FINAL

January 20, 2022

Clarification memo 1

Protocol

Version 1.0

HVTN 805/HPTN 093

Antiretroviral analytical treatment interruption (ATI) to assess immunologic and virologic responses in participants who initiated ART in early HIV infection after having received VRC01 or placebo in HVTN 703/HPTN 081

DAIDS-ES ID 38691

NON-IND PROTOCOL

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

Please distribute this clarification memo to all appropriate staff members, and file with your protocol documents. Consult your local Institutional Review Board (IRB)/Ethics Committee (EC) regarding submission requirements for clarification memos.

List of changes

The changes described herein will be incorporated in the next version of Protocol HVTN /HPTN if it undergoes full protocol amendment at a later time. New text is denoted in **bold underline**, deleted text in ~~strikethrough.~~

Item 1 Corrected in Appendix E, *Laboratory Procedures—Schedule 1: Monitoring ATI:* footnote 9

Footnote 9 in Appendix E, Laboratory Procedures- Schedule 1: Monitoring ATI, has been revised to correct an error. The number of days available for ATI Qualification Procedure prior to visit 4, was corrected from ~~14~~ to **28**, to harmonize with Appendix K: *Visit Windows*.

Footnote 9:

> [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~~**28** days prior to visit 4 (see HVTN 805/HPTN 093 SSP for more information).

The Laboratory Procedures Table with the revised footnote is appended below.

Appendix E Laboratory procedures—Schedule 1: Monitoring ATI

Procedure	Ship to[1]	Assay location[1,2]	Tube Type[3]	Tube size (vol. capacity)[3]	Days on ATI: / Weeks on ATI: Screening visit[15]	ART Switch[8]	ATI qualification[9]	D0 W0 ATI	D7 W1	D14 W2	D21 W3	D28 W4	D35 W5	D42 W6	D49 W7	D56 W8	D70 W10	D84 W12	D98 W14	D112 W16	D126 W18	D140 W20	D154 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	—
Hormone Levels																							
Hormone panel	Local labs	Local labs	SST	5mL	—	—	—	w	—	—	—	w	—	—	—	w	—	w	—	w	—	—	—
Drug levels/detection																							
ARV detection by dry blood spot	CSR	HVTN labs	EDTA	2mL	—	—	—	—	—	—	—	2	—	—	—	2	—	2	—	2	—	2	—
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	77	6	10	6	104	6	104	6	104	6	104	6
56-Day total					38	57	76	210.5	216.5	226.5	232.5	309.5	315.5	325.5	331.5	397.5	225	313	236	324	226	324	226
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]	Local labs	Local labs			X	—	—	X	—	—	—	X	—	—	—	X	—	X	—	X	—	X	—
CERVICAL/VAGINAL SWAB COLLECTION																							
Chlamydia/gonorrhea[7]	Local labs	Local labs			X	—	—	X	—	—	—	X	—	—	—	X	—	X	—	X	—	X	—
Trichomonas vaginalis[7]	Local labs	Local labs			X	—	—	X	—	—	—	X	—	—	—	X	—	X	—	X	—	X	—
OTHER SPECIMEN COLLECTION																							
SARS-CoV-2 testing	Local labs	Local labs			X[18]																		

[2] HVTN Laboratories include: Fred Hutchinson Cancer Research Center (Seattle, Washington, USA); Duke University Medical Center (Durham, North Carolina, USA); South African Immunology Laboratory-National Institute for Communicable Diseases (SAIL-NICD, Johannesburg, South Africa); University of Cape Town (Cape Town, South Africa); Cape Town HVTN Immunology Laboratory (CHIL, Cape Town, South Africa).

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 and may require an additional blood collection.

[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 EITHER urine OR a cervical/vaginal swab; Trichomonas testing will be done on cervical/vaginal swab. In addition to STI testing at the marked visits, STI testing may occur at any visit if clinically indicated. In addition to the listed specimen types (ie, cervical/vaginal swabs), chlamydia/gonorrhea testing may occur on rectal swabs if clinically indicated (see HVTN 805/HPTN 093 SSP for details).

[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 28 days prior to visit 4 (see HVTN 805/HPTN 093 SSP for more information).

[10] In addition to syphilis testing at the marked visits, syphilis 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 805/HPTN 093 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 805/HPTN 093 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 and HVTN 805/HPTN 093 SSP for details).

[14] A confirmatory sample should be 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 and HVTN 805/HPTN 093 SSP 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 805/HPTN 093 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 Protocol Section 6.5), blood should be drawn as shown for Extended follow-up visit type A (see HVTN 805/HPTN 093 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 805/HPTN 093 SSP for more information.

w = SST blood collected for syphilis testing will also cover specimen needs for HBsAg and anti-HCV screening testing. Hormone panel is defined in Protocol Sections 6.1 (Schedule 1: Monitoring ATI) and 6.2 (Schedule 2: Monitoring ATI with viremia).

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.

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 805/HPTN 093 are described below.

Date: January 20, 2022

Protocol version: Version 1.0
Protocol modification: Clarification Memo 1

Item 1 Corrected in Appendix E, *Laboratory Procedures—Schedule 1: Monitoring ATI:* footnote 9

Date: August 27, 2021

Protocol version: Version 1.0
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 Corrected in Section 5.2, *Exclusion criteria*: cardiac or cerebrovascular disease criterion

Item 3 Updated in Appendix A, *Sample Informed Consent Form*: AMP participants currently being unblinded

Item 4 Deleted in Appendices D, H, and I: non-relevant footnotes

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: April 27, 2020

Protocol version: 1.0
Protocol modification: NA

Original protocol