48 and the early discontinuation visit, to be in line with Step 3 - Oral.
i. HIV viral load RNA testing details have been added to footnote 4.

10. Appendix V (Schedule of Additional Procedures for Reactive/Positive HIV Tests):

a. Chemistry and liver function testing have been removed from Weeks +12 and +36 in the Schedule of Evaluations (Appendix V) for participants who acquire HIV during the study. This brings this Schedule of Evaluations (SOE) in line with the counterpart SOE of the parent protocols and in line with the other follow-up (Step 3) SOEs.

11. **Appendix VII (Main Informed Consent):**

a. In the *What Will I Have to Do in The Study?* section, under *Study Visit Schedule* for Step 3, added clarifying details for whether the participant chooses to stay on CAB LA injections in Step 3 or go on oral PrEP (Truvada® or US FDA approved generic).
b. In the Table of Study Visit Procedures, “brief physical exam”, which includes medical history, recording of concomitant medications, and targeted physical exam, has been added to Week +8 for both Step 3 – Oral PrEP and Step 3 – Injection.
c. In the *Permanently Stopping Study Drug* section, deleted a potentially confusing clause about the participant choosing oral PrEP for Step 3, as it is assumed that they would be already going on oral PrEP if they stopped study drug (CAB LA injections).

12. **Appendix VIII (Self-Consent):**

a. In the *What Will I Have to Do in The Study?* section, under *Study Visit Schedule* for Step 3, added clarifying details for whether the participant chooses to stay on CAB LA injections in Step 3 or go on oral PrEP (Truvada® or US FDA approved generic).
b. In the Table of Study Visit Procedures, “brief physical exam”, which includes medical history, recording of concomitant medications, and targeted physical exam, has been added to Week +8 for both Step 3 – Oral PrEP and Step 3 – Injection.In the *Permanently Stopping Study Drug* section, deleted a potentially confusing clause about the participant choosing oral PrEP for Step 3, as it is assumed that they would be already going on oral PrEP if they stopped study drug (CAB LA injections)

13. **Appendix IX (Adolescent 10-13):**

a. More information is given in two areas to clarify details regarding Step 3, given the Schedule (Step 3 – Oral PrEP or Step 3 – Injection) a participant chooses.

14. **Additional changes (not listed in the Implementation Section following this section):**

a. Dates and version numbers have been updated in appropriate places within the protocol.

b. Minor contact detail edited in one cell of the roster (Erica Hamilton) and one former team member, Jean Paul Pease, has been removed, as he is no longer employed at SCHARP, the Statistical and Data Management Center (SDMC).
c. Under Secondary Objectives in the Schema and in Section 2.2 (Secondary Objectives), two references to "unknown" with regards to efficacy of CAB LA have been removed (given HPTN 083 and 084 efficacy results now available).
d. The CAB Investigator's Brochure (IB) has been updated to V11 in Section 1.2.
e. In Sections 1.5, 1.7, and 7.3, links internal (to the document) to certain figures and tables have been updated.
f. Throughout the protocol, any capitalized mentions of "TRADE NAME" or "TRUVADA®" have been made lower-case, also adding that generic Truvada® could be used in Step 3 (if not already noted).
    i. A specification has been included, in appropriate places, that only US FDA approved generic FTC/TDF comparable to Truvada® can be locally sourced and used by the site in HPTN 083-01 setting, in lieu of brand name Truvada®.
g. In Section 5.9.2, fixed one stray lack of mention of the potential for a participant to remain on CAB LA injections during Step 3 (approved in previous V2.0 to V3.0 full amendment).

IMPLEMENTATION SECTION

Deletions to the protocol text are indicated by ~~strikethrough~~; additions are indicated in **bold**. In certain cases, changes are highlighted for clarity.

Revision 1: SCHEMA

- ~~To evaluate the safety of CAB LA for 48 weeks of follow-up after final injection.~~ **To evaluate the safety of oral CAB during step 1 (oral phase) as well as all study products during the aggregate oral + injectable period of all enrolled participants. Additionally, we will include an intention to treat analysis for the primary safety endpoint.**

Revision 2: Section 2.2 Secondary Objectives

- To evaluate the safety of **oral CAB during step 1 (oral phase) as well as all study products during the aggregate oral + injectable period of all enrolled participants. Additionally, we will include an intention to treat analysis for the primary safety endpoint.**

  ~~CAB LA for 48 weeks of follow-up after final injection.~~

Revision 3: Section 2.3 Study Design and Overview

Participants who discontinue study product during Step 2 for any reason other than HIV infection or AE occurrence **related to study product** will be transitioned to open label Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®**; US FDA approved generic FTC/TDF comparable to Truvada® may be used**) for 48 weeks.

Revision 4: Section 5.8 Loading Dose Visit for Injectable Cabotegravir for Participants Restarting CAB Injections

In general, if it has been >15 weeks since a participant's prior CAB LA injection, a reload of CAB LA injections (two injections, 4 weeks apart) will take place. The participant will then continue Step 2 or transition to Step 3 four weeks later. Contact the CMC for guidance regarding all reloading cases.

Revision 5: 5.10 Injection Visit Windows

The target visit windows for all visits, including injection visits, are outlined in the SSP Manual. In brief, the target visit window for **most**~~all~~ injection visits is +/- 3 days.

Revision 6: 7.2.2 Secondary Endpoints

- Proportion of participants experiencing Grade 2 or higher clinical AEs and laboratory abnormalities in the oral phase and the aggregate over the entire study period. **Additionally, we will include an intention to treat analysis for the primary safety endpoint.**

Revision 7: 7.7.1 Safety Endpoints (Primary Analyses)

The primary safety analysis will include Grade 2 or higher clinical and laboratory events that occur from the initial injection to **the last Step 2 safety visit (up to week 34 for participants completing all injections)** ~~48 weeks after the last injection~~ among participants who receive at least one injection.

Revision 8: 7.8.2 Safety Endpoints (Secondary Analyses)

Secondary safety analyses will be summarized using the same method described in section 7.7.1, applied over the oral phase only (week 0 to week 4) and the aggregate oral+injectable+follow-up period~~.~~ **for all enrolled participants. Additionally, we will include an intention to treat analysis for the primary safety endpoint for all participants receiving at least one injection, using the time from first injection to approximately 34 weeks later (or study termination, if terminated early) regardless of whether participants received all 5 injections.**

Revision 9: 8.2 Informed Consent

Participants will document their provision of informed consent and assent by signing their informed consent forms~~.~~ **per site SOPs (refer also to the DAIDS Site Clinical Operations and Research Essentials (SCORE Manual). Site-specific reimbursement amounts will be specified in the study informed consent forms.** All participants will be offered a copy of their informed consent form.

Revision 10: 10.3 Study Coordination

Study implementation will be directed by this protocol as well as the SSP Manual. The SSP Manual, which will include links to the DAIDS **SCORE Manual**~~SOPs for Source Documentation and Essential Documents~~, as well as links to the Manual for Expedited Reporting of AEs to DAIDS and the DAIDS Toxicity Tables, will outline procedures for conducting study visits; data and forms processing; AE assessment, management and reporting; dispensing study products and documenting product accountability; and other study operations.

Revision 11: 12.3 Appendix III. Schedule of Evaluations – Follow-up Phase (Step 3 – Oral PrEP)

WEEKS SINCE LAST INJECTION	Wk +8	Wk +12	Wk +24	Wk +36	Wk +48	Early Discontinuation
ADMINISTRATIVE, BEHAVIORAL, REGULATORY						
Locator information	X	X	X	X	X	X
HIV prevention & risk reduction counseling	X	X	X	X	X	X
Condoms per local SOC	X	X	X	X	X	X
Behavioral/Acceptability assessment (CASI)		X	X	X	X	X
CLINICAL EVALUATIONS & PROCEDURES						
Qualitative interviews continue (approximately)		X	X			
Medical history[1], concomitant medications, targeted physical exam	**X**	X	X	X	X	**X**
Hep B vaccination (if needed) [2]						X
Blood collection	X	X	X	X	X	**X**
Urine collection			X		X	X
Rectal swab collection			X		X	
Provision of Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada® **or US FDA approved generic**) (3 months' worth)		X	X	X		~~X~~
Adherence Counseling[3]		**X**	**X**	**X**	**X[3]**	**X[3]**
LOCAL LABORATORY EVALUATIONS & PROCEDURES						
HIV testing[43]	**X**	X	X	X	X	**X**
CBC with differential			X		X	X
Chemistry testing[54]		~~X~~	X	~~X~~	X	X
Liver function testing[65]		~~X~~	X	~~X~~	X	X
Syphilis testing			X			X

GC/CT testing (urine, rectal, and oral pharyngeal swabs)			X		X	
Urinalysis (protein, glucose; at the clinic or local lab)			X		X	X
Plasma storage[76]	X	X	X	X	X	
DBS storage		X	X		X	
HBsAb and HBcAb[87]					X	X
HCVAb					X	X

FOOTNOTES FOR APPENDIX III:

[3] **At Week +48 and Early Discontinuation visits, Adherence Counseling consists of transition to local care/publicly available product.**

[4] **HIV viral load RNA testing is required for all participants, even those without a known seroconversion, at every visit. Tests include HIV Rapid test, Laboratory-based HIV immunoassay, and HIV viral load (<50 copies/mL).** The HIV testing algorithm is provided in the SSP Manual. If HIV rapid testing is indicated, this testing may be performed in the clinic or the laboratory. At least one HIV assay result must be available and reviewed the same day as sample collection and before product is administered.

[54] Creatinine only (for Step 3-Oral PrEP).

[65] AST, ALT, TBili, and alkaline phosphatase.

[76] Stored plasma will be used for Quality Assurance testing and other assessments at the HPTN LC (see Section 9) including potential assay for plasma CAB concentrations. Assessments will be performed retrospectively; results will not be returned to study sites or participants, except as noted in SSP. Samples cannot be used by site or other lab for local purposes without specific instructions from the LC w/ CMC consult.

[87] HBsAb and HBcAb will be tested in participants who received the HBV vaccine.

Revision 12: 12.4 Appendix IV. Schedule of Evaluations – Follow-up Phase (Step 3 – Injection)

WEEKS SINCE LAST INJECTION	Wk +8	Wk +16	Wk +24	Wk +32	Wk +40	Wk +48	Early Discontinuation
ADMINISTRATIVE, BEHAVIORAL, REGULATORY							
Locator information	X	X	X	X	X	X	X
HIV prevention & risk reduction counseling	X	X	X	X	X	X	X
Condoms per local SOC	X	X	X	X	X	X	X
Behavioral/Acceptability assessment (CASI)		X	X	X	X	X	X
CLINICAL EVALUATIONS & PROCEDURES							
Qualitative interviews continue (approximately)		X	X				
Medical history[1], concomitant medications, targeted physical exam	**X**	X	X	X	X	X	**X**
Hep B vaccination (if needed) [2]							X
Blood collection	X	X	X	X	X	X	**X**
Urine collection			X			X	X
Rectal swab collection			X			X	
Injections (CAB LA)	X	X	X	X	X	X	~~X~~
ISR evaluation	~~X~~	X	X	X	X	X	X
Adherence counselling[3]	X	X	X	X	X	X[3]	X[3]
LOCAL LABORATORY EVALUATIONS & PROCEDURES							
HIV testing[43]	X	X	X	X	X	X	X

CBC with differential			X			X	**X**
Chemistry testing[54]	~~X~~		X			X	X
Liver function testing[65]	~~X~~		X			X	X
Syphilis testing			X				X
GC/CT testing (urine, rectal, and oral pharyngeal swabs)			X			X	X
Urinalysis (protein, glucose; at the clinic or local lab)			**X**			**X**	**X**
Plasma storage[76]	X	X	X	X	X	X	
DBS storage		X	X		X	X	
HBsAb and HBcAb[87]						X	X
HCVAb						X	X

FOOTNOTES FOR APPENDIX IV:

[3] **At Week +48 and Early Discontinuation visits, Adherence Counseling consists of transition to local care/publicly available product.**

[4] **HIV viral load RNA testing is required for all participants, even those without a known seroconversion, at every visit. Tests include HIV Rapid test, Laboratory-based HIV immunoassay, and HIV viral load (<50 copies/mL).** The HIV testing algorithm is provided in the SSP Manual. If HIV rapid testing is indicated, this testing may be performed in the clinic or the laboratory. At least one HIV assay result must be available and reviewed the same day as sample collection and before product is administered.

[45] BUN/urea, creatinine, CPK, calcium, phosphorous, glucose, amylase, and lipase.

[56] AST, ALT, TBili, and alkaline phosphatase.

[67] Stored plasma will be used for Quality Assurance testing and other assessments at the HPTN LC (see Section 9) including potential assay for plasma CAB concentrations. Assessments will be performed retrospectively; results will not be returned to study sites or participants, except as noted in SSP. Samples cannot be used by site or other lab for local purposes without specific instructions from the LC w/ CMC consult. Blood collected for plasma storage must be collected prior to injection.

[87] HBsAb and HBcAb will be tested in participants who received the HBV vaccine.

Revision 13: 12.5 Appendix V. Schedule of Additional Procedures for Reactive/Positive HIV Tests

Participants who acquire HIV infection in Injection and Follow-up Phase only					
	HIV Confirmation Visit	Week 12	Week 24	Week 36	Week 48
ADMININISTRATIVE, BEHAVIORAL, REGULATORY					
Locator information	X	X	X	X	X
Offer condoms	X	X	X	X	X
HIV counseling	X				
CLINICAL EVALUATIONS AND PROCEDURES					

History, con meds, targeted physical exam	X	X	X	X	X
Blood collection	X	X	X	X	X
LOCAL LABORATORY EVALUATIONS					
HIV testing[1]	X				
CD4 cell count	X		X		X
HIV viral load testing	X		X		X
HIV resistance testing[2]	X				
Chemistry testing[3]		~~X~~	X	~~X~~	X
Liver function testing[4]		~~X~~	X	~~X~~	X
Plasma storage[5]	X	X	X	X	X
DBS storage	X				

Revision 14: 12.7 Appendix VII: Informed Consent for Parents/Legal Guardians and Assent for Adolescent Participants Ages 14 – Age of Majority

WHAT WILL I HAVE TO DO IN THE STUDY?
If you want to be in this study, you will sign and date this form before you begin the study.

Study Visit Schedule

- ~~Step 3 (5 or 6 visits) – After a blood draw 8 weeks after your last injection, you will come to the clinic (every 2 or 3 months) for 1 year to check how you are doing and to see how long CAB remains in your body after your last injection (+8, +12, +24, +36, +48 weeks). In most people, CAB disappears from the body slowly over 6 months, but it may last for a year or so. During this Step, you will be provided with Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) to take daily or continue on CAB LA, so we will be following you to see how well things are going on oral PrEP, doing bloodwork, as well as HIV and other STI testing.~~
- **Step 3 (5 or 6 visits, depending on whether you stay on CAB LA injections or move to oral PrEP) – After a visit 8 weeks after your last Step 2 injection, you will come to the clinic (every 2 or 3 months) for 1 year to check how you are doing. In Step 3 – Oral PrEP, you will have 5 visits and be seen quarterly. If you choose the Step 3 – Injection schedule, you will be seen every two months (6 visits total). For those choosing Step 3 – Oral PrEP, CAB disappears from the body slowly over 6 months, but it may last for a year or so. During this Step, you will be provided with Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada® or US FDA approved generic) to take daily, if you don't choose Step 3 – Injection. Either way, we will be following you to see how well things are going, doing bloodwork, as well as HIV and other STI testing.**

Tables of Study Visit Procedures

Step 3: your choice of moving to oral PrEP or remaining on CAB LA injections.

Step 3-Oral PrEP Follow-Up Visits – to see how long the CAB remains in your body

	+8 Weeks	+12 Weeks	+24 Weeks	+36 Weeks	+48 Weeks
Questions/CASI		√	√	√	√
Counselling	√	√	√	√	√
Brief physical exam	√	√	√	√	√
Blood	√	√	√	√	√
Urine			√		√
Rectal and oral pharyngeal swabs			√		√
PrEP pills offered		√	√	√	

OR:

Step 3-Injection Follow-Up Visits – remain on CAB LA, instead of switching to oral PrEP

	+8 Weeks	+16 Weeks	+24 Weeks	+32 Weeks	+40 Weeks	+48 Weeks
Questions/CASI		√	√	√	√	√
Counselling	√	√	√	√	√	√
Brief physical exam	√	√	√	√	√	√
Blood	√	√	√	√	√	√
Urine			√			√
Rectal and oral pharyngeal swabs			√			√
CAB LA injections	√	√	√	√	√	√

Permanently Stopping Study Drug

CAB pills are only given in Step 1, and then stopped permanently. If you need to leave the study before you receive any CAB injections, we'd still like to do a final study visit, which will include the same activities as the Step 3 Follow-Up Visits. If you permanently stop taking CAB after you had at least 1 CAB injection, then you will move straight to Step 3 follow-up visits, if you agree to stay in the study. ~~If you choose oral PrEP for Step 3, then 3~~ **In this case, three** months' supply of Truvada® **(or US FDA approved generic)** will be provided at Week 34.

Revision 15: 12.8 Appendix VIII: Informed Consent for Adolescent Participants Able to Consent for Themselves (Self-Consent) and Participants who Reach the Age of Majority

WHAT WILL I HAVE TO DO IN THE STUDY?

If you want to be in this study, you will sign and date this form before you begin the study.

Study Visit Schedule

Step 3 (5 or 6 visits**, depending on whether you stay on CAB LA injections or move to oral PrEP**) – After a **visit** ~~blood draw~~ 8 weeks after your last **Step 2** injection, you will come to the clinic (every 2 or 3 months) for 1 year to check how you are doing~~and to see how long CAB remains in your body after your last injection (+8, +12, +24, +36, +48 weeks)~~. **In Step 3 – Oral PrEP, you will have 5 visits and be seen quarterly. If you**

choose the Step 3 – Injection schedule, you will be seen every two months (6 visits total). ~~In most people~~**For those choosing Step 3 – Oral PrEP**, CAB disappears from the body slowly over 6 months, but it may last for a year or so. During this Step, you will be provided with Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada® **or US FDA approved generic**) to take daily**, if you don't choose Step 3 – Injection**. ~~or have the opportunity to continue on CAB LA injections, so~~ **Either way,** we will be following you to see how well things are going, doing bloodwork, as well as HIV and other STI testing.

Tables of Study Visit Procedures

Step 3: your choice of moving to oral PrEP or remaining on CAB LA injections.

Step 3- Oral PrEP Follow-Up Visits – to see how long the CAB remains in your body

	+8 Weeks	+12 Weeks	+24 Weeks	+36 Weeks	+48 Weeks
Questions/CASI		√	√	√	√
Counselling	√	√	√	√	√
Brief physical exam	√	√	√	√	√
Blood	√	√	√	√	√
Urine			√		√
Rectal and oral pharyngeal swabs			√		√
PrEP pills offered		√	√	√	

OR:

Step 3-Injection Follow-Up Visits – remain on CAB LA, instead of switching to oral PrEP

	+8 Weeks	+16 Weeks	+24 Weeks	+32 Weeks	+40 Weeks	+48 Weeks
Questions/CASI		√	√	√	√	√
Counselling	√	√	√	√	√	√
Brief physical exam	√	√	√	√	√	√
Blood	√	√	√	√	√	√
Urine			√			√
Rectal and oral pharyngeal swabs			√			√
CAB LA injections	√	√	√	√	√	√

Permanently Stopping Study Drug

CAB pills are only given in Step 1, and then stopped permanently. If you need to leave the study before you receive any CAB injections, we'd still like to do a final study visit, which will include the same activities as the Step 3 Follow-Up Visits. If you permanently stop taking CAB after you had at least 1 CAB injection, then you will move straight to Step 3 follow-up visits, if you agree to stay in the study. ~~If you choose oral PrEP for Step 3, then 3~~ **In this case, three** months' supply of Truvada® **(or US FDA approved generic)** will be provided at Week 34.

Revision 16: 12.9 Appendix IX: Information Sheet and Assent for Adolescent Participants Ages 10-13

If you join, you will complete about 18 study visits over the next 1½ years. You will move through the study in 3 steps:

- Step 1: You will take one CAB pill every day for five weeks.
- Step 2: You will receive a total of 5 CAB injections in your butt over 6 months.
- Step 3: You will come to the clinic for study visits every **2 or** 3 months for up to one year. You can choose either to continue CAB LA in this step, or choose to start taking the Truvada® **(or US FDA approved generic)** PrEP pill instead.

Different procedures are done at different study visits. The procedures include:

- *HIV Prevention* – We will offer you Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada® **or US FDA approved generic**) tablets as pre-exposure prophylaxis (PrEP) **or you may remain on CAB LA injections.** ~~after you stop the CAB injections or you may be able to join another CAB study.~~