FINAL

August 27, 2021

Letter of Amendment 01

Protocol

Version 2.0

HVTN 804/HPTN 095

Antiretroviral analytical treatment interruption (ATI) to assess immunologic and virologic responses in participants who received VRC01 or placebo and became HIV-infected during HVTN 704/HPTN 085

DAIDS-ES ID 38632

NON-IND PROTOCOL

HIV Vaccine Trials Network (HVTN) and HIV Prevention Trials Network (HPTN) Clinical Research Site (CRS) filing instructions

The following information impacts the HVTN 804/HPTN 095 study and must be forwarded to your Institutional Review Board (IRB)/Ethics Committee (EC) and any other applicable Regulatory Entity (RE) as soon as possible for their information and review. Their approval is required before implementation. Upon receiving final IRB/EC and any other RE approval(s) for this LOA, CRSs must implement the LOA immediately.

Upon receiving final IRB/EC and any other applicable RE approval(s), CRSs are required to submit LOA registration documents to the DAIDS Protocol Registration Office (PRO) at the Regulatory Support Center (RSC). CRSs will receive an LOA Registration Notification once the DAIDS PRO verifies that all the required LOA registration documents have been received and are complete. A Registration Notification from the DAIDS PRO is not required prior to implementing the LOA. A copy of the LOA Registration Notification, along with this LOA and any IRB/EC and RE correspondence, should be retained in the CRS's regulatory files.

For additional information on the registration process and specific documents required for LOA registration, refer to the current version of the DAIDS Protocol Registration Manual.

The following information affects the sample informed consent. The CRS's IRB/EC is responsible for determining the process of informing study participants of the contents of this LOA.

List of changes

The changes described herein will be incorporated in the next version of Protocol HVTN 804/HPTN 095 if it undergoes full protocol amendment at a later time. New text is denoted in **bold underline**, deleted text in ~~strikethrough,~~ and intervening text not shown is denoted by '….'.

Item 1 Added in Section 5.2, *Exclusion criteria,* Section 6.1.1, *Screening,* Section 6.1.3, *ART switch,* Section 6.1.4*, ATI,* Section 6.2, *Schedule 2: Monitoring ATI with viremia,* Section 6.3, *Schedule 3: Follow-up on ART,* Section 10.1.1, *Risks of ATI*, Section 14, *Acronyms and abbreviations*, Appendix A: *Sample informed consent form*, and Appendices D through J: monitoring for SARS-CoV-2 infection during the study

In view of the COVID-19 pandemic, we have included language throughout the protocol that aims to mitigate the risk of a SARS-CoV-2 infection for participants who will be screened and enrolled in the ATI study. The specific sections revised are noted below.

A Revised in Section 5.2, Exclusion criteria

Two new criteria were added (new #10 and #13) and subsequent criterion numbers were revised accordingly.

5.2 Exclusion criteria

10. **Receipt of any emergency-use authorized, WHO emergency use listed, licensed or registered SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) vaccine within 4 weeks before planned ART interruption. Note: SARS-CoV-2 vaccination is not required for HVTN 804/HPTN 095 eligibility.**

~~10~~**11**. **Significant or unstable cardiac or cerebrovascular disease** (eg, angina, congestive heart failure [CHF], recent cerebrovascular accident [CVA], or myocardial infarction [MI]).

~~11~~**12**. **Hepatitis B surface antigen (HBsAg) or positive HCV RNA** (Not exclusionary: positive HCV Ab with negative HCV RNA).

13. **Volunteers who have:**

- **a SARS-CoV-2 positive test (direct viral detection, eg, viral nucleic acid or antigen detection) ≤ 14 days of enrollment, if asymptomatic**

OR

- **unresolved COVID-19 (ie, SARS-CoV-2 positive test AND symptoms) ≤ 14 days of enrollment (not excluded: individuals with symptoms consistent with residual sequelae of resolved COVID-19, in the clinical judgement of the investigator)**

~~12~~**14.** **Pregnant or breastfeeding**.

B Revised in Section 6.1.1, Screening:

Screening may occur over the course of several contacts/visits. All inclusion and exclusion criteria must be assessed within 8 weeks (56 days) prior to enrollment, unless otherwise specified in the eligibility criteria (Section 5).

After signing informed consent, volunteers will undergo the following procedures, as shown in Appendix E and Appendix H:

- Assessment of Understanding

….

- HIV transmission risk behavior assessment and counseling

- **SARS-CoV-2 risk reduction counseling (per clinician judgement based on local epidemiology, see HVTN 804/HPTN 095 SSP)**

- Contraception status assessment (for volunteers assigned female sex at birth and who are sexually active in a way that could lead to pregnancy; see Section 6.5 and Appendix B)

- Decision aid

- Blood collection for:

    - HIV PCR viral load
    - CD4+ and CD8+ T-cell counts
    - HBsAg and hepatitis C serology
    - QuantiFERON TB test
    - Hgb, ANC, platelets
    - ALT, direct bilirubin, eGFR
    - Syphilis testing

- **SARS-CoV-2 testing (direct viral detection, eg, viral nucleic acid or antigen detection) for volunteers who, by self-report, have not received a SARS-CoV-2 vaccine**

- Urine pregnancy test (for volunteers assigned female sex at birth; persons not of reproductive potential due to having reached menopause (no menses for 1 year), or having undergone hysterectomy or bilateral oophorectomy or tubal ligation [verified by medical records], are not required to undergo pregnancy testing)

- Gonorrhea/chlamydia testing by urine, rectal swabs, and oropharyngeal swabs

- Tuberculin skin test (TST; only if QuantiFERON TB test not available)

- Confirm volunteer eligibility to enroll

C Revised in Section 6.1.3, ART switch and ATI qualification visit:

ART switch

At the clinic visit initiating the ART switch, the participant will undergo the following procedures (see Appendix E and Appendix H):

- Targeted (ie, symptom directed) physical examination, including weight and vital signs

- Assessment of concomitant medications
- Intercurrent illness/adverse experiences (AEs)
- HIV transmission risk behavior assessment and counseling
- **SARS-CoV-2 risk reduction counseling (per clinician judgement based on local epidemiology, see HVTN 804/HPTN 095 SSP)**
- Contraception status assessment (for participants assigned female sex at birth and who are sexually active in a way that could lead to pregnancy; see Section 6.5 and Appendix B)
- Decision-making assessment
- Psychosocial assessment
    - Blood collection for:
        - HIV PCR viral load
        - CD4+ and CD8+ T-cell counts
        - Hgb, ANC, platelets
        - ALT, direct bilirubin, eGFR
- **SARS-CoV-2 testing (direct viral detection, eg, nucleic acid or antigen detection) per clinician judgement based on local epidemiology and/or symptom presentation, see HVTN 804/HPTN 095 SSP**
- Urine pregnancy test (for volunteers assigned female sex at birth; persons not of reproductive potential due to having reached menopause (no menses for 1 year), or having undergone hysterectomy or bilateral oophorectomy or tubal ligation [verified by medical records], are not required to undergo pregnancy testing)

ATI qualification visit

Four weeks or more after initiation of the new ART regimen, participants undergoing an ART switch will return for a clinic visit during which they will undergo the following procedures (see Appendix E and Appendix H):

- Targeted (ie, symptom directed) physical examination, including weight and vital signs
- Assessment of concomitant medications
- Intercurrent illness/adverse experiences (AEs)

- HIV transmission risk behavior assessment and counseling
- **SARS-CoV-2 risk reduction counseling (per clinician judgement based on local epidemiology, see HVTN 804/HPTN 095 SSP)**
- Contraception status assessment (for participants assigned female sex at birth and who are sexually active in a way that could lead to pregnancy; see Appendix B)
    - Blood collection for:
        - HIV PCR viral load
        - CD4+ and CD8+ T-cell counts
        - Hgb, ANC, platelets
        - ALT, direct bilirubin, eGFR
- **SARS-CoV-2 testing (direct viral detection, eg, nucleic acid or antigen detection) per clinician judgement based on local epidemiology and/or symptom presentation, see HVTN 804/HPTN 095 SSP**
- Urine pregnancy test (for volunteers assigned female sex at birth; persons not of reproductive potential due to having reached menopause (no menses for 1 year), or having undergone hysterectomy or bilateral oophorectomy or tubal ligation [verified by medical records], are not required to undergo pregnancy testing)

D Revised in Section 6.1.4, ATI:

For all participants, initiation of ATI is defined as Day 0.

While on Schedule 1, participants will undergo the following procedures, as specified in Appendix E and Appendix H:

- Complete physical examination OR Targeted (ie, symptom directed) physical examination, including weight and vital signs
- Assessment of concomitant medications
- Intercurrent illness/adverse experiences (AEs)
- ART re-initiation assessment
- HIV transmission risk behavior assessment and counseling
- **SARS-CoV-2 risk reduction counseling (per clinician judgement based on local epidemiology, see HVTN 804/HPTN 095 SSP)**

- Contraception status assessment (for participants assigned female sex at birth and who are sexually active in a way that could lead to pregnancy; see Section 6.5 and Appendix B)
- Decision-making assessment
- Psychosocial assessment
- Social impact assessment
- Social impact assessment questionnaire
- Blood collection per Appendix E for:
    - HIV PCR viral load
    - CD4+ and CD8+ T-cell counts
    - Hgb, ANC, platelets
    - ALT, direct bilirubin, eGFR
    - Syphilis testing
    - ARV detection
    - Intracellular cytokine staining (ICS)
    - Immune cell phenotyping
    - Neutralizing antibodies (nAb)
    - FcR-mediated effector functions
    - HIV reservoir assessment
    - Serum, plasma, and PBMC storage
- **SARS-CoV-2 testing (direct viral detection, eg, nucleic acid or antigen detection) per clinician judgement based on local epidemiology and/or symptom presentation, see HVTN 804/HPTN 095 SSP**
- Urine pregnancy test (for volunteers assigned female sex at birth; persons not of reproductive potential due to having reached menopause (no menses for 1 year), or having undergone hysterectomy or bilateral oophorectomy or tubal ligation [verified by medical records], are not required to undergo pregnancy testing)
- Gonorrhea/chlamydia testing by urine, rectal swabs, and oropharyngeal swabs

E Revised in Section 6.2, Schedule 2: Monitoring ATI with viremia

As soon as participants demonstrate viral load ≥ 200 copies/mL, they will transition to Schedule 2, during which they will continue ATI while viremia is monitored. At Schedule 2 timepoints specified in Appendix F and Appendix I, participants will undergo the following procedures:

- Complete physical examination OR targeted (ie, symptom directed) physical examination, including weight and vital signs.
- Assessment of concomitant medications
- Intercurrent illness/adverse experiences (AEs)
- ART re-initiation assessment
- HIV transmission risk behavior assessment and counseling
- **SARS-CoV-2 risk reduction counseling (per clinician judgement based on local epidemiology, see HVTN 804/HPTN 095 SSP)**
- Contraception status assessment (for participants who were assigned female sex at birth and who are sexually active in a way that could lead to pregnancy; see Section 6.4 and Appendix B).
- Decision-making assessment
- Psychosocial assessment
- Social impact assessment
- Social impact assessment questionnaire
- Blood collection for:
    - HIV PCR viral load
    - CD4+ and CD8+ T-cell counts
    - Hgb, ANC, platelets
    - ALT, direct bilirubin, eGFR
    - Syphilis testing
    - ARV detection
    - Intracellular cytokine staining (ICS)

- Immune cell phenotyping
- Neutralizing antibodies (nAb)
- FcR-mediated effector functions
- Serum, plasma, and PBMC storage

- **SARS-CoV-2 testing (direct viral detection, eg, nucleic acid or antigen detection) per clinician judgement based on local epidemiology and/or symptom presentation, see HVTN 804/HPTN 095 SSP**

- Urine pregnancy test (persons assigned female sex at birth; persons not of reproductive potential due to having undergone hysterectomy or bilateral oophorectomy [verified by medical records], are not required to undergo pregnancy testing).

- Gonorrhea/chlamydia testing by urine, rectal swabs, and oropharyngeal swabs

F Revised in Section 6.3, Schedule 3: Follow-up on ART

At Schedule 3 timepoints specified in Appendix G and Appendix J, participants will undergo the following procedures:

- Complete physical examination OR targeted (ie, symptom directed) physical examination, including weight and vital signs.

- Assessment of concomitant medications

- Intercurrent illness/adverse experiences (AEs)

- HIV transmission risk behavior assessment and counseling

- **SARS-CoV-2 risk reduction counseling (per clinician judgement based on local epidemiology, see HVTN 804/HPTN 095 SSP)**

- Contraception status assessment (for participants who were assigned female sex at birth and who are sexually active in a way that could lead to pregnancy; see Section 6.5 and Appendix B).

- Decision-making assessment

- Psychosocial assessment

- Social impact assessment

- Social impact assessment questionnaire

- Blood collection for:
    - HIV PCR viral load
    - CD4+ and CD8+ T-cell counts
    - Hgb, ANC, platelets
    - ALT, direct bilirubin, eGFR
    - Syphilis testing
    - HIV genotypic antiretroviral resistance
    - Viral isolation and sequencing
    - Intracellular cytokine staining (ICS)
    - Immune cell phenotyping
    - Neutralizing antibodies (nAb)
    - FcR-mediated effector functions
    - HIV reservoir assessment
    - Serum, plasma, and PBMC storage
- **SARS-CoV-2 testing (direct viral detection, eg, nucleic acid or antigen detection) per clinician judgement based on local epidemiology and/or symptom presentation, see HVTN 804/HPTN 095 SSP**
- Urine pregnancy test (persons assigned female sex at birth; persons not of reproductive potential due to having undergone hysterectomy or bilateral oophorectomy [verified by medical records], are not required to undergo pregnancy testing).
- Gonorrhea/chlamydia testing by urine, rectal swabs, and oropharyngeal swabs

G Revised in Section 10.1.1, Risks of ATI

10.1.1 Risks of ATI

The risks from a closely monitored ATI are minimal in this study population. There is a theoretical risk that such an interruption could lead to the development of HIV drug resistance (130). This may be a particular concern for individuals taking NNRTIs. However, this potential risk is substantially mitigated by the procedures described in Section 6.1.1. Given the study population as restricted by the eligibility criteria, the frequency of immunological and virologic monitoring,

and the criteria for restarting ART, it is extremely unlikely that such an ART interruption will lead to the development of any opportunistic infections or AIDS-defining conditions. **The risks of SARS-CoV-2 infection or COVID-19 for people living with HIV during a closely monitored ATI are currently unknown.**

H Added in Section 14, Acronyms and abbreviations

SARS-CoV-2 severe acute respiratory syndrome coronavirus 2

I Revised in Appendix A, Key information

These are some of the things you should know about this study:

- One purpose of the study is to learn whether having the AMP Study antibody in a person's body might help the immune system control HIV better if that person gets HIV.

….

- There may also be risks we don't know about, even serious ones, including death.
- **The risks of SARS-CoV-2 infection or having COVID-19 while you are not taking HIV medication are currently unknown**.
- There is no direct benefit to you from being in the study.

J Revised in Appendix A, Joining the study, item 4, 2nd paragraph

4. If you want to join the study, we will screen you to see if you are eligible.

We will also do blood and urine tests. These tests tell us about some aspects of your health, such as how healthy your kidneys, liver, and immune system are. We will also test you for hepatitis B, hepatitis C, tuberculosis (TB), gonorrhea, chlamydia, and syphilis. **We will also test you for SARS-CoV-2 and provide risk reduction counseling (if you have not been vaccinated)**. We will ask you about medications you are taking. If you were assigned female sex at birth and can become pregnant, we will test you for pregnancy. If you are pregnant, you cannot join the study.

K Revised in Appendix A, Being in the study

8. If you join the study, we will collect some basic information.

We will record your medical history and give you a physical examination, including checking your weight and vital signs. We will ask about other medications you are taking and about any illnesses you may have. We will also collect blood and urine, and if you were assigned female sex at birth and can become pregnant, we will give you a pregnancy test. We will test you for

gonorrhea and chlamydia using urine, rectal swabs, and oral swabs. We will test you for syphilis using a blood sample. **Testing for SARS-CoV-2 and risk reduction counseling will be provided as needed.**

L Revised in Appendix A, section 19:

Risks

19. There are risks to being in this study.

This study is designed to minimize the risks of stopping your HIV medication. This depends on you following the instructions from the clinic staff and attending all your study visits.

This section describes the risks we know about. There may also be risks we don't know about, even serious ones. **The risks of SARS-CoV-2 infection or having COVID-19 while you are not taking HIV medication are currently unknown. This is why we will monitor you for COVID-19 during the study**. We will tell you if we learn anything new that may affect your willingness to stay in the study.

M Added in Appendix D, Tables of procedures for sample informed consent form:

SARS-CoV-2 testing and risk reduction counseling at screening or any study visit as needed, has been added as a new study procedure to all the tables in Appendix D. The revised tables with footnotes are appended.

N Added in Appendix E, Laboratory procedures — Schedule 1: Monitoring ATI:

Specimen collection for SARS-CoV-2 testing has been added to both tables in Appendix E with a new associated footnote:

[18] SARS-CoV-2 testing may be performed at the screening visit and at any other visit, if clinically indicated. Testing must be by direct detection of SARS-CoV-2 (eg, nucleic acid or antigen detection). See HVTN 804/HPTN 095 SSP for more information.

The revised tables with footnotes are appended.

O Added in Appendix F, Laboratory procedures — Schedule 2: Monitoring ATI with viremia

Specimen collection for SARS-CoV-2 testing has been added to both tables in Appendix F with a new associated footnote:

[14] SARS-CoV-2 testing may be performed at the screening visit and at any other visit, if clinically indicated. Testing must be by direct detection of

SARS-CoV-2 (eg, nucleic acid or antigen detection). See HVTN 804/HPTN 095 SSP for more information.

The revised tables with footnotes are appended.

P Added in Appendix G, Laboratory procedures — Schedule 3: Follow-up on ART

Specimen collection for SARS-CoV-2 testing has been added to the table in Appendix G with a new associated footnote:

[14] SARS-CoV-2 testing may be performed at the screening visit and at any other visit, if clinically indicated. Testing must be by direct detection of SARS-CoV-2 (eg, nucleic acid or antigen detection). See HVTN 804/HPTN 095 SSP for more information.

The revised table with footnotes is appended.

Q Added in Appendix H, Procedures at CRS — Schedule 1: Monitoring ATI

"SARS-CoV-2 risk reduction counseling" with checkmarks at all visits has been added as a study procedure to **all the tables** in Appendix H. A new associated footnote # 5, has been added to the footnote list and subsequent footnotes have been renumbered accordingly. The revised tables with footnotes are appended.

[5] SARS-CoV-2 risk reduction counseling will be provided at any visit, if indicated. See HVTN 804/HPTN 095 SSP for more information.

R Added in Appendix I, Procedures at CRS — Schedule 2: Monitoring ATI with viremia

"SARS-CoV-2 risk reduction counseling" with checkmarks at all visits has been added as a study procedure to **all the tables** in Appendix I. A new associated footnote # 2, has been added to the footnote list and subsequent footnotes have been renumbered accordingly. The revised tables with footnotes are appended.

[2] SARS-CoV-2 risk reduction counseling will be provided at any visit, if indicated. See HVTN 804/HPTN 095 SSP for more information.

S Added in Appendix J, Procedures at CRS — Schedule 3: Follow-up on ART

"SARS-CoV-2 risk reduction counseling" with checkmarks at all visits has been added as a study procedure to the table in Appendix I. A new associated footnote # 2, has been added to the footnote list and subsequent footnotes have been renumbered accordingly. The revised table with footnotes is appended.

[2] SARS-CoV-2 risk reduction counseling will be provided at any visit, if indicated. See HVTN 804/HPTN 095 SSP for more information.

Item 2 Updated in Section 2.10, *The necessity of the AMP placebo control group* and Appendix A, *Sample Informed Consent Form*: AMP participants have been unblinded

The AMP study is unblinded and participants are being informed if they received the study antibody or a placebo. We have updated Section 2.10 and Appendix A to reflect this information.

A Revised in Section 2.10, last sentence of 10th paragraph

AMP is ~~projected to be unblinded in Q4 2020~~ **unblinded**.

B Revised in Appendix A, paragraph 3

You are being asked to take part in this study because you got HIV while you were enrolled in the AMP Study, have been taking HIV medication (also known as "ART" or anti-retroviral treatment) and because your HIV has been kept at a very low level or "undetectable" for at least the past year. We will enroll people who got the study antibody and people who got placebo. ~~Since the AMP Study is still blinded, we don't know~~ **You will know** whether you got the study antibody or not **before joining this study**.

Item 3 Deleted in Appendices D, H, and I: non-relevant footnotes

Appendices D, H, and I have multiple tables within one appendix. Some footnotes are not relevant to all the tables within the given appendix. We have corrected this by deleting non-relevant footnotes from the footnote list. All updated tables with footnotes are appended. The specific changes are listed below:

A Deleted in Appendix D, Tables of procedures for sample informed consent form:

Footnote d has been deleted from the footnote list in the first table titled "Table of procedures for Part 1: Screening and stopping your HIV medications".

~~[d] Extra visits every 3 months for people do not meet criteria for moving to Part 2 or Part 3.~~

Footnote c has been deleted from the footnote list in the table titled "Table of procedures for Part 2: Monitoring your health and your HIV".

~~[e] Extra visits every 3 months for people do not meet criteria for moving to Part 3.~~

B Deleted in Appendix H, Procedures at CRS—Schedule 1: Monitoring ATI

The last 3 footnotes, numbered 8, 9, and 10, have been deleted from the footnote list in **first** table of the Appendix.

~~[8] Extended follow-up visit type A will occur every 6 months starting with 3 months after visit 27, continuing up to 3 years of this schedule. This follow-up visit may be performed for participants who have not met ART re-initiation criteria (see Protocol Section 3.3 and HVTN 804/HPTN 095 SSP for details).~~

~~[9] Extended follow-up visit type B will occur every 6 months starting with 6 months after visit 27, continuing up 3 years of this schedule and then every 3 months thereafter. This follow-up visit may be performed for participants who have not met ART re-initiation criteria (see Protocol Section 3.3 and HVTN 804/HPTN 095 SSP for details).~~

~~[10] At an early termination visit for a withdrawn or terminated participant, CRS staff should consider performing procedures specified for Extended follow-up visit Type A (see Section 6.5 and HVTN 804/HPTN 095 SSP for details).~~

C Deleted in Appendix I, Procedures at CRS— Schedule 2: Monitoring ATI with viremia

The last 3 footnotes, numbered 4, 5 and 6, have been deleted from the footnote list in first table of the Appendix.

~~[4] Extended follow-up visit type A will occur every 6 months starting with 3 months after visit 66, continuing up to 3 years of this schedule. This follow-up visit may be performed for participants who have not met ART re-initiation criteria (see Protocol Section 3.3 and HVTN 804/HPTN 095 SSP for details).~~

~~[5] Extended follow-up visit type B will occur every 6 months starting with 6 months after visit 66, continuing up 3 years of this schedule and then every 3 months thereafter. This follow-up visit may be performed for participants who have not met ART re-initiation criteria (see Protocol Section 3.3 and HVTN 804/HPTN 095 SSP for details).~~

~~[6] At an early termination visit for a withdrawn or terminated participant, CRS staff should consider performing procedures specified for Extended follow-up visit Type A (see Section 6.5 and HVTN 804/HPTN 095 SSP for details).~~

Item 4 Corrected in Section 6.1, *Schedule 1: Monitoring ATI*, and Section 6.3, *Schedule 3: Follow-up on ART*: cross reference to contraception status section

A Section 6.1.1, 6th bullet

- Contraception status assessment (for volunteers assigned female sex at birth and who are sexually active in a way that could lead to pregnancy; see Section ~~6.5~~ **6.6** and Appendix B)

B Section 6.1.3, 5th bullet

- Contraception status assessment (for participants assigned female sex at birth and who are sexually active in a way that could lead to pregnancy; see Section ~~6.5~~ **6.6** and Appendix B)

C Section 6.1.4, 6th bullet

- Contraception status assessment (for participants assigned female sex at birth and who are sexually active in a way that could lead to pregnancy; see Section ~~6.5~~ **6.6** and Appendix B)

D Section 6.3, 5th bullet

- Contraception status assessment (for participants who were assigned female sex at birth and who are sexually active in a way that could lead to pregnancy; see Section ~~6.4~~ **6.6** and Appendix B)

Item 5 Corrected in Appendix J, *Procedures at CRS—Schedule 3: Follow-up on ART*: placement of footnote 4 to visit 92 column

Footnote 4 notes that visit 92 procedures will be followed if there is early termination visit for a withdrawn or terminated participant. Therefore, the placement of this footnote (originally #4 but per this LoA item 1 now #5) has been moved from visit 91 column to visit 92 column.

Item 6 Updated in Section 1.3, *Protocol team*: protocol leadership members

There has been a change in the Medical Officers overseeing this study. The Protocol Leadership table has been updated to reflect this change.

Protocol leadership

Co-chairs	Shelly Karuna HVTN Core, Fred Hutch 206-667-4355 skaruna@fredhutch.org Katharine Bar Univ. of Pennsylvania 215-573-8497 bark@pennmedicine.upenn.edu
Protocol Team leaders	Shelly Karuna HVTN Core, Fred Hutch 206-667-4355 skaruna@fredhutch.org Phil Andrew HPTN LOC, FHI 360 919.544.7040 x11213 pandrew@fhi360.org
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Medical Officers	Randall Tressler DAIDS Therapeutics Research Program 240-627-3072 randall.tressler@nih.gov **Lydia Soto-Torres** **International HIV Research\Latin American HIV Research Liaison, NIAID** **lsoto-torres@niaid.nih.gov** **301-213-1154** ~~David Burns~~ ~~DAIDS Prevention Sciences Program (PSP), NIAID~~ ~~301-435-8896~~ ~~burnsda@niaid.nih.gov~~ ~~Margarita Gomez Lorenzo~~ ~~DAIDS Vaccine Research Program (VRP), NIAID~~ ~~240-627-3510~~ ~~gomezmm@niaid.nih.gov~~

Appendix D Tables of procedures for sample informed consent form

Table of procedures for Part 1: Screening and stopping your HIV medications

	Screening	HIV medication switch[a]	Pre-stop visit about 4 weeks later	Time after stopping HIV medications: Day 0	Week 1	Week 2	Week 3	~1 month	Week 5	Week 6	Week 7	~2 months	Week 10	~3 months	Week 14	~4 months	Week 18	~5 months	Week 22
Study procedures																			
HIV medication switch (if required)		✓	✓																
Medical history	✓																		
Complete physical exam	✓			✓															
Brief physical exam		✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Pregnancy test and contraception review[b]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Blood drawn	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
STI testing (blood, urine, and oral & rectal swabs)[c]	✓			✓				✓				✓		✓		✓		✓	
Transmission risk reduction counseling	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Interview/questionnaire	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
TB test	✓																		
Blood drawn	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
SARS-CoV-2 risk reduction counseling	at screening or any study visit as needed																		
SARS-CoV-2 testing	at screening or any study visit as needed																		

Procedures in gray only for participants switching HIV medications.

[a] We will contact you about 2 weeks after you start the new HIV medication to check to see if you have had any side effects or have other concerns.

[b] Persons assigned female sex at birth who have reached menopause or who had a hysterectomy, oophorectomy, or tubal ligation verified by medical records are not required to have a pregnancy test or contraception review.

[c] In addition to STI testing at the checked visits, we will test at other visits if you show symptoms of an STI.

Appendix D Tables of procedures for sample informed consent form

Table of procedures for Part 1: Screening and stopping your HIV medications (continued)

	Time after stopping HIV medications								
	~6 months	Week 28	Week 32	Week 36	~ 9 months	Week 44	Week 48	1 year	Extra visits[d]
Study procedures									
Complete physical exam									
Brief physical exam	✓	✓	✓	✓	✓	✓	✓	✓	✓
Pregnancy test and contraception review[b]	✓	✓	✓	✓	✓	✓	✓	✓	✓
Transmission risk reduction counseling	✓	✓	✓	✓	✓	✓	✓	✓	✓
Interview/questionnaire	✓	✓	✓	✓	✓	✓	✓	✓	✓
STI testing (blood, urine, and oral & rectal swabs)[c]	✓	✓	✓	✓	✓	✓	✓	✓	✓
Blood Drawn	✓	✓	✓	✓	✓	✓	✓	✓	✓
SARS-CoV-2 risk reduction counseling	at screening or any study visit as needed								
SARS-CoV-2 testing	at screening or any study visit as needed								

[a] We will contact you about 2 weeks after you start the new HIV medication to check to see if you have had any side effects or have other concerns.

[b] Persons assigned female sex at birth who have reached menopause or who had a hysterectomy, oophorectomy, or tubal ligation verified by medical records are not required to have a pregnancy test or contraception review.

[c] In addition to STI testing at the checked visits, we will test at other visits if you show symptoms of an STI.

[d] Extra visits every 3 months for people do not meet criteria for moving to Part 2 or Part 3

Appendix D Tables of procedures for sample informed consent form

Table of procedures for Part 2: Monitoring your health and your HIV

	Time after starting Part 2															
	Day 0	Week 1	Week 2	Week 3	~1 month	Week 5	Week 6	Week 7	~2 months	Week 10	~3 months	Week 14	~4 months	Week 18	~5 months	Week 22
Study procedures																
Complete physical exam	✓															
Brief physical exam		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Pregnancy test and contraception review[a]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Blood drawn	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
STI testing (blood, urine, and oral & rectal swabs)[b]	✓				✓				✓		✓		✓		✓	
Transmission risk reduction counseling	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Interview/questionnaire	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Blood drawn	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
SARS-CoV-2 risk reduction counseling	at screening or any study visit as needed															
SARS-CoV-2 testing	at screening or any study visit as needed															

[a] Persons assigned female sex at birth who have reached menopause or who had a hysterectomy, oophorectomy, or tubal ligation verified by medical records are not required to have a pregnancy test or contraception review.

[b] In addition to STI testing at the checked visits, we will test at other visits if you show symptoms of an STI.

Appendix D Tables of procedures for sample informed consent form

Table of procedures for Part 2: Monitoring your health and your HIV (continued)

	Time after starting Part 2											
	Week 24	6 months	Week 28	Week 30	Week 32	Week 34	Week 36	~9 months	Week 44	Week 48	1 year	Extra visits[d]
Study procedures												
Complete physical exam												
Brief physical exam	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Pregnancy test and contraception review[a]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Blood drawn	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
STI testing (blood, urine, and oral & rectal swabs)[b]	✓		✓		✓		✓	✓	✓	✓	✓	✓
Transmission risk reduction counseling	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Interview/questionnaire	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Blood drawn	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
SARS-CoV-2 risk reduction counseling	at screening or any study visit as needed											
SARS-CoV-2 testing	at screening or any study visit as needed											

[a] Persons assigned female sex at birth who have reached menopause or who had a hysterectomy, oophorectomy, or tubal ligation verified by medical records are not required to have a pregnancy test or contraception review.

[b] In addition to STI testing at the checked visits, we will test if you show symptoms of an STI.[d] Extra visits every 3 months for people do not meet criteria for moving to Part 3.

Appendix D Tables of procedures for sample informed consent form

Table of procedures for Part 3: Restart HIV medications

	Time after restarting HIV medications												
	Week 0	Week 2	~1 month	Week 6	~2 months	Week 10	Week 12	~4 months	Week 20	~6 months	Week 28	~9 months	1 year
Study procedures													
Complete physical exam													✓
Brief physical exam	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Pregnancy test & contraception review[a]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Transmission risk reduction counseling	✓	✓	✓		✓		✓		✓		✓		✓
Interview/Questionnaire	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
STI testing (blood, urine, and oral & rectal swabs)[b]	✓		✓		✓		✓	✓[c]	✓[c]	✓	✓[c]	✓	
Blood Drawn	✓	✓	✓	✓	✓	✓	✓	✓	✓	ü	✓	✓	✓
SARS-CoV-2 risk reduction counseling	at screening or any study visit as needed												
SARS-CoV-2 testing	at screening or any study visit as needed												

[a] Persons assigned female sex at birth who have reached menopause or who had a hysterectomy, oophorectomy, or tubal ligation verified by medical records are not required to have a pregnancy test or contraception review. Pregnancy test and contraceptive review are not required once viral load drops to undetectable after restarting HIV medication.

[b] In addition to STI testing at the checked visits, we will test if you show symptoms of an STI.

[c] STI testing is not required at this visit if viral load has returned to undetectable.

Appendix E Laboratory procedures—Schedule 1: Monitoring ATI

Procedure	Ship to[1]	Assay location[1,2]	Tube Type[3]	Tube size (vol. capacity)[3]	Visit:	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
					Days on ATI:				D0	D7	D14	D21	D28	D35	D42	D49	D56	D70	D84	D98	D112	D126	D140	D154
					Weeks on ATI:	Screening visit[15]	ART Switch[8]	ATI qualification[9]	W0 ATI	W1	W2	W3	W4	W5	W6	W7	W8	W10	W12	W14	W16	W18	W20	W22
BLOOD COLLECTION																								
Screening or diagnostic assays																								
HIV PCR viral load[13]	Local labs	Local labs	EDTA	6mL		6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
CD4+/CD8+ T-cell count[14]	Local labs	Local labs	EDTA	4mL		4	4	4	4	—	4	—	4	—	4	—	4	—	4	—	4	—	4	—
HBsAg/anti-HCV[4]	Local labs	Local labs	SST	5mL		10	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
QuantiFERON TB testing[5]	Local labs	Local labs	QFT Gold/Gold-Plus	1mL		4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Safety labs																								
Hgb / ANC / PLT	Local labs	Local labs	EDTA	4mL		4	4	4	4	—	—	—	4	—	—	—	4	—	4	—	4	—	4	—
ALT / direct bilirubin / eGFR	Local labs	Local labs	SST	5mL		5	5	5	5	—	—	—	5	—	—	—	5	—	5	—	5	—	5	—
Syphilis[10]	Local labs	Local labs	SST	5mL		5	—	—	5	—	—	—	5	—	—	—	5	—	5	—	5	—	5	—
Drug levels																								
ARV detection	CSR	TBD	EDTA	4mL		—	—	—	—	—	—	—	4	—	—	—	4	—	4	—	4	—	4	—
Immunogenicity & Virologic Assays																								
Cellular assays																								
ICS	CSR	HVTN labs	ACD	8.5mL		—	—	—	42.5	—	—	—	42.5	—	—	—	42.5	—	42.5	—	42.5	—	42.5	—
Phenotyping	CSR	HVTN labs	ACD	8.5mL		—	—	—	z	—	—	—	z	—	—	—	z	—	z	—	z	—	z	—
Humoral assays																								
Neutralizing antibody	CSR	HVTN labs	SST	8.5mL		—	—	—	8.5	—	—	—	8.5	—	—	—	8.5	—	8.5	—	8.5	—	8.5	—
FcR-mediated effector functions[6]	CSR	HVTN labs	SST	8.5mL		—	—	—	y	—	—	—	y	—	—	—	y	—	y	—	y	—	y	—
HIV reservoir assays	CSR	TBD	ACD	8.5mL		—	—	—	51	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Storage																								
Serum	CSR		SST	8.5mL		—	—	—	8.5	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Plasma	CSR		EDTA	10mL		—	—	—	—	—	—	—	—	—	—	—	10	—	10	—	10	—	10	—
PBMC	CSR		ACD	8.5mL		—	—	—	—	—	—	—	—	—	—	—	17	—	17	—	17	—	17	—
Visit total						38	19	19	134.5	6	10	6	79	6	10	6	106	6	106	6	106	6	106	6
56-Day total						38	57	76	210.5	216.5	226.5	232.5	311.5	317.5	327.5	333.5	401.5	229	319	240	330	230	330	230
URINE COLLECTION																								
Pregnancy Test[16]	Local labs	Local labs				X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Chlamydia/gonorrhea[7,10]	Local labs	Local labs				X	—	—	X	—	—	—	X	—	—	—	X	—	X	—	X	—	X	—
RECTAL SWAB COLLECTION																								
Chlamydia/gonorrhea[7,10]	Local labs	Local labs				X	—	—	X	—	—	—	X	—	—	—	X	—	X	—	X	—	X	—
OROPHARYNGEAL SWAB COLLECTION																								
Chlamydia/gonorrhea[7,10]	Local labs	Local labs				X	—	—	X	—	—	—	X	—	—	—	X	—	X	—	X	—	X	—
OTHER SPECIMEN COLLECTION																								
SARS-CoV-2 testing	Local labs	Local labs													X[18]									

[1] CSR = central specimen repository.

[2] HVTN Laboratories include: Fred Hutchinson Cancer Research Center (Seattle, Washington, USA); Duke University Medical Center (Durham, North Carolina, USA). Non-HVTN laboratories: TBD.

[3] Local labs may assign appropriate alternative tube types for locally performed tests.

[4] HCV RNA PCR testing will be performed as a reflex test if indicated by anti-HCV antibody results.

[5] Tuberculin skin test (TST) will be performed if QuantiFERON TB testing is not available. See Procedures at CRS (Appendix H).

[6] FcR-mediated effector function assays may include ADCC, virion capture, and phagocytosis assays.

[7] Chlamydia/gonorrhea testing will be done on urine, and rectal and oropharyngeal swabs.

[8] The "ART switch" phase will only be performed for participants on NNRTIs. These participants will be considered enrolled on the first day of the new ART medication.

[9] The ATI Qualification visit specimens must be obtained at least 28 days after ART switch. If needed, VL retesting may continue until viral suppression has been achieved (up to 84 days after ART switch). The last ATI qualification procedures must take place no more than 14 days prior to visit 4 (see HVTN 804/HPTN 095 SSP for more information).

[10] In addition to STI testing at the marked visits, STI testing may occur at any visit if clinically indicated.

[11] Extended follow-up visit type A will occur every 6 months starting with 3 months after visit 27 continuing up to 3 years of this schedule. This follow-up visit may be performed for participants who have not met criteria to transition to Schedule 2 or Schedule 3 (see Protocol Section 3.3 and HVTN 804/HPTN 095 SSP for details).

[12] Extended follow-up visit type B will occur every 6 months starting with 6 months after visit 27 continuing up to 3 years of this schedule, and then every 3 months thereafter. This follow-up visit may be performed for participants who have not met criteria to transition to Schedule 2 or Schedule 3 (see Protocol Section 3.3 and HVTN 804/HPTN 095 SSP for details).

[13] A confirmatory sample should be drawn at the next visit (within approximately 1-2 weeks) following the first VL result ≥ 200 copies/mL (see Protocol Section 3.3.1 for details.

[14] A confirmatory sample should be drawn at the next visit (within approximately 1-2 weeks) following the first CD4+ T-cell count < 350 cells/mm^3 (see Protocol Section 3.3.2 for details.

[15] Screening visit specimens for participants not undergoing an NNRTI switch should be obtained no later than 2 weeks before Visit 4; see HVTN 804/HPTN 095 for more information.

[16] For persons capable of becoming pregnant, pregnancy test may be performed on urine or blood specimens.

[17] At an early termination visit for a withdrawn or terminated participant (see Protocol Section 6.5), blood should be drawn as shown for Extended follow-up visit type A (see HVTN 804/HPTN 095 SSP for more information).

[18] SARS-CoV-2 testing may be performed at the screening visit and at any other visit, if clinically indicated. Testing must be by direct detection of SARS-CoV-2 (eg, nucleic acid or antigen detection). See HVTN 804/HPTN 095 SSP for more information.

y = SST blood collected for neutralizing antibody will also cover specimen needs for FcR-mediated effector functions; no separate blood draw is needed.

z = PBMC blood collected for ICS will also cover specimen needs for phenotyping; no separate blood draw is needed.

Appendix E Laboratory procedures—Schedule 1: Monitoring ATI (continued)

Procedure	Ship to[1]	Assay location[1,2]	Tube Type[3]	Tube size (vol. capacity)[3]	Visit: 20	21	22	23	24	25	26	27	Visit Type A[11,17]	Visit Type B[12]	Total
					Days on ATI: D168	D196	D224	D252	D280	D308	D336	D364			
					Weeks on ATI: W24	W28	W32	W36	W40	W44	W48	W52			
BLOOD COLLECTION															
Screening or diagnostic assays															
HIV PCR viral load[13]	Local labs	Local labs	EDTA	6mL	6	6	6	6	6	6	6	6	6	6	174
CD4+/CD8+ T-cell count[14]	Local labs	Local labs	EDTA	4mL	4	4	4	4	—	4	—	4	4	4	76
HBsAg/anti-HCV	Local labs	Local labs	SST	5mL	—	—	—	—	—	—	—	—	—	—	10
QuantiFERON TB testing[5]	Local labs	Local labs	QFT Gold/Gold-Plus	1mL	—	—	—	—	—	—	—	—	—	—	4
Safety labs															
Hgb / ANC / PLT	Local labs	Local labs	EDTA	4mL	4	4	4	4	—	4	—	4	4	4	68
ALT / direct bilirubin / eGFR	Local labs	Local labs	SST	5mL	5	5	5	5	—	5	—	5	5	5	85
Syphilis[10]	Local labs	Local labs	SST	5mL	5	5	5	5	5	5	5	5	5	5	85
Drug levels															
ARV detection	CSR	TBD	EDTA	4mL	4	4	4	4	4	4	4	4	4	4	60
Immunogenicity & Virologic Assays															
Cellular assays															
ICS	CSR	HVTN labs	ACD	8.5mL	42.5	42.5	42.5	42.5	42.5	42.5	42.5	42.5	—	—	595
Phenotyping	CSR	HVTN labs	ACD	8.5mL	z	z	z	z	z	z	z	z	—	—	0
Humoral assays															
Neutralizing antibody	CSR	HVTN labs	SST	8.5mL	8.5	8.5	8.5	8.5	8.5	8.5	8.5	8.5	—	—	119
FcR-mediated effector functions[6]	CSR	HVTN labs	SST	8.5mL	y	y	y	y	y	y	y	y	—	—	0
HIV reservoir assays	CSR	TBD	ACD	8.5mL	—	—	—	—	—	—	—	—	—	—	51
Storage															
Serum	CSR		SST	8.5mL	—	—	—	—	—	—	—	—	8.5	—	17
Plasma	CSR		EDTA	10mL	10	10	10	10	10	10	10	10	10	—	130
PBMC	CSR		ACD	8.5mL	17	17	17	17	17	17	17	17	59.5	—	263.5
Visit total					106	106	106	106	93	106	93	106	106	28	
56-Day total					330	324	318	318	305	305	292	305	106	28	
URINE COLLECTION															
Pregnancy Test[16]	Local labs	Local labs			X	X	X	X	X	X	X	X	X	X	
Chlamydia/gonorrhea[7,10]	Local labs	Local labs			X	X	X	X	X	X	X	X	X	X	
RECTAL SWAB COLLECTION															
Chlamydia/gonorrhea[7,10]	Local labs	Local labs			X	X	X	X	X	X	X	X	X	X	
OROPHARYNGEAL SWAB COLLECTION															
Chlamydia/gonorrhea[7,10]	Local labs	Local labs			X	X	X	X	X	X	X	X	X	X	
OTHER SPECIMEN COLLECTION															
SARS-CoV-2 testing	Local labs	Local labs			X[18]										

[1] CSR = central specimen repository.

[2] HVTN Laboratories include: Fred Hutchinson Cancer Research Center (Seattle, Washington, USA); Duke University Medical Center (Durham, North Carolina, USA). Non-HVTN laboratories: TBD.

[3] Local labs may assign appropriate alternative tube types for locally performed tests.

[4] HCV RNA PCR testing will be performed as a reflex test if indicated by anti-HCV antibody results.

[5] Tuberculin skin test (TST) will be performed if QuantiFERON TB testing is not available. See Procedures at CRS Appendix H).

[6] FcR-mediated effector function assays may include ADCC, virion capture, and phagocytosis assays.

[7] Chlamydia/gonorrhea testing will be done on urine, and rectal and oropharyngeal swabs.

[8] The "ART switch" phase will only be performed for participants on NNRTIs. These participants will be considered enrolled on the first day of the new ART medication.

[9] The ATI Qualification visit specimens must be obtained at least 28 days after ART switch. If needed, VL retesting may continue until viral suppression has been achieved (up to 84 days after ART switch). The last ATI qualification procedures must take place no more than 14 days prior to visit 4 (see HVTN 804/HPTN 095 SSP for more information).

[10] In addition to STI testing at the marked visits, STI testing may occur at any visit if clinically indicated.

[11] Extended follow-up visit type A will occur every 6 months starting with 3 months after visit 27 continuing up to 3 years of this schedule. This follow-up visit may be performed for participants who have not met criteria to transition to Schedule 2 or Schedule 3 (see Protocol Section 3.3 and HVTN 804/HPTN 095 SSP for details).

[12] Extended follow-up visit type B will occur every 6 months starting with 6 months after visit 27 continuing up to 3 years of this schedule, and then every 3 months thereafter. This follow-up visit may be performed for participants who have not met criteria to transition to Schedule 2 or Schedule 3 (see Protocol Section 3.3 and HVTN 804/HPTN 095 SSP for details).

[13] A confirmatory sample should be drawn at the next visit (within approximately 1-2 weeks) following the first VL result ≥ 200 copies/mL (see Protocol Section 3.3.1 for details.

[14] A confirmatory sample should be drawn at the next visit (within approximately 1-2 weeks) following the first CD4+ T-cell count < 350 cells/mm^3. See Protocol Section 3.3.2 for details.

[15] Screening visit specimens for participants not undergoing an NNRTI switch should be obtained no later than 2 weeks before Visit 4; see HVTN 804/HPTN 095 SSP for more information.

[16] For persons capable of becoming pregnant, pregnancy test may be performed on urine or blood specimens.

[17] At an early termination visit for a withdrawn or terminated participant (see Section 6.5), blood should be drawn as shown for Extended follow-up visit type A (see HVTN 804/HPTN 095 SSP for more information).

[18] SARS-CoV-2 testing may be performed at the screening visit and at any other visit, if clinically indicated. Testing must be by direct detection of SARS-CoV-2 (eg, nucleic acid or antigen detection). See HVTN 804/HPTN 095 SSP for more information.

y = SST blood collected for neutralizing antibody will also cover specimen needs for FcR-mediated effector functions; no separate blood draw is needed.

z = PBMC blood collected for ICS will also cover specimen needs for phenotyping; no separate blood draw is needed.

Appendix F Laboratory procedures—Schedule 2: Monitoring ATI with viremia

				Visit:	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55
				Days on ATI with viremia	D0	D7	D14	D21	D28	D35	D42	D49	D56	D70	D84	D98	D112	D126	D140	D154
				Weeks on ATI with viremia	W0	W1	W2	W3	W4	W5	W6	W7	W8	W10	W12	W14	W16	W18	W20	W22
Procedure	**Ship to[1]**	**Assay location[1,2]**	**Tube Type[3]**	**Tube size (vol. capacity)[3]**																
BLOOD COLLECTION																				
Screening or diagnostic assays																				
HIV PCR viral load[10]	Local labs	Local labs	EDTA	6mL	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
CD4+/CD8+ T-cell count[11]	Local labs	Local labs	EDTA	4mL	4	—	4	—	4	—	4	—	4	—	4	—	4	—	4	—
Safety labs																				
Hgb / ANC / PLT	Local labs	Local labs	EDTA	4mL	4	—	—	—	4	—	—	—	4	—	4	—	4	—	4	—
ALT / direct bilirubin / eGFR	Local labs	Local labs	SST	5mL	5	—	—	—	5	—	—	—	5	—	5	—	5	—	5	—
Syphilis[7]	Local labs	Local labs	SST	5mL	5	—	—	—	5	—	—	—	5	—	5	—	5	—	5	—
Drug levels																				
ARV detection	CSR	TBD	EDTA	4mL	—	—	—	—	4	—	—	—	4	—	4	—	4	—	4	—
Immunogenicity & Virologic Assays																				
Cellular assays																				
ICS	CSR	HVTN labs	ACD	8.5mL	42.5	—	42.5	—	42.5	—	—	—	42.5	—	42.5	—	42.5	—	42.5	—
Phenotyping	CSR	HVTN labs	ACD	8.5mL	z	—	z	—	z	—	—	—	z	—	z	—	z	—	z	—
Humoral assays																				
Neutralizing antibody	CSR	HVTN labs	SST	8.5mL	8.5	—	8.5	—	8.5	—	—	—	8.5	—	8.5	—	8.5	—	8.5	—
FcR-mediated effector functions[4]	CSR	HVTN labs	SST	8.5mL	y	—	y	—	y	—	—	—	y	—	y	—	y	—	y	—
Storage																				
Serum	CSR		SST	8.5mL	8.5	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Plasma	CSR		EDTA	10mL	10	—	—	—	—	—	—	—	10	—	10	—	10	—	10	—
PBMC	CSR		ACD	8.5mL	—	—	—	—	—	—	—	—	17	—	17	—	17	—	17	—
Visit total					93.5	6	61	6	79	6	10	6	106	6	106	6	106	6	106	6
56-Day total[6,10,11]					93.5	99.5	160.5	166.5	245.5	251.5	261.5	267.5	373.5	280	319	240	330	230	330	230
URINE COLLECTION																				
Pregnancy Test[12]	Local labs	Local labs			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Chlamydia/gonorrhea[5,7]	Local labs	Local labs			X	—	—	—	X	—	—	—	X	—	X	—	X	—	X	—
RECTAL SWAB COLLECTION																				
Chlamydia/gonorrhea[5,7]	Local labs	Local labs			X	—	—	—	X	—	—	—	X	—	X	—	X	—	X	—
OROPHARYNGEAL SWAB COLLECTION																				
Chlamydia/gonorrhea[5,7]	Local labs	Local labs			X	—	—	—	X	—	—	—	X	—	X	—	X	—	X	—
OTHER SPECIMEN COLLECTION																				
SARS-CoV-2 testing	Local labs	Local labs			X[14]															

[1] CSR = central specimen repository.

[2] HVTN Laboratories include: Fred Hutchinson Cancer Research Center (Seattle, Washington, USA); Duke University Medical Center (Durham, North Carolina, USA). Non-HVTN laboratories: TBD.

[3] Local labs may assign appropriate alternative tube types for locally performed tests.

[4] FcR-mediated effector function assays may include ADCC, virion capture, and phagocytosis assays.

[5] Chlamydia/gonorrhea testing will be done on urine, and rectal and oropharyngeal swabs.

[6] The 56-day blood draw limit also does not include visits from Schedule 1; please see HVTN 804/HPTN 095 SSP for details on prioritizing collections to avoid exceeding the 56-day limit.

[7] In addition to STI testing at the marked visits, STI testing may occur at any visit if clinically indicated.

[8] Extended follow-up visit type A will occur every 6 months starting with 3 months after visit 66 continuing up to 3 years of this schedule. This follow-up visit may be performed for participants who have not met criteria to transition to Schedule 2 or Schedule 3 (see Protocol Section 3.3 and HVTN 804/HPTN 095 SSP for details).

[9] Extended follow-up visit type B will occur every 6 months starting with 6 months after visit 66 continuing up to 3 years of this schedule, and then every 3 months thereafter. This follow-up visit may be performed for participants who have not met criteria to transition to Schedule 2 or Schedule 3 (see Protocol Section 3.3 and HVTN 804/HPTN 095 SSP for details).

[10] Additional weekly viral load monitoring may be required between weeks 8 and 24; after week 24, a confirmatory sample should be drawn at the next visit (within approximately 1-2 weeks) following the first VL result ≥ 200 copies/mL (see Protocol Section 3.3.3 and HVTN 804/HPTN 095 SSP for details). The 56-day blood draw limit does not include up to 10mL blood collected per visit for this additional monitoring; however, the 56-day limit is not exceeded at any visit by these collections.

[11] A confirmatory sample should be drawn at the next visit (within approximately 1-2 weeks) following the first CD4+ T-cell count < 350 cells/mm^3 (see Protocol Section 3.3.3 and HVTN 804/HPTN 095 SSP for details).

[12] For persons capable of becoming pregnant, pregnancy test may be performed on urine or blood specimens.

[13] At an early termination visit for a withdrawn or terminated participant (see Section 6.5), blood should be drawn as shown for Extended follow-up visit type A (see HVTN 804/HPTN 095 SSP for more information).

[14] SARS-CoV-2 testing may be performed at the screening visit and at any other visit, if clinically indicated. Testing must be by direct detection of SARS-CoV-2 (eg, nucleic acid or antigen detection). See HVTN 804/HPTN 095 SSP for more information.

y = SST blood collected for neutralizing antibody will also cover specimen needs for FcR-mediated effector functions; no separate blood draw is needed.

z = PBMC blood collected for ICS will also cover specimen needs for phenotyping; no separate blood draw is needed.

Appendix F Laboratory procedures—Schedule 2: Monitoring ATI with viremia (continued)

Procedure	Ship to[1]	Assay location[1,2]	Tube Type[3]	Tube size (vol. capacity)[3]	Visit:	56	57	58	59	60	61	62	63	64	65	66	Visit Type A[8,13]	Visit type B[9]	Total
					Days on ATI with viremia	D168	D182	D196	D210	D224	D238	D252	D280	D308	D336	D364			
					Weeks on ATI with viremia	W24	W26	W28	W30	W32	W34	W36	W40	W44	W48	W52			
BLOOD COLLECTION																			
Screening or diagnostic assays																			
HIV PCR viral load[10]	Local labs	Local labs	EDTA	6mL		6	6	6	6	6	6	6	6	6	6	6	6	6	174
CD4+/CD8+ T-cell count[11]	Local labs	Local labs	EDTA	4mL		4	—	4	—	4	—	4	—	4	—	4	4	4	64
Safety labs																			
Hgb / ANC / PLT	Local labs	Local labs	EDTA	4mL		4	—	4	—	4	—	4	—	4	—	4	4	4	56
ALT / direct bilirubin / eGFR	Local labs	Local labs	SST	5mL		5	—	5	—	5	—	5	—	5	—	5	5	5	70
Syphilis[7]	Local labs	Local labs	SST	5mL		5	—	5	—	5	—	5	5	5	5	5	5	5	80
Drug levels																			
ARV detection	CSR	TBD	EDTA	4mL		4	—	4	—	4	—	4	4	4	4	4	4	4	60
Immunogenicity & Virologic Assays																			
Cellular assays																			
ICS	CSR	HVTN labs	ACD	8.5mL		42.5	—	42.5	—	42.5	—	42.5	42.5	42.5	42.5	42.5	—	—	637.5
Phenotyping	CSR	HVTN labs	ACD	8.5mL		z	—	z	—	z	—	z	z	z	z	z	—	—	0
Humoral assays																			
Neutralizing antibody	CSR	HVTN labs	SST	8.5mL		8.5	—	8.5	—	8.5	—	8.5	8.5	8.5	8.5	8.5	—	—	127.5
FcR-mediated effector functions[4]	CSR	HVTN labs	SST	8.5mL		y	—	y	—	y	—	y	y	y	y	y	—	—	0
Storage																			
Serum	CSR		SST	8.5mL		—	—	—	—	—	—	—	—	—	—	—	8.5	—	17
Plasma	CSR		EDTA	10mL		10	—	10	—	10	—	10	10	10	10	10	10	—	140
PBMC	CSR		ACD	8.5mL		17	—	17	—	17	—	17	17	17	17	17	59.5	—	263.5
Visit total						106	6	106	6	106	6	106	93	106	93	106	106	28	
56-Day total[6,10,11]						330	230	330	230	330	230	330	311	305	292	305	106	28	
URINE COLLECTION																			
Pregnancy Test[12]	Local labs	Local labs				X	X	X	X	X	X	X	X	X	X	X	X	X	
Chlamydia/gonorrhea[5,7]	Local labs	Local labs				X	—	X	—	X	—	X	X	X	X	X	X	X	
RECTAL SWAB COLLECTION																			
Chlamydia/gonorrhea[5,7]	Local labs	Local labs				X	—	X	—	X	—	X	X	X	X	X	X	X	
OROPHARYNGEAL SWAB COLLECTION																			
Chlamydia/gonorrhea[5,7]	Local labs	Local labs				X	—	X	—	X	—	X	X	X	X	X	X	X	
OTHER SPECIMEN COLLECTION																			
SARS-CoV-2 testing	Local labs	Local labs										X[14]							

[1] CSR = central specimen repository.

[2] HVTN Laboratories include: Fred Hutchinson Cancer Research Center (Seattle, Washington, USA); Duke University Medical Center (Durham, North Carolina, USA). Non-HVTN laboratories: TBD.

[3] Local labs may assign appropriate alternative tube types for locally performed tests.

[4] FcR-mediated effector function assays may include ADCC, virion capture, and phagocytosis assays.

[5] Chlamydia/gonorrhea testing will be done on urine, and rectal and oropharyngeal swabs.

[6] The 56-day blood draw limit also does not include visits from Schedule 1; please see HVTN 804/HPTN 095 SSP for details on prioritizing collections to avoid exceeding the 56-day limit.

[7] In addition to STI testing at the marked visits, STI testing may occur at any visit if clinically indicated.

[8] Extended follow-up visit type A will occur every 6 months starting with 3 months after visit 66 continuing up to 3 years of this schedule. This follow-up visit may be performed for participants who have not met criteria to transition to Schedule 2 or Schedule 3 (see Protocol Section 3.3 and HVTN 804/HPTN 095 SSP for details).

[9] Extended follow-up visit type B will occur every 6 months starting with 6 months after visit 66 continuing up to 3 years of this schedule, and then every 3 months thereafter. This follow-up visit may be performed for participants who have not met criteria to transition to Schedule 2 or Schedule 3 (see Protocol Section 3.3 and HVTN 804/HPTN 095 SSP for details).

[10] Additional weekly viral load monitoring may be required between weeks 8 and 24; after week 24, a confirmatory sample should be drawn at the next visit (within approximately 1-2 weeks) following the first VL result ≥ 200 copies/mL (see Protocol Section 3.3.3 and HVTN 804/HPTN 095 for details). The 56-day blood draw limit does not include up to 10mL blood collected per visit for this additional monitoring; however, the 56-day limit is not exceeded at any visit by these collections.

[11] A confirmatory sample should be drawn at the next visit (within approximately 1-2 weeks) following the first CD4+ T-cell count < 350 cells/mm^3 (see Protocol Section 3.3.3 and HVTN 804/HPTN 095 SSP for details).

[12] For persons capable of becoming pregnant, pregnancy test may be performed on urine or blood specimens.

[13] At an early termination visit for a withdrawn or terminated participant (see Section 6.5), blood should be drawn as shown for Extended follow-up visit type A (see HVTN 804/HPTN 095 SSP for more information).

[14] SARS-CoV-2 testing may be performed at the screening visit and at any other visit, if clinically indicated. Testing must be by direct detection of SARS-CoV-2 (eg, nucleic acid or antigen detection). See HVTN 804/HPTN 095 SSP for more information.

y = SST blood collected for neutralizing antibody will also cover specimen needs for FcR-mediated effector functions; no separate blood draw is needed.
z = PBMC blood collected for ICS will also cover specimen needs for phenotyping; no separate blood draw is needed.

Appendix G Laboratory procedures—Schedule 3: Follow-up on ART

				Visit:	80[7]	81	82	83	84	85	86	87	88	89	90	91[12]	92	
				Days post ART re-initiation	D0	D14	D28	D42	D56	D70	D84	D112	D140	D168	D196	D280	D364	
				Weeks post ART re-initiation:	W0	W2	W4	W6	W8	W10	W12	W16	W20	W24	W28	W40	W52	
Procedure	**Ship to[1]**	**Assay location[1,2]**	**Tube Type[3]**	**Tube size (vol. capacity)[3]**	ART re-initiation visit													**Total**
BLOOD COLLECTION																		
Screening or diagnostic assays																		
HIV PCR viral load	Local labs	Local labs	EDTA	6mL	6	6	6	6	6	6	6	6	6	6	6	6	6	78
CD4+/CD8+ T-cell count	Local labs	Local labs	EDTA	4mL	4	—	4	—	4	—	4	—	4	—	4	4	4	32
Safety labs																		
Hgb / ANC / PLT	Local labs	Local labs	EDTA	4mL	—	—	4	—	4	—	4	—	—	4	—	4	—	20
ALT / direct bilirubin / eGFR	Local labs	Local labs	SST	5mL	—	—	5	—	5	—	5	—	—	5	—	5	—	25
Syphilis[9]	Local labs	Local labs	SST	5mL	5	—	5	—	5	—	5	5[13]	5[13]	5	5[13]	5	—	45
HIV genotypic antiretroviral resistance[8]	CSR	TBD	EDTA	5mL	—	—	—	—	15	—	—	—	—	—	—	—	—	15
Immunogenicity & Virologic Assays																		
Viral isolation/sequencing	CSR	HVTN Labs	EDTA	10mL	10	10	—	—	—	—	10	—	—	10	—	10	10	60
Cellular assays																		
ICS	CSR	HVTN Labs	ACD	8.5mL	—	—	—	—	—	—	42.5	—	—	42.5	—	42.5	42.5	170
Phenotyping	CSR	HVTN Labs	ACD	8.5mL	—	—	—	—	—	—	z	—	—	z	—	z	z	0
Humoral assays																		
Neutralizing antibody	CSR	HVTN Labs	SST	8.5mL	—	—	—	—	—	—	8.5	—	—	8.5	—	8.5	8.5	34
FcR-mediated effector functions[4]	CSR	HVTN Labs	SST	8.5mL	—	—	—	—	—	—	y	—	—	y	—	y	y	0
HIV reservoir assays	CSR	TBD	ACD	8.5mL	34	—	—	—	—	—	—	—	—	51	—	51	51	187
Storage																		
Serum	CSR		SST	8.5mL	8.5	—	—	—	—	—	8.5	—	—	8.5	—	8.5	8.5	42.5
Plasma	CSR		EDTA	10mL	—	—	—	—	—	—	10	—	—	10	—	10	10	40
PBMC	CSR		ACD	8.5mL	42.5	—	—	—	—	—	102	—	—	51	—	51	51	297.5
Visit total					110	16	24	6	39	6	205.5	11	15	201.5	15	205.5	191.5	
56-Day total[5]						126	150	156	195	91	280.5	261.5	231.5	227.5	231.5	205.5	191.5	
URINE COLLECTION																		
Pregnancy Test[11]	Local labs	Local labs			X	X[10]	X[10]	X[10]	X[10]	X[10]	X	X[10]	X[10]	X	X[10]	X	X	
Chlamydia/gonorrhea[6,9]	Local labs	Local labs			X	—	X	—	X	—	X	X[13]	X[13]	X	X[13]	X	—	
RECTAL SWAB COLLECTION																		
Chlamydia/gonorrhea[6,9]	Local labs	Local labs			X	—	X	—	X	—	X	X[13]	X[13]	X	X[13]	X	—	
OROPHARYNGEAL SWAB COLLECTION																		
Chlamydia/gonorrhea[6,9]	Local labs	Local labs			X	—	X	—	X	—	X	X[13]	X[13]	X	X[13]	X	—	
OTHER SPECIMEN COLLECTION																		
SARS-CoV-2 testing	Local labs	Local labs									X[14]							

[1] CSR = central specimen repository.

[2] HVTN Laboratories include: Fred Hutchinson Cancer Research Center (Seattle, Washington, USA); Duke University Medical Center (Durham, North Carolina, USA). Non-HVTN laboratories: TBD

[3] Local labs may assign appropriate alternative tube types for locally performed tests.

[4] FcR-mediated effector function assays may include ADCC, virion capture, and phagocytosis assays.

[5] 56-day totals do not include visit totals from Schedule 1 or 2. Please see HVTN 804/HPTN 095 SSP for details on prioritizing collections to avoid exceeding the 56-day limit.

[6] Chlamydia/gonorrhea testing will be done on both urine, and rectal and oropharyngeal swabs; in addition, testing may occur at any visit if clinically indicated.

[7] Samples for visit 80 should be collected after ART re-initiation criteria have been met, but prior to ART re-initiation.

[8] HIV antiretroviral resistance testing will be tested only if indicated by viral load results.

[9] In addition to STI testing at the marked visits, STI testing may occur at any visit if clinically indicated.

[10] Pregnancy testing is not required if viral load has returned to undetectable.

[11] For persons capable of becoming pregnant, pregnancy test may be performed on urine or blood specimens.

[12] At an early termination visit for a withdrawn or terminated participant (see Section 6.5), blood should be drawn as shown for Visit 91 (see HVTN 804/HPTN 095 SSP for more information).

[13] Syphilis, chlamydia, and gonorrhea testing is not required at this visit if viral load has returned to undetectable.

[14] SARS-CoV-2 testing may be performed at the screening visit and at any other visit, if clinically indicated. Testing must be by direct detection of SARS-CoV-2 (eg, nucleic acid or antigen detection). See HVTN 804/HPTN 095 SSP for more information.

y = SST blood collected for neutralizing antibody will also cover specimen needs for FcR-mediated effector functions; no separate blood draw is needed.

z = PBMC blood collected for ICS will also cover specimen needs for phenotyping; no separate blood draw is needed.

Appendix H Procedures at CRS—Schedule 1: Monitoring ATI

Visit: Days on ATI: Weeks on ATI:	**01**[1] Screening	**02** ART Switch[2]	**03** ATI qualification	**04**[3] D0 W0	**05** D7 W1	**06** D14 W2	**07** D21 W3	**08** D28 W4	**09** D35 W5	**10** D42 W6	**11** D49 W7	**12** D56 W8	**13** D70 W10	**14** D84 W12	**15** D98 W14	**16** D112 W16	**17** D126 W18	**18** D140 W20	**19** D154 W22
Study procedures																			
Screening consent (if used)	✓																		
Protocol consent	✓																		
Assessment of understanding	✓																		
Medical history	✓																		
Complete physical exam	✓			✓															
Targeted physical exam[4]		✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Concomitant medications[4]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Intercurrent illness/adverse experience[4]		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
ART re-initiation assessment[4]					✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Transmission risk reduction counseling[4]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
SARS-CoV-2 risk reduction counseling[5]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Contraception status assessment[6]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Decision aid	✓																		
Decision-making assessment		✓		✓										✓					
Psychosocial assessment		✓		✓										✓					
Social impact assessment[4]				✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Social impact assessment questionnaire														✓					
QuantiFERON tuberculosis test[7]	✓																		
Confirm eligibility	✓																		
Specimen collection[8]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

[1] Screening procedures may occur over the course of several contacts/visits up to and including the day of enrollment, except for blood collection for participants not on NNRTIs, which may occur up to 14 days before enrollment, as defined in Section 6.1.2.

[2] For participants undergoing switch from NNRTI-based to protease- or integrase-based ART regimen. Participants undergoing an "ART switch" will be considered enrolled on first day of the new ART medication. The "ART switch" phase will not be performed for participants not on NNRTIs. For procedure timing during the "ART switch," see Section 6.1.3 and HVTN 804/HPTN 095 SSP.

[3] Enrollment visit for participants who do not undergo ART switch.

[4] Procedure to be performed at interim visits held to draw confirmatory viral load samples or confirmatory samples for CD4+ T cell counts (see Sections 3.3.1, 3.3.2, and 3.3.3).

[5] SARS-CoV-2 risk reduction counseling will be provided at any visit, if indicated. See HVTN 804/HPTN 095 SSP for more information.

[6] Contraception status assessment is required only for participants who were assigned female sex at birth and who can become pregnant (does not include those persons not of reproductive potential due to having undergone hysterectomy or bilateral oophorectomy [verified by medical records]).

[7] If QuantiFERON TB testing cannot be performed, a tuberculin skin test (TST) should be conducted. Additional risk/clinical/diagnostic assessment may be performed at the discretion of the clinician to meet institutional standard of care for evaluation and treatment of latent TB.

[8] For specimen collection requirements, see Appendix E.

Appendix H Procedures at CRS—Schedule 1: Monitoring ATI (continued)

Visit:	**20**	**21**	**22**	**23**	**24**	**25**	**26**	**27**	**Visit Type A[11]**	**Visit Type B[10]**
Days on ATI:	D168	D196	D224	D252	D280	D308	D336	D364		
Weeks on ATI:	W24	W28	W32	W36	W40	W44	W48	W52		
Study procedures										
Screening consent (if used)										
Protocol consent										
Assessment of understanding										
Medical history										
Complete physical exam										
Targeted physical exam[4]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Concomitant medications[4]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Intercurrent illness/adverse experience[4]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
ART re-initiation assessment[4]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Transmission risk reduction counseling[4]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
SARS-CoV-2 risk reduction counseling[5]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Contraception status assessment[6]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Decision aid										
Decision-making assessment	✓			✓				✓		✓
Psychosocial assessment	✓			✓				✓		✓
Social impact assessment[4]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Social impact assessment questionnaire	✓			✓				✓		✓
QuantiFERON tuberculosis test [7]										
Confirm eligibility										
Specimen collection[8]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

[1] Screening procedures may occur over the course of several contacts/visits up to and including the day of enrollment, except for blood collection for participants not on NNRTIs, which may occur up to 14 days before enrollment, as defined in Section 6.1.2.

[2] For participants undergoing switch from NNRTI-based to protease- or integrase-based ART regimen. Participants undergoing an "ART switch" will be considered enrolled on first day of the new ART medication. The "ART switch" phase will not be performed for participants not on NNRTIs. For procedure timing during the "ART switch," see Section 6.1.3 and HVTN 804/HPTN 095 SSP.

[3] Enrollment visit for participants who do not undergo ART switch.

[4] Procedure to be performed at interim visits held to draw confirmatory viral load samples or confirmatory samples for CD4+ T cell counts (see Sections 3.3.1, 3.3.2, and 3.3.3).

[5] SARS-CoV-2 risk reduction counseling will be provided at any visit, if indicated. See HVTN 804/HPTN 095 SSP for more information.

[6] Contraception status assessment is required only for participants who were assigned female sex at birth and who can become pregnant (does not include those persons not of reproductive potential due to having undergone hysterectomy or bilateral oophorectomy [verified by medical records]).

[7] If QuantiFERON TB testing cannot be performed (see Appendix E), TST should be conducted. Additional risk/clinical/diagnostic assessment may be performed at the discretion of the clinician to meet institutional standard of care for treatment of latent TB.

[8] For specimen collection requirements, see Appendix E.

[9] Extended follow-up visit type A will occur every 6 months starting with 3 months after visit 27, continuing up to 3 years of this schedule. This follow-up visit may be performed for participants who have not met ART re-initiation criteria (see Protocol Section 3.3 and HVTN 804/HPTN 095 SSP for details).

[10] Extended follow-up visit type B will occur every 6 months starting with 6 months after visit 27, continuing up 3 years of this schedule and then every 3 months thereafter. This follow-up visit may be performed for participants who have not met ART re-initiation criteria (see Protocol Section 3.3 and HVTN 804/HPTN 095 SSP for details).

[11] At an early termination visit for a withdrawn or terminated participant, CRS staff should consider performing procedures specified for Extended follow-up visit Type A (see Section 6.5 and HVTN 804/HPTN 095 SSP for details).

Appendix I Procedures at CRS—Schedule 2: Monitoring ATI with viremia

Visit:	**40**	**41**	**42**	**43**	**44**	**45**	**46**	**47**	**48**	**49**	**50**	**51**	**52**	**53**	**54**	**55**
Days on ATI with viremia:	D0	D7	D14	D21	D28	D35	D42	D49	D56	D70	D84	D98	D112	D126	D140	D154
Weeks on ATI with viremia:	W0	W1	W2	W3	W4	W5	W6	W7	W8	W10	W12	W14	W16	W18	W20	W22
Study procedures																
Complete physical exam	✓															
Targeted physical exam[1]		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Concomitant medications[1]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Intercurrent illness/adverse experience[1]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
ART re-initiation assessment[1]		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Transmission risk reduction counseling[1]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
SARS-CoV-2 risk reduction counseling[2]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Contraception status assessment[3]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Decision-making assessment	✓															
Psychosocial assessment	✓										✓					
Social impact assessment[1]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Social impact assessment questionnaire											✓					
Specimen collection[4]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

[1] Procedure to be performed at interim visits held to draw confirmatory viral load samples or confirmatory samples for CD4+ T cell counts (see Sections 3.3.1, 3.3.2, and 3.3.3).

[2] SARS-CoV-2 risk reduction counseling will be provided at any visit, if indicated. See HVTN 804/HPTN 095 SSP for more information.

[3] Contraception status assessment is required only for participants who were assigned female sex at birth and who can become pregnant (does not include those persons not of reproductive potential due to having undergone hysterectomy or bilateral oophorectomy [verified by medical records]).

[4] For specimen collection requirements, see Appendix F.

Appendix I Procedures at CRS—Schedule 2: Monitoring ATI with viremia (continued)

Visit:	**56**	**57**	**58**	**59**	**60**	**61**	**62**	**63**	**64**	**65**	**66**	**Visit Type A[7]**	**Visit Type B[6]**
Days on ATI with viremia:	D168	D182	D196	D210	D224	D238	D252	D280	D308	D336	D364		
Weeks on ATI with viremia:	W24	W26	W28	W30	W32	W34	W36	W40	W44	W48	W52		
Study procedures													
Targeted physical exam[1]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Concomitant medications[1]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Intercurrent illness/adverse experience[1]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
ART re-initiation assessment[1]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Transmission risk reduction counseling[1]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
SARS-CoV-2 risk reduction counseling[2]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Contraception status assessment[3]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Decision-making assessment	✓						✓				✓		✓
Psychosocial assessment	✓						✓				✓		✓
Social impact assessment[1]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Social impact assessment questionnaire	✓						✓				✓		✓
Specimen collection[4]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

[1] Procedure to be performed at interim visits held to draw confirmatory viral load samples or confirmatory samples for CD4+ T cell counts (see Sections 3.3.1, 3.3.2, and 3.3.3).

[2] SARS-CoV-2 risk reduction counseling will be provided at any visit, if indicated. See HVTN 804/HPTN 095 SSP for more information.

[3] Contraception status assessment is required only for participants who were assigned female sex at birth and who can become pregnant (does not include those persons not of reproductive potential due to having undergone hysterectomy or bilateral oophorectomy [verified by medical records]).

[4] For specimen collection requirements, see Appendix F.

[5] Extended follow-up visit type A will occur every 6 months starting with 3 months after visit 66, continuing up to 3 years of this schedule. This follow-up visit may be performed for participants who have not met ART re-initiation criteria (see Protocol Section 3.3 and HVTN 804/HPTN 095 SSP for details).

[6] Extended follow-up visit type B will occur every 6 months starting with 6 months after visit 66, continuing up 3 years of this schedule and then every 3 months thereafter. This follow-up visit may be performed for participants who have not met ART re-initiation criteria (see Protocol Section 3.3 and HVTN 804/HPTN 095 SSP for details).

[7] At an early termination visit for a withdrawn or terminated participant, CRS staff should consider performing procedures specified for Extended follow-up visit Type A (see Section 6.5 and HVTN 804/HPTN 095 SSP for details).

Appendix J Procedures at CRS—Schedule 3: Follow-up on ART

Visit:	**80**[1]	**81**	**82**	**83**	**84**	**85**	**86**	**87**	**88**	**89**	**90**	**91**	**92**[5]
Days after ART re-initiation:	D0	D14	D28	D42	D56	D70	D84	D112	D140	D168	D196	D280	D364
Weeks after ART re-initiation:	W0	W2	W4	W6	W8	W10	W12	W16	W20	W24	W28	W40	W52
Study procedures													
Complete physical exam													✓
Targeted physical exam	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Concomitant medications	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Intercurrent illness/adverse experience	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Transmission risk reduction counseling	✓	✓	✓		✓		✓		✓		✓		✓
SARS-CoV-2 risk reduction counseling[2]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Contraception status assessment[3]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Decision-making assessment	✓						✓			✓			✓
Psychosocial assessment	✓						✓			✓			✓
Social impact assessment	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Social impact assessment questionnaire							✓			✓			✓
Specimen collection[4]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

[1] ART re-initiation visit.

[2] SARS-CoV-2 risk reduction counseling will be provided at any visit, if indicated. See HVTN 804/HPTN 095 SSP for more information.

[3] Contraception status assessment is required only for participants who were assigned female sex at birth and who can become pregnant (does not include those persons not of reproductive potential due to having undergone hysterectomy or bilateral oophorectomy [verified by medical records]). Contraception status assessment is not required if participant VL has returned to undetectable.

[4] For specimen collection requirements, see Appendix G.

[5] At an early termination visit for a withdrawn or terminated participant, CRS staff should consider performing procedures specified for Visit 92 (see Section 6.5 and HVTN 804/HPTN 095 SSP for more details).

Protocol modification history

Protocol modifications are made via clarification memos, letters of amendment, or full protocol amendments. The version history of, and modifications to, Protocol HVTN 804/HPTN 095 are described below.

Date: August 27, 2021

Protocol version: Version 2.0
Protocol modification: Letter of Amendment 01

Item 1 Added in Section 5.2, *Exclusion criteria,* Section 6.1.1, *Screening,* Section 6.1.3, *ART switch,* Section 6.1.4*, ATI,* Section 6.2, *Schedule 2: Monitoring ATI with viremia,* Section 6.3, *Schedule 3: Follow-up on ART,* Section 10.1.1, *Risks of ATI*, Section 14, *Acronyms and abbreviations*, Appendix A: *Sample informed consent form*, and Appendices D through J: monitoring for SARS-CoV-2 infection during the study

Item 2 Updated in Section 2.10, *The necessity of the AMP placebo control group* and Appendix A, *Sample Informed Consent Form*: AMP participants have been unblinded

Item 3 Deleted in Appendices D, H, and I: non-relevant footnotes

Item 4 Corrected in Section 6.1, *Schedule 1: Monitoring ATI*, and Section 6.3, *Schedule 3: Follow-up on ART*: cross reference to contraception status section

Item 5 Corrected in Appendix J, *Procedures at CRS—Schedule 3: Follow-up on ART*: placement of footnote 4 to visit 92 column

Item 6 Updated in Section 1.3, *Protocol team*: protocol leadership members

Date: March 16, 2020

Protocol version: 2.0
Protocol modification: Full Protocol Amendment 1

Item 1 Clarified in Section 1, *Protocol summary*: Study population description

Item 2 Revised in Sections 3.3.1 through 3.3.3 and in footnotes to Appendices E and F: Timing for viral load and CD4 count confirmatory testing

Item 3 Revised in Sections 5.1, *Inclusion criteria* and 5.2, *Exclusion criteria*: VL assay qualification

Item 4 Updated in Sections 5.3 and 16: Document reference

Item 5 Clarified in Section 6.5 and footnote to Appendix J: Procedures at early termination visit

Item 6 Clarified in Section 11.1.1: PSRT meeting frequency

Item 7 Added in Section 11.2.3, *AE reporting*: Exception for eGFR reporting

Item 8 Removed in Section 13, *Protocol conduct*: Reference to randomization

Item 9 Updated in Section 15: Protocol version history

Item 10 Corrected and clarified in Appendix A, *Sample informed consent form*: Study objectives, ATI duration, ATI qualification visit, follow-up for those who decline ART restart, data provision to participants, follow-up till viral resuppression, lab locations, and potential other studies

Item 11 Corrected in Appendix C, *Sample consent form for use of samples and information in other studies*: Section 13 checkbox text

Item 12 Corrected in Appendix D: Table of procedures for Part 2

Item 13 Added to HVTN Laboratories in Appendices E, F, and G: Fred Hutchinson Cancer Research Center (Seattle, Washington, USA)

Item 14 Corrected in Appendix G, *Laboratory procedures—Schedule 3: Follow-up on ART*: CT/GC testing by urine at Visits 87, 88, and 90

Item 15 Corrected in Appendix H footnotes: Visit number reference and typographical error

Item 16 Corrected: Typographical and copy-editing errors

Item 17 Corrected in Section 3.3.4: Visit schedule references

Item 18 Corrected in Section 5: Study population description

Date: November 13, 2019

Protocol version: 1.0
Protocol modification: Original protocol

Protocol Signature Page

Antiretroviral analytical treatment interruption (ATI) to assess immunologic and virologic responses in participants who received VRC01 or placebo and became HIV-infected during HVTN 704/HPTN 085

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

Investigator of Record Name (print)	Investigator of Record Signature	Date

DAIDS Protocol Number: HVTN 804/HPTN 095

DAIDS Protocol Version: Version 2.0

Protocol Date: March 16, 2020