

FINAL
SUMMARY OF CHANGES
INCLUDED IN THE FULL PROTOCOL AMENDMENT OF:
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, Version 1.0, 03 October 2019

DAIDS Document ID: 38654

THE AMENDED PROTOCOL IS IDENTIFIED AS:

Final Version 2.0

23 August 2020

IND #122,744

Information/Instructions to the Study Sites from the Division of AIDS

The information contained in this protocol amendment impacts the HPTN 083-01 study and must be submitted to site Institutional Review Boards and/or Ethics Committees (IRBs/ECs) as required as soon as possible for review and approval. This amendment impacts the study informed consent forms (ICFs) and related assent forms. Approval must be obtained from other site regulatory entities if applicable per the policies and procedures of the regulatory entities. All IRB/EC and regulatory entity requirements must be followed.

Upon obtaining all required IRB/EC approvals and any other applicable regulatory entity approvals, each site should immediately begin implementing this amendment, using site-specific Version 2.0 ICFs when obtaining informed consent and assent under protocol Version 2.0.

Upon receiving IRB/EC approvals and any other applicable regulatory entity approvals, all sites are required to submit an amendment registration packet to the DAIDS Protocol Registration Office (DAIDS PRO) at the Regulatory Support Center. Sites will then receive a registration notification for the amendment after the DAIDS PRO verifies that all required registration documents have been received and are complete. Sites should not await this notification before implementing this amendment.

This Summary of Changes, Protocol Version 2.0, corresponding site-specific informed consent and assent forms, and all associated IRB/EC and regulatory entity correspondence should be retained in each site's essential document files for HPTN 083-01.

The Division of AIDS Regulatory Affairs Branch will submit this amendment to the United States Food and Drug Administration (FDA) for inclusion in Investigational New Drug application (IND) #122,744.

Summary of Revisions and Rationale

The modifications included in this protocol amendment and the rationale are summarized below and detailed in the ‘implementation’ section that follows. The modifications are presented generally in order of their appearance in the study protocol. The major items included in this protocol amendment are as follows:

1. The protocol title and signature pages are updated for the current version of the protocol.
See revision 1 and revision 1 (continued).
2. Section 1.2 is updated to remove reference to an outdated version of the cabotegravir Investigator’s Brochure.
See revision 2.
3. Section 1.7 now has three new sub-sections. Section 1.7.1 is a new section which includes PK data on adolescents <50kg from the MOCHA Study. Section 1.7.2 is updated to include new data on HPTN 077 participants. Section 1.7.3 is a new section added to include preliminary (non-inferiority) and official (superiority) results from HPTN 083.
See revision 3.
4. Section 2.3 is updated to remove language that indicated that the team would broaden the sexual risk profile of participants in the future, if results show CAB LA is effective at preventing HIV. This is now the case, so this language has been removed.
See revision 4.
5. Section 3.1, Inclusion Criteria, is updated in two areas:
 - 3.1.3 Decreased weight criterion from ≥ 50 kg (110 lbs) to ≥ 35 kg (77 lbs).
 - 3.1.8 Added new inclusion criterion: If currently on PrEP from a non-study source, willing to stop said PrEP prior to enrollment and agree to switch to oral CAB for the lead-in period and CAB LA injections.See revision 5.
6. Section 3.2, Exclusion Criteria, is updated in two areas:
 - 3.2.2 “Currently receiving PrEP from a non-study source” has been removed.
 - 3.2.5 Three exclusion criteria have been removed, to broaden the sexual risk profile for participants, due to the superiority results from HPTN 083.See revision 6.
7. Section 4.1, Study Product Regimens/Administration/Formulation Content, Step 3 - Follow-up Phase has been updated to include the potential for participants to enroll in an open label CAB study during Step 3, if available. This update also applies to Section 5.7, Step 3, Follow-up Phase, 1st Paragraph, 2nd Sentence.
 - a. Note that “if available” has been incorporated post-ARR (see Appendix I of the Team Response to the ARR).See revision 7.
8. Section 5.2, Enrollment, now clarifies that the PHQ-9 must be administered at the Enrollment visit.

- See revision 8.
9. Edits to Section 5.8 reflect superiority findings from HPTN 083.
See revision 9.
10. Section 5.9, Injection Visit Windows: Change made to target visit windows. Target should be +/- 3 days for all injection visits, since there is only 1 week between each safety visit (and not 2 weeks in between, like in the parent protocol).
See revision 10.
11. Section 5.16 now includes clarifying language regarding early study termination taken from the full protocol amendment (V2.0 to 3.0, 31 October 2019) of the parent study, HPTN 083.
See revision 11.
12. In Section 6.4, Clinical Data Review, the section describing the Study Monitoring Committee (SMC) was removed, since the SMC will not be reviewing safety data for this trial.
See revision 12.
13. Section 7, the Statistical Considerations Section, now includes the possibility for a participant to join an open label CAB study during Step 3, if available locally, desired, and warranted. Other clarifications are also made within this section.
See revision 13.
14. Section 8.1, Ethical Review: Removed inclusion of SRC and PSRC review of any subsequent modifications of the protocol and template informed consent forms.
See revision 14.
15. The Virology section (Section 9.3) now includes language permitting the HPTN Laboratory Center to periodically conduct resistance testing, instead of conducting it retrospectively. This was a change in the parent protocol, given DSMB feedback.
See revision 15.
16. The Study Monitoring section, 10.4, has been updated to ensure that Westat (on behalf of NICHD), which will be monitoring this study, will have access to study files.
See revision 16.
17. Record Retention, in Section 10.6, was changed to incorporate potential European Medicines Agency (EMA) requirements.
See revision 17.
18. Appendix I has been changed to allow for collection of demographic information at Screening or Enrollment and administering the PHQ-9 at Enrollment.
See revision 18.
19. The fasting lipid requirement has been removed at every visit except Enrollment and Week 34 (Appendices II and III).

See revisions 19 and 20.

20. Seven consents/assents have been added to the protocol, as initially approved by HPTN’s new Single IRB (sIRB), Advarra, after they were approved by DAIDS. These consents/assents are very similar to the ICF templates already approved by DAIDS, with minimal changes made, mostly including template formatting and headers.

Since the results from HPTN 083 have been released, we have now included mention of those in these ICFs, as well as included the possibility for a participant to join and open label CAB study in Step 3 (if available locally and if desired and warranted). After DAIDS review, these ICFs will be sent back to Advarra for approval again.

See revision 21.

21. Other minor changes have been made (not included in the Implementation Section below):

1. The designation of Version 1.4, Regulatory Review Version, has been added to the title page.
2. The Table of Contents has been updated to reflect corrected linked page numbers.
3. Patient Health Questionnaire-9 (PHQ-9) has been added to the Acronyms list.
4. The Protocol Team Roster information is updated for Lynda Emel, Lisa Hightow-Weidman, and Marcus Bryan. Julie Ngo, Jean Paul Pease, and Kathryn Myers are added as protocol team members. Heather Noble was removed from the roster. External links to email addresses were removed.
5. Section 1: Table numbers have been updated. Table 1.1 was moved accordingly.
6. Section 1.9, Weight Gain: Typo corrected in paragraph one: “integrate inhibitors” corrected to “integrase”.
7. Section 3.1.6: Platelet count is clarified to **cells/mm³**.
8. Section 4.4: Descovy® and atazanavir spelling errors were corrected.
9. Section 5.8.2: references to orphan “/FTC” were removed.
10. Various sections: Changes made to clarify that a participant may join an open-label CAB study during Step 3 only **if available** in their area:
 - Section 2.3, Study Design and Overview: added the phrase “**if such a study is being implemented in their area at the time**” to the end of the next to last sentence of the second paragraph.
 - Section 4.1, Step 3 – Follow-up Phase: added the phrase “**if available**” to the end of the last sentence of that paragraph.
 - Section 5.7, Step 3, Follow-up Phase: clarification to note that a participant may join, instead of be offered enrollment, an open-label CAB study and added the phrase “**if available**” (last sentence of first paragraph).
 - Section 7.1, Review of Study Design, end of the last sentence of second paragraph: This language now states, “...for daily use or **participation** in an open-label CAB study for 48

- weeks, **if available.**” This replaces the previous language in that section, which stated “...for daily use for 48 weeks or ~~offered enrollment~~ into local open label CAB study.”
- Appendix VI, Important Information (*HIV Prevention*): added the phrase “**if available**” to the end of the last sentence of that paragraph.
 - Appendix VI, Step 3 information under Study Visit Schedule: clarification added to the last sentence of that paragraph, so that it now reads “...to take daily or have ~~be offered~~ the opportunity to join an open label CAB study (**if available**),...”.
 - Appendix VI, *HIV Prevention* section of Study Visit Procedures: added the phrase “**if available**” to the end of the next to last sentence of that paragraph.

11. Appendix III: a blank row in Appendix III was removed.

12. A new reference has been added. (37. Landovitz, AIDS 2020.)

Implementation of Modifications

Modifications of protocol text are described below. Modifications are generally listed in order of appearance in the protocol. Where applicable, modified protocol text is shown using strikethrough for deletions and bold type for additions.

Revision 1: Protocol Title Page

The protocol title page is updated for Version 2.0.

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 Document ID: 38654

A Study by the HIV Prevention Trials Network (HPTN)

Sponsored by:

Division of AIDS (DAIDS), United States (US) National Institute of Allergy and Infectious Diseases (NIAID), Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD),
US National Institutes of Health (NIH)

Support Provided by:

ViiV Healthcare

IND Holder:

DAIDS, NIAID, NIH

IND #: 122,744

Protocol Chair:

Sybil Hosek, PhD

Protocol Co-Chair:

Lynda Stranix-Chibanda, MBChB, MMED

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Revision 1 (continued): Protocol Signature Page

The protocol signature page is updated for V 2.0.

**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**

Protocol Signature Page

Version 2.0, dated 03 October 2019

23 August ~~XX~~ Month 2020

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Division of AIDS (DAIDS), United States (US) National Institute of Allergy and Infectious Diseases (NIAID), Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD),
US National Institutes of Health (NIH)

Support Provided by:

ViiV Healthcare

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.

Name of Investigator of Record (print name)

Signature of Investigator of Record

Date (DD/MM/YYYY)

Revision 2: Removal of reference to outdated CAB IB.

1.2 Overview of Oral CAB and CAB LA

The majority of information contained in this section of the protocol is a summary of information provided in the CAB Investigator's Brochure (IB), ~~V8.0, Effective Dated 17 December 2018~~ unless otherwise noted.

Revision 3: Section 1.7 is updated to include HPTN 077, HPTN 083, and MOCHA (IMPAACT 2017) results. Table 1.1 has been moved accordingly, to Section 1.5.2. Previously titled Table 2 has been moved accordingly, to Section 1.5.2, and is now Table 1.1.

1.7 Pediatric Dosing

Currently, there is no previous clinical trial experience with oral CAB or CAB LA in humans under 18 years of age. This protocol will enroll using a weight-based approach rather than age based. This allows for an eventual adolescent indication for LA CAB in adolescents at-risk, regardless of age. The supplemental adolescent indication for Truvada® was entirely weight-based (down to 35 kg) for adolescents at risk of HIV. Also, by not specifying a lower limit of age, this allows sites the flexibility to enroll participants that meet the behavioral and physical criteria necessary to qualify. Each site will have ethics review and will consider these criteria in light of community standards; and each investigator of record will be able to determine whether a candidate is appropriate for enrollment or not. These decisions will then be made with consideration for the local context of each site/community, rather than arbitrarily choosing what age should be the lower limit.

1.7.1 Preliminary Results MOCHA (IMPAACT 2017)

The IMPAACT 2017 trial began enrolling in April 2019. IMPAACT 2017 (NCT03497676) is a Phase I/II, multi-center, open-label, non-comparative study to confirm the dose and evaluate the safety, tolerability, acceptability, and PK of oral CAB, long-acting injectable CAB (CAB LA), and long-acting injectable RPV (RPV LA) administered monthly among up to 155 virologically suppressed HIV-1 infected children and adolescents aged 12 to <18.

As of January 2020, 7 adolescent HIV infected participants in IMPAACT 2017 (MOCHA) aged 12 to 17 years (40 to <50kg: n=4, >50 kg: n=3) had PK collected and analyzed following oral CAB 30 mg once daily and three injections of the CAB LA adult monthly regimen (600 mg IM initiation injection, followed by two monthly 400 mg IM injections). Median (range) CAB PK parameters were within the desired target ranges, specifically Week 2 oral AUC 167.0 (131.1-326.8) µg•h/mL and Week 16 IM trough 2.9 (1.2-6.2) µg/mL, and were similar to adult exposures (Table 1.2).

Table 1.2: Pharmacokinetic Parameters following Cabotegravir Orally Once Daily and Initiation and Monthly Continuation Intramuscular Injections in Adults

Dosing Phase	Dosage Regimen	Geometric Mean (5 th , 95 th Percentile) ^a	
		AUC _(0-tau) ^b (mcg•h/mL)	C _{tau} ^b (mcg/mL)
Oral Lead-In ^c	30 mg once daily	145 (93.5, 224)	4.6 (2.8, 7.5)
Initial Injection ^d	600 mg IM Initial Dose	1,591 (714, 3,245)	1.5 (0.65, 2.9)
Monthly Injection ^e	400 mg IM monthly	2,415 (1,494, 3,645)	2.8 (1.7, 4.6)

^a All pharmacokinetic parameter values based on pooled FLAIR and ATLAS individual post-hoc estimates from cabotegravir population pharmacokinetic model (n = 581, 2018N384611_01).

^b tau is dosing interval: 24 hours for oral administration; 1 month for IM injections of extended-release injectable suspension.

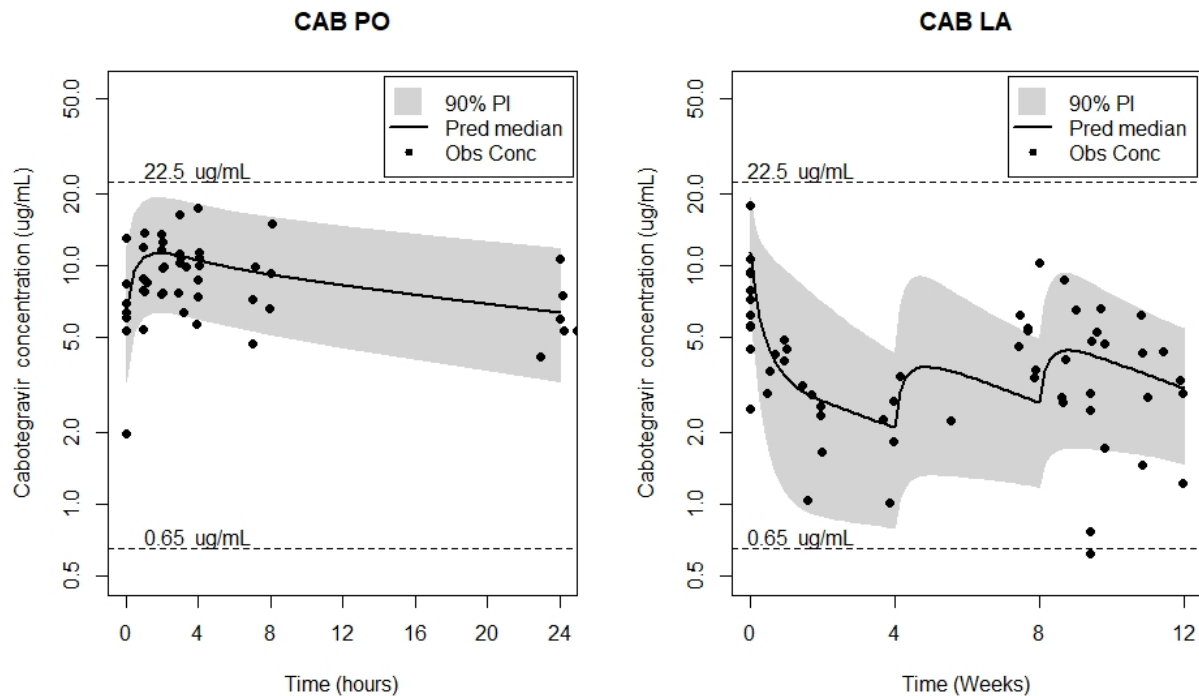
^c Oral lead-in pharmacokinetic parameter values represent steady-state.

^d Initial injection AUC_(0-tau) value includes contribution following oral dosing because the initial injection was administered on the same day as the last oral dose; however, the C_{tau} value at Week 4 reflects the initial injection.

^e Monthly pharmacokinetic parameter values represent Week 48 data.

Preliminary CAB data observed in adolescent participants were compared to *a priori* predictions in adolescents from population PK (POP PK) modelling and simulation (Figure 1.2). The CAB POP PK model was developed utilizing exposure data from adult participants (n=1647) in clinical studies with efficacious dosing regimens having an acceptable safety profile with Q4W and Q8W injections, and simulations were conducted taking into account any potential age and weight related impact on PK, to recommend appropriate doses in adolescents that achieve comparable exposures to those seen in adults. The preliminary adolescent PK data are in agreement with the predicted exposure range and within thresholds (Figure 1.2). Given the strong agreement of observed data with predictions, the model is considered suitable to predict exposure in adolescents ≥35 kg for any dosing regimen. Predicted exposures following CAB LA Q8W administration in adolescents are shown in Table 1.2.

Figure 1.2: Preliminary Observed CAB concentrations in adolescents compared to model predictions based on POP PK analyses from adult studies (IMPAACT 2017 Cohort 1C)



Note: The plots represent the CAB systemic exposure: solid line and shaded band reflect the population pharmacokinetic model predictions (median and 90% interval); the dots represent the observed individual subject data. The dashed lines represent the maximum observed geometric mean exposure from the TQT study at (22.5 $\mu\text{g/mL}$) at suprathreshold doses following 150 mg q12h x 3 and the target threshold concentrations at trough (0.65 $\mu\text{g/mL}$).

Table 1.3: Predicted Steady State CAB Parameters following CAB LA IM Q8W regimen compared with Observed and Estimated data in Adults

		Predicted C_{τ} ($\mu\text{g/mL}$) ^b	
		Post First Injection	Post Second Injection ^c
Adolescent Body weight	35 to <50kg	2.49 [0.98, 4.72]	2.34 [0.84, 3.98]
	$\geq 50\text{kg}$	1.76 [0.69, 3.49]	1.76 [0.77, 3.05]
Observed adult data		1.50 [0.65, 2.90] ^a	1.61 [0.80, 2.99] ^d
<p>a. Geometric mean [5th and 95th percentile] - Week 8 pre-dose concentrations were obtained following a CAB 600 mg IM dose.)</p> <p>b. Median [90% prediction Interval]</p> <p>c. C_{τ} after second injection is 8 weeks post injection</p> <p>d. Geometric mean [5th and 95th percentile] - C_{τ} at Week 48 with Q8W dosing regimen (ATLAS 2M, 207966)</p>			

1.7.2 Results from HPTN 077

A population PK model (n=1647) that included data from HPTN 077 (n=134, 89 females, 45 males) and 15 other studies was used to predict exposures following the proposed CAB LA Q8W regimen in adolescents. Gender and BMI are significant covariates affecting the absorption rate following IM administration and were retained in the model to extrapolate to smaller adolescent males expected to enroll in HPTN 083-01. Model predicted concentrations in adolescent males (simulated with median weight and BMI of 63 kg and 21 kg/m², respectively) to enroll in HPTN 083-01 are similar to adult males in HPTN 077 (median weight and BMI of 77kg and 24 kg/m², respectively) receiving the same regimen and below oral dosing, and therefore are expected to be safe in this population (Table 1.4). Approximately 95% of male subjects are expected to achieve trough concentrations > 4x PA-IC90 following the 5th injection. This regimen is currently being evaluated in uninfected adult males and females in HTPN 083 and HPTN 084, respectively, and has maintained HIV suppression in infected adults when combined with RPV LA (LATTE-2).

Table 1.4: Predicted CAB Parameters following Injection 5 of the CAB LA 600mg IM Q8W Regimen in Male Adolescents compared with Predicted and Observed Data in Male Adults in HPTN 077

Plasma CAB Parameter ((µg/mL)	Male Participants in HPTN 077 Median (range)		Predicted Exposures Male Adolescents ≥50kg (110 lbs.)		
	Predicted Parameters 30 mg Once Daily	Observed Data 600mg IM Q8W (Injection 5)	Median (90% PI)	Peds:Adults Relative Exposure	
				Vs 30mg	Vs 600mg
Oral C _{max} or C, Wk 34 (1-week post Inj5)	7.6 (4.6 - 12.0)	3.4 (1.6 - 12.9)	5.0 (2.7, 9.1)	0.7	1.5
Oral C _τ or C, Wk 41 (8-weeks post Inj5)	4.5 (2.3 - 7.6)	1.78 (0.50 - 4.2)	1.8 (0.5, 3.4)	0.4	1.0

Plasma CAB will be evaluated during follow up period and but is not expected to be detectable in a majority of subjects one year after the final injection.

Based on adult dosing data and pharmacokinetic modeling, oral CAB 30mg and CAB LA 600mg IM are expected to be safe in adolescents and have been selected as the initial regimen for the IMPAACT 2017 study - the same as the adult CAB regimen in current Phase III studies. While somewhat higher CAB plasma concentrations are expected in lower weight adolescent participants, the safety and tolerability seen in adults at the higher oral CAB dose of 60 mg daily and CAB LA dose of 800mg q 8 weeks tempers any safety concerns.

Seven uninfected participants in HPTN 077 weighing <50kg at baseline received CAB LA injections during the study. Individual W41 Ctau values following final injections in participants <50 kg ranged from 0.616 µg/mL to 4.17 µg/mL (

Table), which is within the range of W41 Ctau for the study population overall of 0.203 to 4.72 µg/mL for Cohort 1 (n=57) and 0.503 to 4.62 µg/mL for Cohort 2 (n=52) and are consistent with expected concentration targets. Individual t1/2 estimates ranged from 13.6 days to 90.4 days in participants <50 kg and from 19.8 to 183 days in Cohort 1 overall and from 13.6 to 241 days in Cohort 2 overall.

Table 1.5: Select PK Parameters in Participants with Baseline Weight <50kg

Cohort	Sex	Subject	Baseline Weight (kg)	Baseline BMI (kg/m ²)	Ctau (µg/mL)		T1/2 (day)
					Week 9 (Initial Injection)	Week 41 (Final Injection)	
Cohort 1	F	257000081	42.7	16.5	0.655	1.73	28.3
	F	264000146	41.4	18.2	1.36	3.13	50.3
Cohort 2	F	261000208	46.5	19.4	4.41	4.02	90.4
	M	261000299	49.7	17.0	2.22	4.17	60.8
	F	263000215	46.5	19.4	2.74	0.616	13.6
	F	263000350	47.5	20.3	2.27	2.67	21.9
	F	264000392	49.5	18.4	3.68	1.04	14.5

Source Data: Listings 6.4, 8.23, 8.24

Cohort 1: 800mg Q12W x 3 doses

Cohort 2: 600mg Q8W (Injections 2 administered 4 weeks following injection 1, Injections 3-5 administered 8 week following prior injections).

1.7.3 Results from HPTN 083

On 14 May 2020, the international DSMB met to review safety and efficacy data for the HPTN 083 and 084 study trials. In HPTN 083, a study among cisgender men and transgender women who have sex with men, they reviewed 50 overall HIV infections for an overall HIV incidence of 0.79%. Of those infections, 38 occurred in the TDF/FTC arm compared to 12 in the CAB LA arm. Based on this data, the DSMB agreed that CAB LA had crossed the prespecified non-inferiority margin and was highly effective in preventing HIV infections. The DSMB recommended unblinding of all study participants and providing them their choice of study product in HPTN 083. In addition, the DSMB reported no safety concerns for either the HPTN 083 or 084 trials.

On 7 July 2020, at the 23rd International AIDS Conference (AIDS 2020: Virtual), the HPTN 083 study team announced that the HPTN 083 clinical trial showed that CAB LA, injected once every 8 weeks, was superior to daily oral tenofovir/emtricitabine (TDF/FTC) for HIV prevention amongst the HPTN 083 study population. A total of 52 HIV infections occurred during follow-up, with 13 infections in the CAB arm (incidence rate 0.41%) and 39 infections in the TDF/FTC arm (incidence rate 1.22%). The hazard ratio in the CAB versus TDF/FTC arms was 0.34 (95% CI 0.18-0.62), corresponding to a 66% reduction in incident HIV infections in study participants given CAB compared to TDF/FTC. These

results meet the statistical criteria for superiority of the regimen containing CAB compared to TDF/FTC in the HPTN 083 study population.

Revision 4: Removed language referring to broadening sexual risk profile in the future, if results show CAB LA is effective at preventing HIV, since this is now the case.

2.3 Study Design and Overview

We propose a single arm, open label, safety, tolerability, and acceptability study (n= approximately 50) in sexually-active, healthy adolescents assigned male sex at birth. ~~We have chosen to enroll an adolescent population that is sexually active, yet not at the highest risk for HIV exposure due to several reasons. First, this is the first protocol to study a new prevention product (CAB LA) among adolescent minors—and the primary outcome of interest is safety. Safety studies within a new population with an unproven product typically enroll “healthy” volunteers. The adult safety study for CAB LA was HPTN 077, which enrolled lower risk adults in a manner similar to the approach adopted for these sub-studies. Second, adolescents are considered a vulnerable population and the efficacy of CAB LA has yet to be proven. Thus, a young person at very high risk would potentially benefit more from oral Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®), which is highly efficacious and approved for use by adolescents to prevent HIV infection. Finally, adolescent sexual activity is highly variable, and we will likely see individual variation in sexual risk over the course of the study visits. Should promising efficacy data from adult populations become available during the implementation of this study, the protocol team will consult with the DSMB to consider broadening the sexual risk criteria to enroll high-risk adolescents.~~

Study participation includes, Step 1: a 5-week oral CAB 30mg QD safety lead-in followed by a series of 5 intramuscular (IM) injections of 3 mL (600 mg), administered at 8-week intervals after a 4-week loading dose (injections at weeks 5, 9, 17, 25 & 33) in Step 2. Adherence support strategies (e.g., counseling, reminders, pill cases) will be included to support pill-taking during the first five weeks and to support retention during the injectable phase. A safety visit will follow each injection to ascertain pharmacokinetic-peak safety data, including injection site reactions. Step 3: a blood draw visit, the +8 Week Visit, will follow the last injection to monitor CAB drug levels. All participants who have received at least one injection will be followed for 48 weeks after their last injection. Waning levels of cabotegravir (the PK tail) will be covered with locally sourced oral Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) for daily use for 48 weeks. **Participants may be offered the opportunity to join an open label CAB study instead, if such a study is being implemented in their area at the time.** Behavioral and acceptability data will be collected via computer-assisted self-interview (CASI).

Revision 5: Changed weight criterion from ≥ 50 kg (110 lbs) to ≥ 35 kg (77 lbs) and now allowing participants already on PrEP to join the study

3.1 Inclusion Criteria

Male adolescents who meet the following criteria are eligible for inclusion in this study:

- 3.1.1 Assigned male at birth (includes MSM, TGW, and gender non-conforming people)
- 3.1.2 At enrollment, aged below 18 years*
- 3.1.3 At enrollment, body weight ≥ 50 **35** kg (~~± 10~~ **77** lbs.)*

3.1.8 If currently on PrEP from a non-study source, willing to stop said PrEP prior to enrollment and agree to switch to oral CAB for the lead-in period and CAB LA injections.

Revision 6: Section 3.2, Exclusion Criteria, is updated now include those participants who may have been receiving PrEP from a non-study source and to broaden the sexual risk profile for participants, due to the superiority results from HPTN 083.

3.2 Exclusion Criteria

Male adolescents with any of the following criteria will be excluded from the study:

~~3.2.2 Currently receiving PrEP from a non-study source;~~

3.2.3 Past or current participation in HIV vaccine trial with exception for participants who can provide documentation of receipt of placebo;

3.2.4 Exclusively had sex with biological females in lifetime;

3.2.5 In the last 6 months (at the time of screening):

- ~~• self-reported unprotected anal intercourse with someone known to be HIV-infected;~~
- ~~• self-reported illicit injection drug use of any kind or stimulant use (including inhaled nitrate, cocaine in any form, methamphetamine, or non-physician-prescribed pharmaceutical-grade stimulants);~~
- active or planned use of any substance use which would, in the opinion of the site investigator, would hinder study participation (including herbal remedies), as described in the IB or listed in the SSP, and/ or Protocol Section 4.4,
- ~~• self-report of greater than 5 different sexual partners (anal or vaginal), regardless of use of protection or knowledge of HIV status;~~

Revision 7: Addition to Section 4.1, Step 3 – Follow-up Phase,-1st Paragraph, Last Sentence:

Step 3 – Follow-up Phase

All participants who have received at least one injection will be followed for 48 weeks after their last injection, beginning with a blood draw visit, +8 Week Visit, that will follow eight weeks after the last injection to monitor CAB drug levels. Waning levels of cabotegravir (the PK tail) will be covered with locally sourced oral Tenofovir/Emtricitabine (TRADE NAME: TDF/FTC, TRUVADA®) for daily use for 48 weeks. **Participants may also be provided the opportunity to enroll in a local open label study of CAB, if available.****Revision 7 (continued):** Addition to Section 5.7, Step 3, Follow-up Phase, 1st Paragraph, 2nd Sentence:

Step 3, Follow-up Phase

Follow-up Phase

All participants will be followed quarterly for 48 weeks following their last injection and provided with Tenofovir/Emtricitabine [TRADE NAME: TDF/FTC, TRUVADA®)]. Participants may also **join a be-offered enrollment into local open label CAB studies, if available.**

Revision 8: Clarification in Section 5.2, Enrollment.

5.2 Enrollment

Baseline/Enrollment/Week 0 Visit

Both clinical and laboratory evaluations will occur at this visit, along with behavioral and acceptability assessments, **including administration of the Patient Health Questionnaire-9 (PHQ-9)**. (See Appendix I Schedule of Evaluations for Oral Phase – Step 1 for details).

All behavioral assessment measures will be programmed into CASI, **with the exception of the PHQ-9, which is an eCRF administered only at Enrollment**. Measures have been previously used either in adolescent biomedical prevention trials or in the Phase III adult trials of cabotegravir (HPTN 083/084).

Revision 9: Edits to Section 5.8 to reflect superiority findings from HPTN 083.

5.8.1 HIV and Risk Reduction Counseling

HIV testing and risk reduction counseling will be provided at each study visit, in accordance with local SOC, and will include messaging about consistent condom use ~~and the current lack of efficacy data for CAB-LA~~. Condoms will be offered to all participants at each study visit consistent with local standards and **oral PrEP referrals made as warranteddesired**.

Increase in Risk for HIV Infection

~~At any time during study participation, any participant whose risk for HIV increases such that they qualify for PrEP by local guidelines will permanently discontinue study product and receive ongoing risk reduction counselling. Step 1 participants will be switched to open label Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®)/FTC PrEP and not transition to Step 2. They will be referred for further HIV prevention services and exit the study. Step 2 participants will switch to open label Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®)/FTC PrEP and remain in follow up in Step 3. All cases should be communicated to the HPTN 083-01 CMC at 083-01eme@hptn.org.~~

5.8.2 Adherence Counseling and Monitoring

The study will provide adherence support/counseling at baseline and at all follow-up visits for all participants and will be tailored to participants' current study Step. During Step 1, participants will receive counseling focused on adherence to the oral CAB and messages about ~~insuring~~**ensuring** adequate dosing for safety prior to proceeding to Step 2. During Step 2, the importance of returning for injection visits on or as close to the scheduled date as practical will be emphasized. During Step 3, the focus will be on adherence to oral Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®)~~/FTC PrEP~~. ~~Throughout the study, participants will be reminded that efficacy of CAB-LA for HIV prevention has yet to be established.~~

Revision 10: Change to target visit windows for injections in Section 5.9.

5.9 Injection Visit Windows

The visit windows for all visits, including injection visits, are outlined in the SSP Manual. Refer to SSP for instruction on managing participants who report to clinic outside of injection window.

The target visit windows for all visits, including injection visits, are outlined in the SSP Manual. In brief, the target visit window for **all** injection visits ~~for the Week 5 and 9 injections~~ is +/- 3 days ~~and is +/- 7 days for all other injection visits.~~ Visits conducted outside of the target visit windows are allowable without restriction and are also defined in the SSP Manual for scheduling guidance. Each study visit, including the injection visit, should ideally be conducted within the target date range. When that is not possible, visits outside of the target dates may be completed.

Revision 11: Updates to Section 5.16, Early Termination.

5.16 Criteria for Early Termination of Study Participation

Participants may voluntarily withdraw from the study for any reason at any time (or their parents/guardians may, if they are under the legal age of consent). **In general, for participants who withdraw consent from the study prematurely during a study visit, the requirements for that visit should be completed to the extent possible except for provision of study product and will be considered their final visit. When possible, a plan should be made to provide final laboratory results to the participant. For participants who inform the site in between visits that they wish to withdraw consent from the study, sites should make every effort to have the participant return any unused study product.** Study staff will record the reason(s) for all withdrawals in participants' study records: **and consult procedures for early discontinuation.**

Site IoRs may, with the agreement of the CMC, Protocol Chairs, DAIDS MO, and study statistician, withdraw participants before their scheduled termination visit to protect their safety, the safety of the staff, and/or if participants are unable or unwilling to comply with study procedures. Participants also may be withdrawn if the study sponsors, government or regulatory authorities (including the OHRP and US FDA), or site IRBs/ECs or ViiV terminate the study prior to its planned end date.

Revision 12: Removal of description of SMC from Clinical Data Review section.

6.4 Clinical Data Review

A multi-tiered safety review process will be followed for the duration of this study. The study site investigators are responsible for the initial evaluation and reporting of safety information at the participant level, and for alerting the CMC if unexpected concerns arise.

Participant safety data is also monitored by the SDMC Clinical Affairs staff who review incoming safety data for completeness and consistency on an ongoing basis. Events identified as questionable, inconsistent, or unexplained will be queried for verification.

AE reports submitted in an expedited manner to the DAIDS Safety Office will be forwarded to the DAIDS Medical Officer for review and possible reporting to the FDA as a Safety Report.

~~The SDMC will prepare routine reports of study conduct for the Safety Study Monitoring Committee (SMC), which will meet by conference call approximately every 6 months and will review accrual and retention data, as well as other aspects of study conduct. More frequent or ad hoc reviews of safety data may be conducted by the SMC as needed.~~

This study ~~also~~ 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 13: Update to Statistical Considerations Section.

7.0 STATISTICAL CONSIDERATIONS

7.1 Review of Study Design

This is a single arm, open label, safety, tolerability, and acceptability study of CAB LA for prevention of HIV-acquisition in sexually-active, HIV-uninfected adolescents (below aged 18 years old at time of enrollment).

The study includes a 5-week oral CAB 30mg QD safety lead-in followed by a series of 5 intramuscular (IM) injections of 3 mL (600 mg) CAB LA administered at 8-week intervals after a 4-week loading dose (injections at weeks 5, 9, 17, 25 & 33). Follow up on study product (oral and injectable) will occur for 34 weeks. All participants who have received at least one injection will be followed for 48 weeks after their last injection. Waning levels of cabotegravir (the PK tail) will be covered with locally sourced oral Tenofovir/Emtricitabine ~~TENOFOVIR/EMTRICITABINE~~ (TRADE NAME: TDF/FTC, TRUVADA®) for daily use **or participation in an open-label CAB study (if available)** for 48 weeks.

7.2 Endpoints

7.2.2 Secondary Endpoints

- Plasma CAB pharmacokinetics
- Proportion of participants experiencing Grade 2 or higher clinical AEs and laboratory abnormalities in the **oral phase 48 weeks following final injection and the aggregate over the entire study period**
- Proportion of injection visits that occurred “on-time”
- Change from enrollment of self-reported sexual behavior (number of sexual partners, increased episodes of unprotected vaginal or anal intercourse) during the study period

7.7 Primary Analyses

All participants who receive at least one injection will contribute to the primary analyses. ~~The safety and tolerability will be analyzed in aggregate.~~ When the use of descriptive statistics to assess group characteristics or differences is required, the following methods will be used: for categorical variables, the number and percent in each category; for continuous variables, the mean, median, standard deviation, quartiles and range (minimum, maximum).

7.7.1 Safety Endpoints

The primary safety analysis will include Grade 2 or higher clinical and laboratory events that occur from the initial injection to 48 weeks after the last injection among participants who receive at least one injection. ~~Secondary safety analyses will include the same definition applied over the oral phase only (week 0 to week 4) and the aggregate oral + injectable + follow-up period.~~

To assess safety, the number and the percent of participants experiencing each safety endpoint will be tabulated. Each participant will contribute once in each category (for example, only for the highest severity AE for each participant) for the calculation of event rates. Exact binomial confidence intervals will be calculated for each safety endpoint.

7.7.2 Injection Site Reaction (ISR)

The number and percentage of participants experiencing each type of injection site reaction sign or symptom will be tabulated by severity. For a given sign or symptom, each participant's ISR will be counted once under the maximum severity for all injection visits as well as by each successive injection.

In addition, we will report the proportion of injections (over all participants) that resulted in an ISR. A 95% CI (using a robust variance) will be computed.

7.7.3 AEs and Serious Adverse Events (SAEs)

AEs will be tabulated using MedDRA preferred terms. The number and percentage of participants experiencing each specific AE (All AEs, Grade 2 or higher, and SAEs) will be tabulated by severity and by relationship to study product. For the calculations in these tables, each participant's AEs will be counted once as the maximum severity and relationship to study product. AEs leading to temporarily or permanently stopping drug will also be summarized. AEs will be summarized for those that are treatment emergent during LA dosing. ~~separately from those that are treatment emergent during oral dosing and also for those that are treatment emergent across the entire treatment phase of the study (combining both LA and oral dosing).~~

A listing of EAEs reported to the DAIDS RSC Safety Office will provide details of the events including severity, relationship to study product, time between onset and last injection, number of injections received, and a summary of the event.

7.7.5 Acceptability

To assess acceptability, the number and **percentage of participants who complete all scheduled injections will be described.** ~~To assess acceptability, the number and the percent of participants who receive at least one injection that would consider using CAB LA for HIV prevention in the future will be tabulated. Acceptability will be assessed by age and in aggregate.~~

7.7.6 Local Laboratory Values

The number (percentage) of participants with local laboratory values recorded as meeting Grade 2 AE criteria or above as specified in the DAIDS AE Grading Table will be tabulated ~~by treatment arm~~ for follow-up time points.

7.8 Secondary Analyses

7.8.1 Plasma Drug-Level Concentrations

Descriptive analyses of plasma concentration of CAB LA will be performed using mean, median, standard deviation, coefficient of variation (%CV) and range, for example. Graphical displays of

the data based on appropriate techniques (e.g., boxplots, histograms, kernel density estimates, probability plots, scatterplots) will be generated to visually explore distributional properties of the data. Statistics and graphical displays will be produced for plasma concentrations within and across timepoints. In addition, proportion of participants with plasma CAB concentrations <LLQ, between LLQ and PA-IC90, 1-4X PA-IC90, and >4X PA-IC90 will be calculated at pre-specified time points after the final injection.

In addition to concentration summaries, parameters may be derived by non-compartmental pharmacokinetic methods.

7.8.2 Safety Endpoints

Secondary safety analyses will ~~include~~ **be summarized using the same definition 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.

7.8.3 AEs and Serious Adverse Events (SAEs)

AEs and SAEs will be summarized using the same method described in section 7.7.3, applied over the oral phase only (week 0 to week 4) and the aggregate oral+injectable+follow-up period.

7.8.4 Injection adherence

The number and the percent of injection visits that occur within the injection visit window will be tabulated.

7.8.5 Sexual Risk Behaviors

Change in sexual risk behavior (number of sexual partners, episodes of unprotected anal and/or vaginal intercourse) during the injection phase will be measured by summarizing the change from baseline by visit. ~~Sexual risk behavior will be analyzed in aggregate.~~

~~7.6.107.8.5~~ Plasma Drug Level Concentrations

~~Descriptive analyses of plasma concentration of CAB LA will be performed using mean, median, standard deviation, coefficient of variation (%CV) and range, for example. Graphical displays of the data based on appropriate techniques (e.g., boxplots, histograms, kernel density estimates, probability plots, scatterplots) will be generated to visually explore distributional properties of the data. Statistics and graphical displays will be produced for plasma concentrations within and across timepoints. In addition, proportion of participants with plasma CAB concentrations <LLQ, between LLQ and PA-IC90, 1-4X PA-IC90, and >4X PA-IC90 will be calculated at pre-specified time points after the final injection.~~

~~In addition to concentration summaries, parameters may be derived by non-compartmental methods. Details of the analysis will be described in the study Reporting and Analysis Plan (RAP), separately.~~

Revision 14: Update to Section 8.1, Ethical Review.

8.1 Ethical Review

This protocol and the template informed consent form contained in [Appendix V](#) ~~—and any subsequent modifications—~~ will be reviewed and approved by the HPTN Scientific Review Committee (SRC) and DAIDS Prevention Science Review Committee (PSRC) with respect to scientific content and compliance with applicable research and human subjects regulations.

Revision 15: Update to Virology Section.

9.3 Virology

The HPTN LC will perform QA testing, including testing to determine HIV infection status in selected cases. Additional assays may be performed at the HPTN LC or a laboratory designated by the HPTN LC. This testing may include the following tests for participants who acquire HIV infection: HIV viral load, HIV resistance testing, HIV subtyping, and other tests to characterize HIV viruses and/or the host response to HIV infection. Results will not be returned to the sites or study participants, with the exception of HIV diagnostic testing (if results obtained at the HPTN LC do not agree with site results).

Resistance testing will be performed at the HPTN LC or a laboratory designated by the HPTN LC. This testing will be performed **periodically during** ~~retrospectively at the end of~~ the study. Results of this testing will not be returned to study sites. Because real-time resistance testing may be needed for clinical management in the event of HIV infection, each site will have an SOP as to how they will accomplish real-time local or regional resistance testing to assist with clinical decision making; separate specimens should be collected for that testing.

Revision 16: Updates to Section 10.4, Study Monitoring

Site investigators will allow study monitors to inspect study facilities and documentation (e.g., informed consent forms, clinic and laboratory records, other source documents, CRFs), as well as observe the performance of study procedures. Investigators also will allow inspection of all study-related documentation by authorized representatives of the HPTN LOC, HPTN SDMC, HPTN LC, NIAID and/or its contractors; **NICHD and/or its contractors (including Westat)**; site IRBs/ECs; other local, US, or international regulatory authorities (including the OHRP and US FDA); or, if appropriate, ViiV. A site visit log will be maintained at each study site to document all visits.

Revision 17: Section 10.6 is updated to provide additional guidance regarding retention of study records following completion of a study.

Investigator's Records

The IoR will maintain, and store in a secure manner, complete, accurate, and current study records throughout the study. In accordance with Federal regulations, for each of the investigational products tested, the IoR will retain all study records for at least two years following the date of marketing approval for the study product for the indication in which it was studied, or if other applicable laws, regulations, policies, or other requirements (e.g., State, country-specific, and local laws, and sponsor or institutional policies) exist, the most stringent retention period will be followed. **European Medicines Authority (EMA) requirements, which will apply to the parent protocol (HPTN 083), were the most demanding identified by DAIDS at the study-wide level. Based upon EMA requirements,**

sites should therefore plan to retain files (and any other study documentation) for more than 15 years from the end of data collection, or longer if required by local regulations.

If no marketing application is filed, or if the application is not approved, the records must be retained for two years after the US FDA is notified that the IND is discontinued, or if other applicable laws, regulations, policies, or other requirements (e.g., State, country-specific, and local laws, and sponsor or institutional policies) exist, the most stringent retention period will be followed.

Study records include administrative documentation — including protocol registration documents and all reports and correspondence relating to the study, as well as documentation related to each participant screened and/or enrolled in the study. This includes informed consent forms, locator forms, CRFs, notations of all contacts with the participant, and all other source documents.

Completion of a clinical research study occurs when the following activities have been completed:

- All research-related interventions or interactions with human subjects (e.g. when all subjects are off study);
- All protocol-required data collection of identifiable private information described in the IRB/EC-approved research plan;
- All analysis of identifiable private information described in the IRB/EC-approved research plan;
- Primary analysis of either identifiable private or de-identified information.

Revision 18: Changes to Appendix I.

12.1 APPENDIX I. SCHEDULE OF EVALUATIONS – ORAL PHASE (STEP 1)

WEEKS in Study (Shaded column = dispense oral product)	Screening	WEEK 0 Enrollment	WEEK 2	WEEK 4
ADMINISTRATIVE, BEHAVIORAL, REGULATORY				
Informed consent	X			
Locator information	X	X	X	X
Demographic information ¹	X	X		
HIV prevention counseling	X	X	X	X
Offer condoms	X	X	X	X
Patient Health Questionnaire-9 (PHQ-9)		X		
Behavioral/Acceptability Assessment (CASI)		X		X
CLINICAL EVALUATIONS & PROCEDURES				
Dispense study product (enough for 5 weeks)		X		
Observe participant take oral study product ²¹		X	X [†]	X [†]
Adherence counseling/pill count (pill count Weeks 2 and 4 only)		X	X	X
Medical history, con meds, targeted physical exam ³²	X	X	X	X
Hep B vaccination (if needed) ⁴³			X	
Blood collection	X	X	X	X
Urine collection	X	X		

WEEKS in Study (Shaded column = dispense oral product)	Screening	WEEK 0 Enrollment	WEEK 2	WEEK 4
Rectal swab collection	X			
LOCAL LABORATORY EVALUATIONS & PROCEDURES				
HIV testing ⁵⁴	X	X	X	X
HBV and HCV testing ⁶⁵	X	X		
CBC with differential	X	X	X	X
Chemistry testing ⁷⁶	X	X	X	X
Liver function tests ⁸⁷	X	X		X
Fasting lipid profile ⁹⁸		X		
Syphilis testing	X			
GC/CT testing (urine, rectal, and oral pharyngeal swabs)	X			
Urinalysis (protein and glucose; this test can be done at either the clinic or in the local laboratory)		X		
Plasma storage ¹⁰⁹	X	X	X	X

FOOTNOTES FOR APPENDIX I:

¹ **Demographics may be collected and reported at either Screening or Enrollment.**

² Staff are required to observe participants take one pill at Enrollment. If participants return with their pills at Weeks 2 & 4, staff will observe participant take one pill then as well, unless the participant has already taken oral study product that day. Participants must not be asked to take a second dose of oral study product for the sake of observation.

³² Full physical exam is to be conducted during Enrollment. A targeted physical exam will be done at all other visits. Participant pulse, blood pressure and weight must be recorded at every visit. BMI must be calculated.

⁴³ The initial dose of the Hep B vaccination will ideally be given at Week 2, though there is flexibility around the timing of the vaccination. Subsequent doses may be given at different visits than indicated in this SOE, as long as sites follow manufacturer guideline timing.

⁵⁴ The HIV testing algorithm is provided in the SSP Manual. Testing for acute HIV must be negative and must be performed within the 14 days prior to enrollment of the participant. 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.

⁶⁵ Participants will be tested for Hepatitis B surface antibody (HBsAb), and Hepatitis B core antibody (HBcAb, total) at Screening or Enrollment. HbsAg and HCV Ab must be resulted and reviewed prior to enrollment.

⁷⁶ At Screening: Creatinine. At and after enrollment: BUN/urea, creatinine, CPK, calcium, phosphorous, glucose, amylase, and lipase.

⁸⁷ At Screening: ALT and TBili. At and after Enrollment: AST, ALT, total bilirubin, and alkaline phosphatase.

⁹⁸ Total cholesterol, HDL, triglycerides, and LDL (either calculated or measured). Participants must have fasted for at least 8 hours, preferably 12 hours, prior to sample collection. Do not collect or test if <8 hours fasting.

¹⁰⁹ Stored plasma will be used for Quality Assurance testing and other assessments at the HPTN LC (see Section 9).

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.

Revision 19: Changes to Appendix II.

12.2 APPENDIX II. SCHEDULE OF EVALUATIONS – INJECTION PHASE (STEP 2)

WEEKS in Study (shaded column = injection visit)	Wk 5	Wk 6	Wk 9	Wk 10	Wk 17	Wk 18	Wk 25	Wk 26	Wk 33	Wk 34
LOCAL LABORATORY EVALUATIONS & PROCEDURES										

HIV testing ³	X		X		X		X		X	
CBC with differential	X	X	X	X	X	X	X	X	X	X
Chemistry testing ⁴	X	X	X	X	X	X	X	X	X	X
Liver function testing ⁵	X	X	X	X	X	X	X	X	X	X
Fasting lipid profile ⁶	X	X	X	X	X	X	X	X	X	X
Syphilis testing									X	
GC/CT testing (urine, rectal, and oral pharyngeal swabs)					X				X	
Urinalysis (protein, glucose; at the clinic or local lab)	X	X	X	X	X	X	X	X	X	X
Plasma storage ⁷	X	X	X	X	X	X	X	X	X	X

FOOTNOTES FOR APPENDIX II:

¹ Medical history must include pulse, blood pressure, weight and Body Mass Index (BMI) calculated at each visit

² The initial dose of the HBV vaccination is ideally given at Week 2, though there is flexibility around the timing of the vaccination. Subsequent doses may be given at different visits than indicated in this SOE, as long as sites follow manufacturer guideline timing.

³ 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.

⁴ BUN/urea, creatinine, CPK, calcium, phosphorous, glucose, amylase, and lipase.

⁵ AST, ALT, TBili, and alkaline phosphatase.

⁶ Total cholesterol, HDL, triglycerides, and LDL (either calculated or measured). Participants must have fasted for at least 8 hours, preferably 12 hours, prior to sample collection. Do not collect or test if <8 hours fasting. **For participants who switch to Step 3 early (without having completed all 5 injections), the fasting lipid profile will be taken at the first visit after they transition off injections.**

⁷ 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 the SSP Manual. Samples cannot be used by site or other lab for local purposes without specific instructions from the LC w/ CMC consult.

Revision 20: Changes to Appendix III.

12.3 APPENDIX III. SCHEDULE OF EVALUATIONS –FOLLOW-UP PHASE (STEP 3)

WEEKS SINCE LAST INJECTION	Wk +8	Wk +12	Wk +24	Wk +36	Wk +48	Early Discontinuation
LOCAL LABORATORY EVALUATIONS & PROCEDURES						
HIV testing ³		X	X	X	X	
CBC with differential		X	X	X	X	X
Chemistry testing ⁴		X	X	X	X	X
Liver function testing ⁵		X	X	X	X	X
Fasting lipid profile⁶		X				X
Syphilis testing				X		X
GC/CT testing (urine, rectal, and oral pharyngeal swabs)		X	X	X	X	
Urinalysis (protein, glucose; at the clinic or local lab)		X	X	X	X	X

Plasma storage ⁷	X	X	X	X	X	
DBS storage		X	X		X	

FOOTNOTES FOR APPENDIX III:

¹ Medical history must include pulse, blood pressure, weight and Body Mass Index (BMI) calculated at each visit

² The initial dose of the HBV vaccination is ideally given at Week 2, though there is flexibility around the timing of the vaccination. Subsequent doses may be given at different visits than indicated in this SOE, as long as sites follow manufacturer guideline timing.

³ 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.

⁴ BUN/urea, creatinine, CPK, calcium, phosphorous, glucose, amylase, and lipase.

⁵ AST, ALT, TBili, and alkaline phosphatase.

~~⁶ Total cholesterol, HDL, triglycerides, and LDL (either calculated or measured). Participants must have fasted for at least 8 hours, preferably 12 hours, prior to sample collection. Do not collect or test if <8 hours fasting.~~

⁷ 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.

Revision 21: Addition of seven ICFs, formerly approved by the HPTN’s sIRB (Advarra), and now with the addition of findings from HPTN 083 and the option to join an open label extension trial during Step 3, if available.

12.6 APPENDIX VI: INFORMED CONSENT FOR PARENTS/LEGAL GUARDIANS AND PARTICIPANTS WHO REACH THE AGE OF MAJORITY AND ASSENT FOR ADOLESCENT PARTICIPANTS AGES 14 – AGE OF MAJORITY

Sponsor / Study Title: Division of AIDS (DAIDS), United States (US) National Institute of Allergy and Infectious Diseases (NIAID), Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), US National Institutes of Health (NIH) / “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”

Protocol Number: HPTN 083-01

Principal Investigator: «PiFullName»
(Study Doctor)

Telephone: «IcfPhoneNumber»

Address: «PiLocations»

If you are a parent or legal guardian of a child participating on this study, throughout this document “you(r)” = “your child.”

Key Information:

The first two pages of this document include summary information about this study that will help you decide whether or not you should participate. More detailed information is provided after this summary section.

About this research

You are being asked to join a research study. Scientists do research to answer important questions which might help change or improve the way we do things in the future. This form explains the research study and your part in the study. Please read it carefully and take as much time as you need. Ask your study doctor or the study team to explain any words or information that you do not understand. You may take this description home and discuss it with your family or friends to help you decide.

Taking part in this research study is voluntary

You may choose not to take part in the study or may choose to leave the study at any time. Deciding not to participate, or deciding to leave the study later, will not result in any penalty or loss of benefits to which you are entitled and will not affect your relationship with the study site.

Important Information

This information gives you an overview of the research. More information about these topics may be found in the pages that follow.

1. Why is this research being done?

There is a new drug called cabotegravir (CAB) that can treat people who have human immunodeficiency virus (HIV) infection. CAB is also being tested to see if it can protect people from getting HIV and has been found to be effective at preventing HIV among adult men and transgender women. In this study, we want to know if it is safe and acceptable for adolescent boys who do not have HIV to take CAB. For more information, please see the *What is this Study About* section below.

2. What will happen to me during the study?

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 over 6 months**
- **Step 3: You will come to the clinic for study visits quarterly for up to one year.**

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

- ***Physical examinations* – We will examine you to check on your health by measuring height, weight, temperature and blood pressure.**
- ***Questions* – We will ask general questions about your age, living situation, medical health, and as well as beliefs about HIV, opinions about taking pills and getting injections, sexual behavior, and any alcohol or drug use.**
- ***Counselling* – We will discuss ways to protect you from getting HIV and offer condoms. We will discuss any challenges you have taking the CAB pill or attending study visits.**
- ***CAB pills or injection* – During Step 1, we will explain how to take the study pills, watch you take a study pill, and explain any side effects the pills may cause. In Step 2, the CAB injection will be given into your buttock.**
- ***Laboratory tests* – We will collect blood, urine, rectal swabs, and oral pharyngeal swabs to test for HIV, Hepatitis, liver and kidney health, cholesterol, and sexually transmitted infections (STIs).**
- ***HIV Prevention* – We will offer you Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) tablets as pre-exposure prophylaxis (PrEP) after you stop the CAB injections. You may, instead, have the opportunity to join an open label CAB study, if available.**

For more information on each procedure and when it happens, please see the *What Will I have to Do in the Study* section below.

3. How long will I participate in the study?

If you decide to join the study, participation will last about 1.5 years and include a maximum of 18 study visits at this clinic.

4. Will I benefit from the study?

It is possible that you may benefit from taking part in this study.. The study medication being used has been shown to prevent HIV infections among some adults. You will get information about your health and the results of the tests, as well as treatment for sexually transmitted infections. The counseling you get during this study may help you avoid HIV and other sexually transmitted infections. For more information, please see the *What are the Potential Benefits of Taking Part in the Study* section below.

5. Will taking part in the study expose me to risks?

Taking part in this research may expose you to risks. We may not know or understand all the risks at this time. Some people may experience side effects or discomfort, some of which may be serious. It is very important that you understand the risks in this research study before you decide whether you will participate. For details and a list of risks you should know about, please see the *What Are the Risks of Taking Part in the Study* section below.

6. Will I be paid to participate?

Payment for your time or travel is available if you decide that you will take part in this study. For more information, please see the *What Will I Get for Taking Part in this Study* section below.

7. Will it cost me anything to participate?

There is no cost to you for taking part in this study.

Please review the rest of this document for details about these topics and additional things you should know before making a decision about whether you will participate in this research.

INTRODUCTION

We invite you to take part in a research study about PrEP for Human Immunodeficiency Virus (HIV). PrEP is short for Pre-Exposure Prophylaxis. Pre-exposure means before being exposed to HIV. Prophylaxis is the way people prevent a disease from infecting them. With PrEP for HIV, medications are being developed to prevent people from getting infected if they are exposed to HIV.

This form gives information about what it means to join the study. Please read it and ask any questions that you may have. You can take as much time as you need to fully understand the study. We will ask questions to see if we have explained the study clearly. After you understand the study, if you decide that you will take part, we will ask you to sign and date this form. You will be offered a copy to keep. Because you are still a minor, we must have permission from a parent or guardian for you to take part. This process is called “informed consent.”

WHAT IS THIS STUDY ABOUT?

In this study, we want to know if it is safe and acceptable for adolescent men who do not have HIV to take an anti-HIV drug called cabotegravir (CAB). We would also like to look at the tolerability, or side effects, of CAB. CAB is a new drug that is still being studied. Other studies showed that

CAB can treat people who have HIV infection and it has recently been shown available way to prevent HIV infection from sex is to use condoms and/or take the PrEP pill called Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) every day. But some people have a hard time remembering to take a pill every day, so it is a good idea to have other HIV prevention options. With CAB, people would get injections every 8 weeks and would not have to remember to take a pill every day. It is important that we learn what happens when adolescents use CAB for HIV prevention and whether it is safe and acceptable.

A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

DO I HAVE TO JOIN THIS STUDY?

You do not have to be in this study. The study staff can tell you about other places where you can get the care you need even if you do not join the study. If you join the study today, you can still change your mind later and leave the study at any time for any reason without penalty. If you decide not to take part in this study, you can join another study at a later time if one is available and you qualify for it.

You can't join this study if you are taking part in another study of drugs, HIV vaccines, or medical devices. You must tell the study staff about any other studies you are taking part in or thinking of taking part in. *This is very important for your safety. [Some sites may have biometric fingerprint screening and, if so, sites should add information regarding that here.]*

HOW LONG WILL THE STUDY LAST?

If you decide to join the study, participation will last about 1.5 years and include about 18 study visits at this clinic. 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 over 6 months

Step 3: You will come to the clinic for study visits quarterly for up to one year

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

Screening (1 visit) – First, we will find out if you qualify to be in the study.

Step 1 (3 visits) – If you qualify and decide to join the study, you will swallow 1 CAB tablet every day for 5 weeks starting at the Entry, or Enrollment, Visit. Step 1 is done to make sure your body is tolerating the CAB well, so you should take the tablets every day. You will come back for a medical check-up at weeks 2 and 4. If Step 1 goes well for you, then you will move to Step 2.

Step 2 (10 visits) – If you qualify, you will get the first CAB injection at week 5, then again at weeks 9, 17, 25 and 33 (5 injection visits). You will come back to the study clinic for a brief check-up 1 week after each injection at weeks 6, 10, 18, 26 and 34 (5 safety visits).

Step 3 (5 visits) – After a blood draw 8 weeks after your last injection, you will come to the clinic quarterly (every 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 have the opportunity to join an open label CAB study (if available), 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.

You will be in the study for the about 1.5 years. Your parent/guardian does not need to come with you to the study visits. The study visits will take from 1 to 4 hours each [*sites to modify accordingly*]. It is important that you attend all of these study visits. If you do not come for a scheduled visit or if a test result comes back abnormal, study staff will contact you or visit you. We will ask for your address and contact information so that we will be able to get in touch with you. You should not join the study if it's not okay for study staff to contact you and visit you where you stay. If at any time you feel sick, you should let the study staff know right away and we may ask you to come back for a check-up.

Study Visit Procedures

Different procedures are done at different study visits. We will now explain each of the procedures and then show you which ones are done at which visits.

Physical examinations – We will examine you to check on your health by measuring height, weight, temperature and blood pressure. At each study visit, we will check on whether CAB may be causing side effects. We will also tell you what to do if you have side effects.

Questions – We will ask general questions about your age, living situation, medical health, and any medications or vitamins that you take. At some visits, you will also answer questions on a computer about your beliefs about HIV, opinions about taking pills and getting injections, sexual behavior, and any alcohol or drug use (we call these questions “CASI” for computer-assisted self-interview).

Counseling – We will discuss ways to protect you from getting HIV and offer condoms. We will discuss any challenges you have about taking the CAB pill or attending study visits.

CAB pills or injection – During Step 1, we will explain how to take the study pills, watch you take a study pill, and explain any side effects the pills may cause. In Step 2, the CAB injection will be given into your buttock.

Laboratory tests – We will collect blood and urine. Some of these tests are done right away and we will tell you the results when they are available. The HIV results will be available before you are given CAB each time. Other tests are stored and then done later in a batch. More details are shown in the table below this section. Some tests are done in laboratories in other states, so your samples may be shipped there for testing. The laboratory tests are done for the following reasons:

Blood – To check for infections (HIV, hepatitis B and C, Syphilis), your general health, the health of the liver and kidneys, the amount of cholesterol (a fatty substance in your blood) and the amount of the study drug that is in your blood. How much blood is taken depends on which tests are due at each visit and is between 1 and 4 teaspoons each time (5-20mL). Study staff will tell you more about fasting before the cholesterol test. The study staff may be required by law to report the result of the HIV and Hepatitis tests to the local health authority.

Urine – To test if there is sugar or protein in your urine and for sexually transmitted infections.

Hepatitis B vaccination – At Week 2 or soon thereafter, you will be given the hepatitis B vaccination if testing shows you are not already immune. Additional vaccination (boosters) will be given at approximately Weeks 6 and 33).

HIV Prevention –The amount of CAB remaining in the body disappears slowly after you stops the CAB injections – it can last in the body for about one year, so you must use other ways of preventing HIV if you are at risk of infection. For this reason, we will offer you Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) tablets as PrEP after you stop the CAB injections or offer you the opportunity to join an open label CAB study, if available. Before you leave the study, we will help you find a place where you can continue getting HIV prevention care [sites to add information here or elsewhere in the consent form].

Tables of Study Visit Procedures

Step 1 – to see if your body is tolerating the CAB well

	screening	entry	Week 2	Week 4
Receive CAB pills (5 weeks' worth)		√		
Pill count			√	√
Questions/CASI	√	√	√	√
Counselling	√	√	√	√
Physical exam	√	√	√	√
Blood	√	√	√	√
Urine	√	√		
Rectal and oral pharyngeal swabs	√			

Step 2 – to give you the CAB injections and check your health (grey columns mean injection weeks)

	Week 5	Week 6	Week 9	Week 10	Week 17	Week 18	Week 25	Week 26	Week 33	Week 34
Questions/CASI	√		√		√		√		√	
Counselling	√	√	√	√	√	√	√	√	√	√
Brief physical exam	√	√	√	√	√	√	√	√	√	√
Blood	√	√	√	√	√	√	√	√	√	√
Urine	√	√	√	√	√	√	√	√	√	√
Rectal and oral pharyngeal swabs					√				√	
CAB injection	√		√		√		√		√	
PrEP pills offered										√

Step 3 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		√	√	√	

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.

WHAT IF I BECOME INFECTED WITH HIV?

Being in this study will not cause HIV infection, but you could become infected with HIV through sex or other activities while in this study. If you get HIV infection, you will stop using CAB, but you should still come for the study visits to make sure that you are doing okay. The study staff will counsel you and refer you for HIV treatment and other available services, but the study will not pay for this treatment. We will share any test results that will help you get the treatment you need. Testing, which will take an additional 1-3 mL of blood, will be done to see if your HIV is resistant to any drugs that are used to treat HIV infection. This testing will help select the best drugs to treat your HIV infection.

Tables of Study Visit Procedures if you become infected with HIV during Step 2 or Step 3

If you become infected with HIV infection before your first injection, you will have the oral CAB stopped permanently and will be referred to local HIV-related care and exit from the study.

	HIV Confirmation Visit	+12 weeks	+24 weeks	+36 weeks	+48 weeks
Questions/CASI	√	√	√	√	√
Counselling	√				
Brief physical exam	√	√	√	√	√
Blood	√	√	√	√	√

WHAT OTHER TESTS WILL BE DONE?

After all the laboratory tests mentioned above for this study have been done, there may be some of your samples left over. We want to keep these in storage for future tests related to HIV and other infections, including testing for the drugs used in this study and other anti-HIV medications, or tests about your genes. There is a separate form with more information about this. We will not use DNA from your stored samples to study your whole genetic sequence (also called your "genome"). If you agree to this future research, identifiers might be removed from your identifiable private

information or identifiable biospecimens collected during this study. That information could then be used for future research studies or distributed to another investigator for future research studies without additional informed consent.

WHAT ARE THE RISKS OF TAKING PART IN THIS STUDY?

Taking part in this study may involve some risks and discomfort.

Risk from Blood Draws – The needle can cause pain, swelling, bruising, or bleeding from the needle site. Drawing blood can cause fainting or infection, but this is very rare.

Risk from Receiving CAB Injections – People who got CAB injections in other studies had pain, skin irritation, skin redness, bumps, swelling, itching, or bruising at the spot where they got the shot. Most reactions go away in a week or less but sometimes they can last a long time. The injection could be given too deeply or not deeply enough, missing the muscle and entering your skin, blood, or a nerve. Everything possible will be done to decrease this risk, including watching you for problems during the study. If we think that the injection was not given the right way, you might be asked to stay in the clinic up to 2 hours after the injection to watch how you are doing. Receiving injections can cause some people to feel lightheaded or feel like they might pass out, or 'faint'. This is called a 'vasovagal reaction' and it can occur with many medical procedures but usually resolves quickly.

Risk of CAB Side Effects – All drugs can cause side effects. Some side effects are minor; others can be severe. Some side effects are common; others are rare. Some people who take the study drug have some of the side effects. Other people have different side effects, or no side effects. The most common side effects for CAB are listed below. It is not known if CAB, other drugs or the participant's other health problems caused these side effects. There may be other side effects that we do not know about now. This may be especially true for adolescents, because this is the first study of CAB in adolescents.

Very Common Side Effects of CAB	Common Side Effects of CAB
<ul style="list-style-type: none"> • Nausea (feeling sick to the stomach) • Diarrhea or loose stools • Runny nose, sore throat/Upper respiratory tract infection • Headache • Fever • Lack of energy 	<ul style="list-style-type: none"> • Rash • Itching • Vomiting (being sick) • Stomach pain and discomfort • Problems sleeping • Abnormal dreams/nightmares • Feeling light headed • Depression • Passing gas or wind • Joint or muscle pain • Increase in the level of enzymes made in the muscles (creatine phosphokinase)

Some of the people who received CAB in other studies also had abnormal liver tests. In most people, this was explained by other things such as a new virus infection with Hepatitis. Very few people did not have another possible reason, so it is possible that a mild form of liver damage happened from taking CAB. In those people, the liver tests got better after stopping CAB, showing that any damage was temporary. Seizures have been seen (rarely) in people who had CAB. They are not thought to be caused by CAB, but the study staff will ask you about them. We have an information sheet about CAB and its side effects for you to keep.

Allergic Reaction Risks – As with taking any drug, there is a risk of allergic reaction. If you have a very serious allergic reaction, you may be at risk of death. Some symptoms of allergic reactions are:

- Rash
- Wheezing and difficulty breathing
- Dizziness and fainting
- Swelling around the mouth, throat or eyes
- A fast pulse
- Sweating

Please seek treatment immediately and tell the study doctor and study staff if you have any of these symptoms.

Risk of HIV Resistance to CAB – We do not know if using CAB for PrEP will mean that CAB will not work to treat the HIV if you get infected with HIV during the study or in the future (this is called drug resistance). Drug resistance usually occurs when the amount of a drug in the body is too low to kill the virus. You will have low levels of CAB in the body for about one year after the last injection, or if you don't get the injections when they are due. This is why it is very important that you use other methods to protect against HIV infection whenever you are at risk, like using condoms and Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) PrEP pills.

Risks potentially related to Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) for PrEP - Like all other drugs, you may have symptoms or side effects while taking PrEP. These symptoms or side effects may be due to participation in the study or due to illnesses that have no

relation to the study, like a cold or flu. You should tell the study staff at the study clinic about any symptoms that you feel while you are participating in the study. In past PrEP research studies, nausea and diarrhea were the most common side effects, and happened in about 10% or 1 in 10 people. Nausea and diarrhea mainly happened in the first month and then went away. A small number (less than 1% or 1 out of 100 people) in PrEP studies showed a small decrease in how their kidneys work, but this stopped when the people stopped taking the study drug. Other side effects were very rare and usually resolved when the study drug was stopped.

Risks of Asking Sensitive Questions – You may feel uncomfortable when we ask personal questions. You do not have to answer any question that you do not want to and you can stop answering the questions at any time.

Risk of Disclosure of Private Information – We will make every effort to keep your information private and confidential. It is possible that others may learn that you are part of this study and they may think that you are infected with HIV or are at high risk for HIV. Because of this you may feel stigma, stress or embarrassment. We will not share any information about you or your health with anyone, even your parent/guardian, without talking to you first, except when *[sites to insert relevant information about any legal obligations for disclosure, for example...your life is thought to be in danger]*.

Risks of Rectal Swabs – You may have mild discomfort when the swab is performed, particularly if you have hemorrhoids. In some cases, a very small amount of bleeding may occur. If you are already having pain in the rectal area, be sure to let the study staff know.

Risks of Oral Pharyngeal Swabs – There are no risks or complications associated with this collection procedure. The procedure may cause momentary gagging because the back of the throat is a sensitive area, but it shouldn't be painful.

Other Risks – There may be uncommon or previously unknown risks that might occur. You should report any problems to the study staff immediately.

WHAT ARE THE BENEFITS OF TAKING PART IN THIS STUDY?

You may get direct benefit from being in this study. CAB LA has been shown to prevent HIV infections among adult men and transgender women. You will get information about your health and the results of the tests, as well as treatment for sexually transmitted infections. The counseling you get during this study may help you avoid HIV and other sexually transmitted infections. You or others in your community may benefit from this study later. The information gathered during this study may help to prevent the spread of HIV. This may be beneficial to you and your community.

ARE THERE ANY COSTS TO ME FOR TAKING PART IN THIS STUDY?

You will pay no money to be in the study. The study drug CAB will be provided and study procedures will be performed at no additional cost to you and/or your insurance company.

WHAT OTHER CHOICES DO I HAVE?

It is possible that Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) PrEP is available in your local area for HIV prevention. If you prefer to take PrEP instead of joining the study, ask the study staff to refer you for HIV prevention medical services.

[Sites to include/amend the following if applicable: There may be other studies going on here or in the community that you may be eligible for. If you wish, we will tell you about other studies that we know about. There also may be other places where you can go for HIV counseling and testing. We will tell you about those places if you wish.]

WILL I BE TOLD IF THERE IS NEW INFORMATION?

You will be told about any new information learned during the course of the study that might cause you to change your mind about being in the study. At the end of the study, you will be told when study results may be available and how we will let you know about the results.

COMMERCIAL PROFIT

Your biospecimens collected during this study will not be used for commercial profit.

CLINICALLY RELEVANT RESULTS

Research results that are clinically relevant, including individual research results, will be disclosed to you under these conditions:

- **HIV diagnostic testing results**
- **Any results that affect the treatment of HIV**

ARE THERE ANY REASONS WHY I MAY BE ASKED TO STOP TAKING PART IN THIS STUDY?

You may be withdrawn from the study if any of the following occur:

- Your parent/guardian decides that they do not want you to participate anymore (if still under the legal age of consent).**
- You are unable or unwilling to attend clinic visits and/or follow all of the study procedures or instructions.**
- You could be harmed by continuing to take the pills or getting an injection.**
- The study is stopped or canceled.**
- The study doctor feels that staying in the study would be harmful to you.**
- Other reasons, as decided by the study staff.**

WHAT WILL I GET FOR TAKING PART IN THIS STUDY?

«Compensation»

You will be paid up to a total of \$xx.xx if you complete this study. You will be paid for the visits you complete according to the following schedule:

- **\$xx.xx for Visits xxx.**
- **\$xx.xx for Visits xxx.**
- **\$xx.xx for Visits xxx.**

If you do not complete the study, for any reason, you will be paid for each study visit you do complete.

You will be paid _____ [*“after each visit,” “annually,” “bi-weekly,” etc.*]

If you have any questions regarding your compensation for participation, please contact the study staff.

HOW WILL MY PRIVACY BE PROTECTED?

To keep your information private, your samples will be labeled with a code that can only be traced back to the study clinic. Your name, where you live, and other personal information will be protected by the study clinic. The results of any tests done will not be included in your health records without your permission. Every effort will be made to keep your personal information confidential, but we cannot guarantee absolute confidentiality. Your records may be reviewed, under guidelines of the United States Federal Privacy Act, by the United States Food and Drug Administration (FDA); the sponsor of the study (United States National Institutes of Health [NIH]), other US, local and international regulatory entities may also review your study records, as well as the Advarra Institutional Review Board (IRB), Ethics Committees (EC), study staff, study monitors, the company that makes CAB, and other local authorities. Groups that oversee the study include:

Advarra IRB

[insert name of other site regulatory entities]

Representatives of the HPTN

The United States National Institutes of Health and its study monitors

The United States Food and Drug Administration

The United States Office for Human Research Protections

Other U.S., local, and international regulatory entities

ViiV Healthcare (the company that makes CAB)

The study staff and these groups are required to keep study records private and confidential. The results of the study may be presented publicly or published. However, no presentation or publication will use your name or identify you personally. Your study information may be given to other authorities if required by law, including diagnoses of sexually transmitted infections. For example, we are required to follow state laws and report any risk of harm to you or others. This would include sexual activity with an adult while you are a minor.

In addition to the efforts made by the study staff to help keep your personal information confidential, we have obtained a Certificate of Confidentiality from the U.S. Federal Government. This Certificate protects researchers from being forced to tell people who are not connected with this study about your participation. The Certificate of Confidentiality does not prevent you from releasing information about yourself and your participation in the study. The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). Even with the Certificate of Confidentiality, if the study staff learns of possible child abuse and/or neglect or a risk of harm to you or others, we will tell the proper authorities.

WHAT HAPPENS IF I AM INJURED DURING THE STUDY?

Your health is important to us. We will make every effort to protect your well-being and minimize risks. It is possible, however, that you could have an illness or injury that is study-related. This means that the illness or injury occurred as a direct result of the study procedures or the study drug.

If a study-related illness or injury occurs, we will treat you or tell you where you can get treatment. The cost for this treatment may be charged to you or your insurance company. There is no program for compensation either through the study site or the U.S. National Institutes of Health.

By signing and dating this document, you will not lose any of your legal rights or release anyone involved in the research from responsibility for mistakes.

WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the study doctor at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, and/or concerns or complaints regarding this research study, contact:

- **By mail:**
Study Subject Adviser
Advarra IRB
6940 Columbia Gateway Drive, Suite 110
Columbia, MD 21046
- **or call toll free: 877-992-4724**
- **or by email: adviser@advarra.com**

Please reference the following number when contacting the Study Subject Adviser: Pro00040790.

SCREENING AND ENROLLMENT CONSENT

Your signature and date on this form means that:

- **You understand the information given to you in this form,**
- **You accept the provisions in the form, on behalf of your child, and**
- **You agree to permit your child to join the study**

You will not give up any of you or your child’s legal rights by signing and dating this consent form.

CONSENT FOR MINOR TO TAKE PART IN THIS STUDY

In consideration of all of the above, I give my consent for my child to participate in this research study. I will be given a copy of this document to keep for my records. I agree to let my child take part in this study.

Name of Participant (print)

PARENT/GUARDIAN INFORMED CONSENT

Relationship to participant

Name (print)

Signature and Date

ASSENT TO TAKE PART IN THIS STUDY FOR ADOLESCENT PARTICIPANTS AGES 14 YEARS – AGE OF MAJORITY

I have read this form. I know that this is a research study. I have been told about the risks and potential benefits of taking part in the study. I have asked all the questions I have about the study and have gotten answers to my questions. I know that I am free to quit the study at any time without any penalties or loss of benefits. I will tell the study doctor, the study staff or my parent(s)/guardian(s), if I choose to stop the study so that I can stop in the best way to not harm my health. I will be given a signed and dated copy of this form to keep.

I agree to take part in this research study.

Participant’s Name (print)

Signature and Date

CONSENT TO TAKE PART IN THIS STUDY FOR ADOLESCENT PARTICIPANTS WHO HAVE REACHED THE AGE OF MAJORITY

I have read this form. I know that this is a research study. I have been told about the risks and potential benefits of taking part in the study. I have asked all the questions I have about the study and have gotten answers to my questions. I know that I am free to quit the study at any time without any penalties or loss of benefits. I will tell the study doctor or the study staff if I choose to

stop the study so that I can stop in the best way to not harm my health. I will be given a signed and dated copy of this form to keep.

I agree to take part in this research study.

Participant's Name (print)

Signature and Date

**Study Staff Conducting
Consent Discussion (print)**

Study Staff Signature and Date

12.7 APPENDIX VII: INFORMATION SHEET AND ASSENT FOR ADOLESCENT PARTICIPANTS AGES 10-13

Sponsor / Study Title: Division of AIDS (DAIDS), United States (US) National Institute of Allergy and Infectious Diseases (NIAID), Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), US National Institutes of Health (NIH) / “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”

Protocol Number: HPTN 083-01

Principal Investigator: «PiFullName»
(Study Doctor)

Telephone: «IcfPhoneNumber»

Address: «PiLocations»

About this research

We are scientists doing a research study that we’d like you to join. This form explains what the study is about and what will happen if you decide to join. Please read it carefully. You can take as much time as you need to decide. Take the form home if you like. Ask the study team to explain any words or information that you do not understand. We will ask questions to see if we have explained the study clearly. After you understand the study, if you decide that you will take part, we will ask you to sign and date this form. You will be offered a copy to keep.

Because you are still a minor, we must have permission from a parent or guardian for you to take part. This process is called “informed consent.” You don’t have to join the study, even if your parent or guardian says you should. You can also quit the study at any time, and it won’t change how you are treated here at the clinic.

This study is about PrEP for HIV (Human Immunodeficiency Virus).

- PrEP is short for Pre-Exposure Prophylaxis.
- Pre-exposure means before being exposed to HIV.
- Prophylaxis is the way people prevent a disease from infecting them.
- With PrEP for HIV, medications are being developed to prevent people from getting HIV if they are exposed to it.
- The usual PrEP medication is a pill called Truvada® that works well if taken every day.
- Some people have a hard time remembering to take a pill every day, so it is a good idea to have choices.

We're testing a new drug called cabotegravir (CAB) to see if it can be used as PrEP to protect people from getting HIV.

- CAB comes in the form of a pill and also as an injection (or 'shot') that's given every 8 weeks.
- In this study, about 50 men under 18 who do not have HIV will take CAB. We want to know:
 - Is it safe for adolescents to take CAB pills and CAB injections?
 - Is it acceptable and tolerable for adolescents to use CAB for HIV prevention?
 - Are adolescents able to make it to the clinic for injection appointments?
 - What do parents/guardians think about their sons using CAB for HIV prevention?
- You can't join this study if you are taking part in another study of drugs, HIV vaccines, or medical devices. You must tell the study staff about any other studies you are taking part in or thinking of taking part in. *This is very important for your safety.*

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 3 months for up to one year. You will take the Truvada® PrEP pill every day while your body clears out the CAB or be offered an opportunity to join another CAB study.

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

- *Physical examinations* – We will examine you to check on your health by measuring height, weight, temperature and blood pressure.
- *Questions* – We will ask general questions about your age, living situation, medical health, and as well as beliefs about HIV, opinions about taking pills and getting injections, sexual behavior, and any alcohol or drug use.
- *Counselling* – We will discuss ways to protect you from getting HIV and offer condoms. We will discuss any challenges you have taking the CAB pill or attending study visits.
- *CAB pills or injection* – During Step 1, we will explain how to take the study pills, watch you take a study pill, and explain any side effects the pills may cause. In Step 2, the CAB injection will be given into your butt using a needle and syringe – this will probably be painful, just like any other shot.
- *Laboratory tests* – We will collect blood, urine, rectal swabs, and oral pharyngeal (throat) swabs to test for HIV, Hepatitis, liver and kidney health, cholesterol, and sexually transmitted infections (STIs). The needle stick can cause pain where it enters the skin and the swabs can be uncomfortable when they're collected. The study staff may be required by law to report the result of the HIV and Hepatitis tests to the local health authority.
- *HIV Prevention* – We will offer you Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) tablets as pre-exposure prophylaxis (PrEP) after you stop the CAB injections or you may be able to join another CAB study.

Your parent or guardian does not need to come with you to the study visits. The study visits will take from 1 to 4 hours each. It is important that you attend all of these study visits. If you do not

come for a scheduled visit or if a test result comes back abnormal, study staff will contact you or visit you. We will ask for your address and contact information so that we will be able to get in touch with you. You should not join the study if it's not okay for study staff to contact you and visit you where you stay. If at any time you feel sick, you should let the study staff know right away and we may ask you to come back for a check-up.

You may benefit from taking part in this study, but there is no guarantee that it will help you. Being in this study may expose you to risks.

- **We may not know all the risks of CAB.**
- **Some people may have bad effects or discomfort, some may be serious.**
- **The most common bad effects include nausea, diarrhea, headaches and flu-like symptoms. You should tell the study staff whenever you don't feel well.**
- **We'll discuss in more detail about these risks with your parent or guardian through the informed consent session before you decide whether you will join the study.**
- **You may feel uncomfortable when we ask personal questions. You do not have to answer any question that you do not want to and you can stop answering the questions at any time.**
- **If others find out that you are on this study, they may think you have HIV and you may feel bad.**

It doesn't cost you anything to be in the study. We will cover your transport costs to come to the study clinic.

«Compensation»

You will be given \$XX each time you complete a study visit.

If you get HIV while you are in this study, you will stop using CAB and will be referred to start HIV treatment. You should still come for the study visits to make sure that you are doing okay.

You might be able to get Truvada® PrEP in your local area for HIV prevention. If you prefer to take PrEP instead of joining the study, ask the study staff to refer you for HIV prevention medical services.

We won't tell anyone else that you are in the study.

- **We won't share anything we find out about you with anyone, even your parent or guardian, without talking to you first.**
- **We use a code number instead of your name on all the study forms.**

Have I explained the study clearly to you? Now you should ask the study staff any questions you have.

If you have more questions later, or have any problems or complaints about the study, please contact the study doctor. If you are seen at another clinic for anything, let them know that you're in this study and we can call them to share details.

ASSENT TO TAKE PART IN THIS STUDY FOR ADOLESCENT PARTICIPANTS AGES 10-13

I have read this form. I know that this is a research study. I have been told about the risks and potential benefits of taking part in the study. I have asked all the questions I have about the study and have gotten answers to my questions. I know that I am free to quit the study at any time without any penalties or loss of benefits. I will tell the study doctor, the study staff or my parent(s)/guardian(s) if I choose to stop the study so that I can stop in the best way to not harm my health. I will be given a signed and dated copy of this form to keep.

I agree to take part in this research study.

Participant's Name (print)

Signature and Date

**Study Staff Conducting
Assent Discussion (print)**

Study Staff Signature and Date

12.8 APPENDIX VIII: INFORMED CONSENT FOR ADOLESCENT INTERVIEW FOR PARENTS/LEGAL GUARDIANS AND PARTICIPANTS WHO REACH THE AGE OF MAJORITY AND ASSENT FOR ADOLESCENT PARTICIPANTS AGES 14 – AGE OF MAJORITY

Sponsor / Study Title: Division of AIDS (DAIDS), United States (US) National Institute of Allergy and Infectious Diseases (NIAID), Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), US National Institutes of Health (NIH) / “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”

Protocol Number: HPTN 083-01

Principal Investigator: «PiFullName»
(Study Doctor)

Telephone: «IcfPhoneNumber»

Address: «PiLocations»

If you are a parent or legal guardian of a child participating on this study, throughout this document “you(r)” = “your child.”

INTRODUCTION

You are being asked to take part in an interview as part of the research study listed above. Participating in this interview is voluntary. You may refuse to join, or you may withdraw your consent to be interviewed for any reason. Before you decide whether to take part in the interview, we would like to explain the purpose of the interview, the risks and benefits to you and what is expected of you.

This consent form gives information about taking part in the interview. We will help you to understand the form and answer your questions before you sign and date this form. Once you understand the details about taking part in the interview, and if you agree to take part, you will be asked to sign your name and date this form. You will be offered a copy of this form to keep. If you are a child, your parent/guardian must also give their permission.

Participation is voluntary

Before you learn about the interview, it is important that you know the following:

Your participation is voluntary. You do not have to take part in this interview if you do not want to. You may decide not to take part in the interview, or you may decide to leave the interview at any time without losing your regular medical care.

You are not required to participate in this interview in order to remain in the rest of the main study.

About the interview

The main study is being done to find out if it is safe and acceptable for adolescent men who do not have HIV to take an experimental HIV drug called cabotegravir (CAB) as PrEP to prevent HIV. The interview portion will ask young men what they like and do not like about getting CAB injections. We will also ask questions to find out what makes some young men more or less interested in starting PrEP. Finally, we will ask about difficulties you had getting CAB injections and things that made that easier.

Entering the interview

In order to understand better what makes it easier or harder for young men in this study to get CAB injections as directed, we will be doing interviews with up to 10 young men at participating sites. You have been selected to take part in one interview sometime after your last CAB injection.

What will happen during the interview

The interview will be led by a member of the research team that you do not work with during the study. It should take about 1 hour and your parent/guardian will not be there. *[To be modified to reflect site practices: The interview will take place in a location that the study staff have determined will provide you with privacy and confidentiality such as the clinic, or another appropriate place. The study team will talk with you about this so you know where to go for the interview].*

During the interview we will ask you questions about:

- **How and when you decided to join the study**
- **Whether you feel that you personally are at risk of HIV**
- **How you made daily pill-taking part of your routine in Step 1**
- **Where you kept your CAB pills**
- **Whether you talked to your family members, peers, or partner(s) about being in this study or getting CAB injections in Step 2**
- **If you had any bad effects from the CAB injections, and if this influenced your decision to keep getting the injections**
- **If you are taking daily Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) pills, how you feel about being on PrEP**
- **Other related topics**

If any of the questions make you upset, either you or the interviewer may stop the interview at any time. You will also be provided with contact and referral information if any of the questions raise issues that you would like to talk about later.

Benefits of taking part in the interview

There may be no benefit from being interviewed. You may not receive any other direct benefit from being in this part of the study; however, you or others in your community may benefit from this study later.

Risk of taking part in the interview

FINAL Summary of Changes for HPTN 083-01
From Version 1.0 to Version 2.0
23 August 2020

There is little risk from the interview. To minimize any discomfort and to protect your privacy, the interview will be conducted in a private area that will allow you to speak comfortably without being overheard. Although we hope that you will be comfortable answering all of the questions openly and honestly, please keep in mind that you may refuse to answer any of the questions, or stop the interview completely, at any time. The greatest risk may involve your privacy and confidentiality. The steps that the study team have taken to protect your privacy are described below.

Other information about the interview

Privacy – Every effort will be made to keep your personal information confidential. Your personal information (name, address, phone number) will be protected by the research clinic. Your name, or anything else that might identify you personally, will not be used in any publication of information about this study.

To help assure that we get the best understanding possible from your answers during the interview, the entire interview will be audio-recorded. After the interview is finished, the recording will be typed (called a transcript) by people who know how to do this. All identifying information will be removed from the transcript. Your name will not be included on the transcript. These recordings will be destroyed after all analysis is completed.

Your records may be reviewed by the following groups, involved with the study:

- **Advarra Institutional Review Board**
- **[insert name of other site regulatory entities]**
- **Representatives of the HPTN**
- **The United States National Institutes of Health and its study monitors**
- **The United States Food and Drug Administration**
- **The United States Office for Human Research Protections**
- **Other U.S., local, and international regulatory entities**
- **ViiV Healthcare (the company that makes CAB)**

If the study staff learns that you are at risk of harm, we will tell the proper authorities as we are required to do by the law. We are also required to follow state laws regarding reporting of sexual activity of minors with adults.

New Information – You will be told any new information learned during this study that might affect your willingness to stay in the study. You will also be told when the results of the study may be available, and how to learn about them.

Alternatives to participating

You can talk to the study staff at any time about your experiences in the study, without taking part in the interview.

There are no costs to you for being interviewed

There will be no cost to you for participating in the in-depth interview.

«Compensation»

FINAL Summary of Changes for HPTN 083-01
From Version 1.0 to Version 2.0
23 August 2020

You will receive \$XX for being interviewed. You will be paid _____ [“after each visit,” “annually,” “bi-weekly,” etc.]

If you have any questions regarding your compensation for participation, please contact the study staff.

Whom to contact

If you have questions about the interview, please contact the study staff listed on page 1 of this document.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, and/or concerns or complaints regarding this research study, contact:

- **By mail:**
Study Subject Adviser
Advarra IRB
6940 Columbia Gateway Drive, Suite 110
Columbia, MD 21046
- **or call toll free:** 877-992-4724
- **or by email:** adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00040790.

SIGNATURE PAGE

ADOLESCENT IN-DEPTH INTERVIEW INFORMED CONSENT FORM

If you decide to join this interview portion of the main study, sign and date below. Before deciding whether to be interviewed, make sure you have read this form, or had it read to you, and that all of your questions have been answered. You should feel that you understand the study, its risks and benefits, and what is expected of you if you decide to join. You can ask questions or request more information at any time. You do not give up any rights by signing and dating this form.

ADOLESCENT ASSENT FOR PARTICIPANTS AGES 14 – AGE OF MAJORITY

Write your initials and sign and date below.

_____ I agree to be interviewed for the study and to have the interview audiotaped.

Name of Participant (print)

Signature and Date

PARENT/GUARDIAN INFORMED CONSENT

Relationship to participant

Name (print)

Signature and Date

CONSENT FOR PARTICIPANTS WHO REACH THE AGE OF MAJORITY

Write your initials and sign and date below.

_____ I agree to be interviewed for the study and to have the interview audiotaped.

Name of Participant (print)

Signature and Date

Study Staff Conducting
Consent Discussion (print)

Study Staff Signature and Date

12.9 APPENDIX IX: INFORMATION SHEET AND ASSENT FOR ADOLESCENT INTERVIEWS FOR PARTICIPANTS AGES 10-13

Sponsor / Study Title: Division of AIDS (DAIDS), United States (US) National Institute of Allergy and Infectious Diseases (NIAID), Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), US National Institutes of Health (NIH) / “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”

Protocol Number: HPTN 083-01

Principal Investigator: «PiFullName»
(Study Doctor)

Telephone: «IcfPhoneNumber»

Address: «PiLocations»

About this form

You have decided to join the study named above, with permission from your parent or guardian. We also invite you to be interviewed for this study. This interview part will ask young men what they like and do not like about getting CAB injections. We will also ask questions to find out what makes some young men more or less interested in starting PrEP. Finally, we will ask about difficulties you had getting CAB injections and things that made that easier. Joining this interview part is voluntary.

- You can take as much time as you need to decide. Take the form home if you like.
- Ask the study team to explain any words or information that you do not understand. We will ask questions to see if we have explained it clearly.
- After you understand the interview part, we will ask you to sign and date this form.
- You will be offered a signed and dated copy to keep.
- It is your decision whether or not to be interviewed. You are free to say yes or no, and to change your mind at any time.
- If you say no, you can still be in the main study.

What will happen if you agree to be interviewed

One of the study staff that you do not work with during the study will interview you at **[Site to insert location]**. It will be for about 1 hour. Your parent or guardian will not be there. We will ask you questions about joining the main study and who you talked to about the study. We will also ask about your experiences with taking the study pills and having the injections. We will ask what you feel about your risk of getting HIV and such topics.

If any of the questions make you upset, either you or the interviewer may stop the interview at any time. You will also be provided with contact and referral information if any of the questions raise issues that you would like to talk about later.

Being interviewed won't benefit you in any way, but the information we get from the interviews may benefit your community later.

«Compensation»

You will be given \$XX for the cost of transport to the clinic for the interview.

Have I explained the interview part of this study clearly to you? Now you should ask the study staff any questions you have.

If you have more questions later, or have any problems or complaints about the study, please contact the study doctor. If you are seen at another clinic for anything, let them know that you're in this study and we can call them to share details.

ASSENT TO TAKE PART IN THIS STUDY FOR ADOLESCENT PARTICIPANTS AGES 10-13

I agree to be interviewed for the study and to have the interview audiotaped.

Participant's Name (print)

Signature and Date

Study Staff Conducting Assent Discussion (print)

Study Staff Signature and Date

12.10 APPENDIX X: INFORMED CONSENT PARENT/GUARDIAN INTERVIEW FOR PARENTS/LEGAL GUARDIANS

Sponsor / Study Title: Division of AIDS (DAIDS), United States (US) National Institute of Allergy and Infectious Diseases (NIAID), Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), US National Institutes of Health (NIH) / “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”

Protocol Number: HPTN 083-01

Principal Investigator: «PiFullName»
(Study Doctor)

Telephone: «IcfPhoneNumber»

Address: «PiLocations»

INTRODUCTION

You are being asked to take part in an interview for the research study listed above. Joining this interview is voluntary. You may refuse to join, or you may withdraw your consent to be interviewed for any reason. Before you decide whether to join the interview, we would like to explain the purpose of the interview, the risks and benefits to you and what is expected of you.

This consent form gives information about being in the interview. We will help you to understand the form and answer your questions before you sign and date this form. Once you understand the interview, and if you agree to take part, you will be asked to sign your name and date this form. You will be offered a copy of this form to keep.

Participation is voluntary

Before you learn about the interview, it is important that you know the following:

Your participation is voluntary. You do not have to take part in the interview if you do not want to. You may decide not to take part in the interview, or you may decide to leave the interview at any time without losing your regular medical care.

You are not required to participate in these interviews in order for your child to remain in the rest of the study.

About the interview

The main study is being done to find out if it is safe and acceptable for adolescent men who do not have HIV to take an experimental HIV drug called cabotegravir (CAB) as PrEP to prevent HIV. This interview will ask parents/guardians questions to find out what it is like to have a child getting CAB injections and things that made that easier. We will also ask young men what they like and do not like about getting CAB injections.

Entering the interview

We will be doing interviews with up to 10 parents/guardians at participating sites (total, across sites). You have been selected to take part in one interview sometime after your child's last CAB injection.

What will happen during the interview

The interview will be led by a member of the research team that you do not work with during the study. It should take about 1 hour and your child will not be there. *[To be modified to reflect site practices: The interview will take place in a location that the study staff have determined will provide you with privacy and confidentiality such as the clinic, or another appropriate place. The study team will talk with you about this so you know where to go for the interview].*

During the interview we will ask you questions about:

- How and when you decided to allow your child to join the study
- Whether you feel that they personally are at risk of HIV
- Whether you talked to your children about sexual activity or preventing HIV
- If your child had any bad effects from being in the study, and if this influenced your decision to keep coming for the study visits
- Other related topics

If any of the questions make you upset, either you or the interviewer may stop the interview at any time. You will also be provided with contact and referral information if any of the questions raise issues that you would like to talk about later.

Benefits of the interview

There may be no benefit from being interviewed. You may not receive any other direct benefit from being in this part of the study; however, you or others in your community may benefit from this study later.

Risk of the interview

There is little risk from the interview. To minimize any discomfort and to protect your privacy, the interview will be conducted in a private area that will allow you to speak comfortably without being overheard. Although we hope that you will be comfortable answering all of the questions openly and honestly, please keep in mind that you may refuse to answer any of the questions, or stop the interview completely, at any time. The greatest risk may involve your privacy and confidentiality. The steps that the study team have taken to protect your privacy are described below.

Other information about the interview

Privacy – Every effort will be made to keep your personal information confidential. Your personal information (name, address, phone number) will be protected by the research clinic. Your name, or anything else that might identify you personally, will not be used in any publication of information about this study.

To help assure that we get the best understanding possible from your answers during the interview, the entire interview **will be audio-recorded**. After the interview is finished, the recording will be typed (called a transcript) by people who know how to do this. All identifying information will be removed from the transcript. Your name will not be included on the transcript. These recordings will be destroyed after all analysis is completed.

Your records may be reviewed by the following groups, involved with the study:

- Advarra Institutional Review Board
- **[insert name of other site regulatory entities]**
- Representatives of the HPTN
- The United States National Institutes of Health and its study monitors
- The United States Food and Drug Administration
- The United States Office for Human Research Protections
- Other U.S., local, and international regulatory entities
- ViiV Healthcare (the company that makes CAB)

If the study staff learns that you are at risk of harm, we will tell the proper authorities as we are required to do by the law.

New Information – You will be told any new information learned during this study that might affect your willingness to stay in the study. You will also be told when the results of the study may be available, and how to learn about them.

Alternatives to participating

You can talk to the study staff at any time about your child’s experiences in the study, without taking part in the interview.

There are no costs to you for being interviewed

There will be no cost to you for participating in the in-depth interview.

«Compensation»

You will receive \$XX for being interviewed. You will be paid _____ [“after each visit,” “annually,” “bi-weekly,” etc.]

If you have any questions regarding your compensation for participation, please contact the study staff.

Whom to contact

If you have questions about the interview, please contact the study staff listed on page 1 of this document.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, and/or concerns or complaints regarding this research study, contact:

- **By mail:**
 Study Subject Adviser
 Advarra IRB
 6940 Columbia Gateway Drive, Suite 110
 Columbia, MD 21046
- **or call toll free: 877-992-4724**
- **or by email: adviser@advarra.com**

Please reference the following number when contacting the Study Subject Adviser: Pro00040790.

SIGNATURE PAGE

PARENT/GUARDIAN IN-DEPTH INTERVIEW INFORMED CONSENT FORM

If you decide to be interviewed, sign and date below. Before deciding whether to join this study, make sure you have read this form and that all of your questions have been answered. You should feel that you understand the study, its risks and benefits, and what is expected of you if you decide to join. You can ask questions or request more information at any time. You do not give up any rights by signing and dating this form.

Name of Parent/Guardian (print)

Signature and Date

**Study Staff Conducting
Consent Discussion (print)**

Study Staff Signature and Date

12.11 APPENDIX XI: INFORMED CONSENT FOR SPECIMEN STORAGE AND FUTURE USE FOR PARENTS/LEGAL GUARDIANS AND PARTICIPANTS WHO REACH THE AGE OF MAJORITY AND ASSENT FOR ADOLESCENT PARTICIPANTS AGES 14 – AGE OF MAJORITY

Sponsor / Study Title: Division of AIDS (DAIDS), United States (US) National Institute of Allergy and Infectious Diseases (NIAID), Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), US National Institutes of Health (NIH) / “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”

Protocol Number: HPTN 083-01

Principal Investigator: «PiFullName»
(Study Doctor)

Telephone: «IcfPhoneNumber»

Address: «PiLocations»

If you are a parent or legal guardian of a child participating on this study, throughout this document “you(r)” = “your child.”

INTRODUCTION

You have decided to join the study named above. As part of the study, you will have blood, urine, rectal swab, and oral pharyngeal swabs collected. After all the tests for this study have been done, there may be some samples left over. We call these left over samples. The study doctor would like to keep these left over samples and use them for other research in the future. This form gives information about use of left over samples. Please read it and ask any questions you may have. After we discuss the information with you, you will record your decisions on use of extra samples at the end of the form.

It is your decision whether or not to allow the left over samples to be used.

You are free to say yes or no, and to change your mind at any time. Your decision will not affect your participation in the study. If you say no, all left over samples will be destroyed.

If you agree, his left over samples will be kept in a repository.

A repository is a secure facility that is used to store samples. The HPTN repository is in the United States. If you agree to have left over samples stored, the samples will be kept in this repository. There is no limit on how long the samples will be kept.

Left over samples could be used for different types of research.

Left over samples may be used for research on HIV and other infections, including testing for the medicines used in this study and other anti-HIV medicines, the immune system, and other diseases. The research may be done in the United States or in other locations. If you agree, the leftover samples could also be used for research that looks at your genes. Genes are passed to children from their birth parents. They affect how people look and how their bodies work. Differences in people's genes can help explain why some people get a disease while others do not. Your samples would only be used to look at genes related to how the body responds to the study drugs and the immune system. These tests would not include whole genome sequencing (WGS).

Any research done with the leftover samples must be reviewed and approved by the HPTN. The research must also be approved by an ethics committee. The role of an ethics committee is to review the research plan and protect the rights and well-being of the people whose samples will be used.

The research done with left over samples is not expected to give any information relevant to your health. Therefore, the results will not be given to the study staff or to you. The results also will not be placed in your study records.

There is little risk to you.

When left over samples are used for research, they are labeled with a code number only. To protect your privacy, no names are used. However, information such as age, gender, HIV status, and other health information may be linked to the samples. There may be some risks from tests of your genes. If others found out the results of these tests, they could treat you badly or unfairly. However, this is almost impossible because the results will not be given to the study staff or to you and will not be in his study records.

Any identifiers will be removed from the identifiable private information or biospecimens and, after removal, the information or biospecimens can be used for future research studies or distributed to another investigator for future research studies without additional informed consent.

There may be no benefit to you or your child.

You will not get direct benefit from storage of the samples. You or others in your community may benefit from this study later. The information gathered during this study may help to prevent the spread of HIV. This may be beneficial to you and your community.

You will not be paid for use of your child's samples.

There is no cost to you for use of your leftover samples. The samples will not be sold, and you will not be paid for use of the samples. It is possible that research done with the samples could lead to a new discovery or a new product. If this happens, there is no plan to share any money with you.

Information from research using extra samples may be reviewed by groups that oversee the research.

These groups include:

- **Advarra Institutional Review Board**
- **[insert name of other site regulatory entities]**

- **Representatives of the HPTN**
- **The United States National Institutes of Health and its study monitors**
- **The United States Food and Drug Administration**
- **The United States Office for Human Research Protections**
- **Other U.S., local, and international regulatory entities**
- **ViiV Healthcare (the company that makes CAB)**

The people who do research with the leftover samples and the groups listed above are required to make efforts to keep information private and confidential.

The results of research done with the leftover samples may be presented publicly or published. However, no presentation or publication will use your name or identify you personally.

Whom to contact about this sub-study

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the study doctor at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, and/or concerns or complaints regarding this research study, contact:

- **By mail:**
Study Subject Adviser
Advarra IRB
6940 Columbia Gateway Drive, Suite 110
Columbia, MD 21046
- **or call toll free:** 877-992-4724
- **or by email:** adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00040790.

SPECIMEN STORAGE AND FUTURE USE INFORMED CONSENT

Before deciding about storage of laboratory specimens, make sure you have read this form and that all of your questions have been answered. You should feel that you understand your options and the possible risks and benefits before making your decision. You and your child do not give up any rights by signing and dating this form.

For your child's leftover samples, write your initials next to your choice (*choose only one*).

_____ **I allow my child's leftover samples to be used for research on HIV and other infections, including testing for the study drugs and other anti-HIV medicines, the immune system, and other diseases. I also allow my child's samples to be used for tests of his genes.**

_____ **I allow my child's leftover samples to be used for research on HIV and other infections, including testing for the study drugs and other anti-HIV medicines, the immune system, and other diseases. I do not allow my child's samples to be used for tests of his genes.**

_____ **I do not allow my child's leftover samples to be used for any research.**

Participant's Name (print)

PARENT/GUARDIAN INFORMED CONSENT

Relationship to participant

Name (print)

Signature and Date

ASSENT FOR ADOLESCENT PARTICIPANTS AGES 14 YEARS – AGE OF MAJORITY
I have read this form. I have asked all the questions I have about the study and have gotten answers to my questions. I will be given a signed and dated copy of this form to keep.

For your leftover samples, write your initials next to your choice (*choose only one*).

_____ **I allow my leftover samples to be used for research on HIV and other infections, including testing for the study drugs and other anti-HIV medicines, the immune system, and other diseases. I also allow my samples to be used for tests of my genes.**

_____ **I allow my leftover samples to be used for research on HIV and other infections, including testing for the study drugs and other anti-HIV medicines, the immune system, and other diseases. I do not allow my samples to be used for tests of my genes.**

_____ **I do not allow my leftover samples to be used for any research.**

Participant's Name (print)

Signature and Date

CONSENT FOR ADOLESCENT PARTICIPANTS WHO REACH THE AGE OF MAJORITY

I have read this form. I have asked all the questions I have about the study and have gotten answers to my questions. I will be given a signed and dated copy of this form to keep.

For your leftover samples, write your initials next to your choice (*choose only one*).

_____ **I allow my leftover samples to be used for research on HIV and other infections, including testing for the study drugs and other anti-HIV medicines, the immune system, and other diseases. I also allow my samples to be used for tests of my genes.**

_____ **I allow my leftover samples to be used for research on HIV and other infections, including testing for the study drugs and other anti-HIV medicines, the immune system, and other diseases. I do not allow my samples to be used for tests of my genes.**

_____ **I do not allow my leftover samples to be used for any research.**

Participant's Name (print)

Signature and Date

**Study Staff Conducting
Consent Discussion (print)**

Study Staff Signature and Date

12.12 APPENDIX XII: INFORMATION SHEET AND ASSENT FOR SPECIMEN STORAGE AND FUTURE USE FOR PARTICIPANTS AGES 10-13

Sponsor / Study Title: Division of AIDS (DAIDS), United States (US) National Institute of Allergy and Infectious Diseases (NIAID), Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), US National Institutes of Health (NIH) / “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”

Protocol Number: HPTN 083-01

Principal Investigator: «PiFullName»
(Study Doctor)

Telephone: «IcfPhoneNumber»

Address: «PiLocations»

About this form

You have decided to join the study named above, with permission from your parent or guardian. As part of the study, we will collect lab samples for the study tests. After all the tests for this study have been done, there may be some of the samples left over. We call these leftover samples. The study doctor would like to keep these leftover samples and use them for other research in the future, if you and your parent or guardian agree.

- You can take as much time as you need to decide. Take the form home if you like.
- Ask the study team to explain any words or information that you do not understand. We will ask questions to see if we have explained it clearly.
- After you understand specimen storage, we will ask you to enter your decision and then sign and date this form.
- You will be offered a signed and dated copy to keep.
- It is your decision whether or not to allow the leftover samples to be used. You are free to say yes or no, and to change your mind at any time.
- If you say no, you can still join the main study and all your leftover samples will be destroyed at the end.

What will happen if you agree to store your leftover samples

If you agree, your leftover samples will be kept in a secure storage lab called a repository in [Sites should insert the location]. There is no limit on how long the samples will be kept. Leftover samples could be used for different types of research, mostly related to HIV, testing for anti-HIV medicines, the immune system, and other diseases. If you agree, the leftover samples could also be used for research that looks at your genes.

This research may be done in the United States or other countries. Any research done with the leftover samples must be reviewed and approved by the HPTN and an ethics committee to protect your rights and well-being. We won't give you the results of any tests done on your leftover samples because they won't be relevant to your health. Leftover samples are labeled with a code number only, not your name. Only your age, gender, HIV status, and other health information may be linked to the samples.

Storing your samples won't benefit you in any way, but the information we get from these future studies may benefit your community later. The samples will not be sold, and you will not be paid for use of the samples.

Have I explained the specimen storage clearly to you? Now you should ask the study staff any questions you have.

If you have more questions later, or have any problems or complaints about the study, please contact the study doctor. If you are seen at another clinic for anything, let them know that you're in this study and we can call them to share details.

ASSENT TO TAKE PART IN THIS STUDY FOR ADOLESCENT PARTICIPANTS AGES 10-13

For your leftover samples, write your initials next to your choice (choose only one).

_____ **I allow my leftover samples to be used for research on HIV and other infections, including testing for the study drugs and other anti-HIV medicines, the immune system, and other diseases. I also allow my samples to be used for tests of my genes.**

_____ **I allow my leftover samples to be used for research on HIV and other infections, including testing for the study drugs and other anti-HIV medicines, the immune system, and other diseases. I do not allow my samples to be used for tests of my genes.**

_____ **I do not allow my leftover samples to be used for any research.**

Participant's Name (print)

Signature and Date

Study Staff Conducting Assent Discussion (print)

Study Staff Signature and Date