HIV VACCINE TRIALS NETWORK

HPTN HIV Prevention Trials Network

March 16, 2020

Full Protocol Amendment 1

A summary of changes to

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

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 amendment, CRSs must implement the amendment immediately.

Upon receiving final IRB/EC and any other applicable RE approval(s), CRSs are required to submit amendment registration documents to the DAIDS Protocol Registration Office (PRO) at the Regulatory Support Center (RSC). CRSs will receive an Amendment Registration Notification once the DAIDS PRO verifies that all the required amendment registration

documents have been received and are complete. A Registration Notification from the DAIDS PRO is not required prior to implementing the amendment. A copy of the Amendment Registration Notification, along with this amendment 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 amendment 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 full protocol amendment.

List of changes

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

The study population description in Section 1 has been revised to more accurately describe persons who are eligible to participate in HVTN 804/HPTN 095 per the criteria listed in Sections 5.1 and 5.2.

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

In order to avoid elevated viral load readings or deviant CD4+ T cell count readings due to transient intercurrent illness rather than recrudescent HIV and because visit schedules have participants coming to the clinic every week or two throughout most of the study, guidance to clinical site staff regarding when confirmatory testing should be performed has been revised from "as soon as possible" to "at the next visit" with the qualification that this visit should take place within approximately 1-2 weeks. Additionally, site staff are referred to the protocol-specific Study Specific Procedures document for additional guidance on this point. This change has been made in protocol Sections 3.3.1, 3.3.2, and 3.3.3, in Appendix E footnotes 13 and 14, and in Appendix F footnotes 10 and 11.

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

In order to accommodate regional differences in qualification of viral load assays, inclusion criterion #17 (Section 5.1) and exclusion criterion #1 (Section 5.2) have been revised so that US volunteers must have viral load results from a CLIA or VQA-approved assay, results from assays approved as standard-of-care by regional governing bodies may be used in sites outside the US. In addition, inclusion criterion #17 has been revised to clarify that one VL test is required from each of the two time periods specified in the bulleted list.

Item 4 Updated in Sections 5.3 and 16: Document reference

Guidance for clinical research site staff regarding participant relocation and possibilities of remote follow-up is found in the Antibody Manual of Operation (MOP) in addition to the Study Specific Procedures. Accordingly, reference to this MOP has been added to the seventh bullet in Section 5.3. The Ab MOP has also been added to the document list in Section 16.

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

In order to complete comprehensive laboratory and clinical assessments at an early termination visit, the **clinical** procedures to consider have been changed (in Section

6.5 concerning early termination visits and in Appendix J footnote 4) from those specified at Week 40 (Visit 91) to those at Week 52 (Visit 92). Note that the instruction to consider Week 40 **laboratory** procedures remains in place.

Item 6 Clarified in Section 11.1.1: PSRT meeting frequency

The fourth paragraph in Section 11.1.1 has been revised to more accurately reflect the planned meeting frequency (ie, twice a month rather than every 2 weeks). In addition, an option has been added for the PSRT to meet less frequently (ie, monthly) once all participants have demonstrated viral resuppression following ART re-initiation on Schedule 3.

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

eGFR (estimated glomerular filtration rate) reporting has been added, in the fourth paragraph of Section 11.2.3, to the list of exceptions to AE reporting per the DAIDS AE grading table.

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

Because randomization does not exist in HVTN 804/HPTN 095 an example of additional instructions is not needed, parenthetical reference to randomization has been removed from the final paragraph in Section 13.

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

A Clarified in *Key information*: Safety study objective

To more clearly identify evaluation of ATI safety as a primary study objective, this has been rephrased and made a separate bullet at the beginning of the *Key information* boxed text in Appendix A.

B Removed in Section 2: Statement regarding ATI duration

The first sentence in Section 2 of Appendix A stated that study participants will be asked to stop taking HIV medication for up to 24 weeks (about 6 months). Because ATI for a participant may continue as long as they demonstrate control of viremia, this statement could mislead potential participants. In addition, information about ATI duration is conveyed accurately in Sections 9, 10, and 12 and Section 13 indicates how long most participants are expected to be in the study. Because this sentence was potentially misleading and is unnecessary, it has been removed.

C Clarified in Section 7: ATI qualification visit

Information about the "ATI qualification visit" about 4 weeks following initiation of a new ART regimen has been added as a new second paragraph in Section 7.

D Clarified in Sections 9, 10, 11, and 12: Provision of physical exam and safety lab results to participants

Text has been added in Sections 9, 10, 11, and 12 in Appendix A to indicate that results of physical exams and safety lab tests will be shared with participants.

E Clarified in Sections 9, 10, and 12: Follow-up for participants who decline to restart ART

For consistency with protocol Section 3.3.4, text has been added in Sections 9, 10, and 12 indicating that participants who meet criteria for ART re-initiation but who decline to do so will be asked to continue clinic visits on their current schedule and that additional visits may be required.

F Corrected in Section 10: Typographical error

In the first paragraph of Section 10 the number of visits over the first 8 weeks in Schedule 2 has been corrected..

G Clarified in Section 11: Follow-up schedule until viral suppression following ART re-initiation

Text has been added to Section 11 to clarify that participants who do not demonstrate viral resuppression within 12 weeks following ART re-initiation will be asked to continue biweekly clinic visits until viral resuppression is achieved.

H Clarified in Section 14: Locations of sample testing

Text indicating the location of laboratories to which participant samples may be shipped for testing has been added as a new first paragraph in Section 14 of Appendix A. In addition, the header sentence for this section has been revised to refer to all endpoint assays (and to all endpoint laboratories), not just those that may perform genetic testing. The former header line has been inserted at the beginning of the second paragraph, which discussed potential genetic testing.

I Clarified in Section 15 of Appendix A and Section 1 of Appendix C:

In Item 15 of Appendix A and in Item 1 of Appendix C, text has been revised to clarify that disposition of extra samples is the responsibility of the HVTN and HPTN. In addition, in Item 15 of Appendix A and in Item 8 of Appendix C, a sentence indicating what information may be shared has been revised to clarify reference to the AMP study product.

J Clarified in Section 25: Other studies using extra samples and information

Reference to "monoclonal antibodies" has been added to the first check box in Section 25 for consistency with the list in Section 15 of studies that may be performed using extra samples and information.

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

The first check box in Section 13 has been revised for consistency with the first sentence in Section 9, which lists the types of studies that may be performed using extra samples and information.

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

The header above the visit schedule in the procedure tables in Appendix D for Schedule 2 inadvertently and incorrectly replicated the header in the tables for Schedule 1. This error has been corrected.

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

The HVTN endpoint laboratories at the Fred Hutchinson Cancer Research Center were inadvertently omitted from the listing of HVTN Laboratories in footnote 2 to the tables in Appendices E, F, and G. This omission has been corrected.

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

Throughout protocol HVTN 804/HPTN 095, tests for Chlamydia and gonorrhea are performed on urine, rectal swabs, and oropharyngeal swabs. However, urine testing was inadvertently omitted at visits 87, 88, and 90 in Appendix G, *Laboratory procedures—Schedule 3: Follow-up on ART*. This omission has been corrected.

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

A typographical error in footnote 2 and an erroneous visit number reference in footnotes 8 and 9 have been corrected.

Item 16 Corrected: Typographical and copy-editing errors

Minor typographical errors, incomplete cross-references, team member email addresses, a small portion of inapplicable text, and deviations from style standards

(eg, failure to define acronyms at first use, failure to superscript exponents, inconsistent character spacing) have been corrected.

Item 17 Corrected in Section 3.3.4: Visit schedule references

Section 3.3.4 has been revised to refer to "Schedule 1 or Schedule 2" for participants who decline to re-initiate ART upon meeting protocol criteria for doing so. This correction reconciles an inconsistency with text in Sections 9 and 12 in Appendix A.

Item 18 Corrected in Section 5: Study population description

The first sentence in Section 5, *Study population*, has been revised for consistency with the description of the study population in Section 1, *Protocol summary*, and with the eligibility criteria in Sections 5.1 and 5.2.

Protocol modification history

Protocol modifications are made to HVTN protocols via clarification memos, letters of amendment, or full protocol amendments. HVTN protocols are modified and distributed according to the standard HVTN procedures as described in the HVTN Manual of Operations (MOP).

The version history of, and modifications to, Protocol HVTN 804/HPTN 095 are described below.

Date: March 16, 2020

Protocol version: Version 2.0
Protocol modification: Full Protocol Amendment 1

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Item 4 Updated in Sections 5.3 and 16: Document reference

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

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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: NA

Original protocol