November 26, 2019

Letter of Amendment 1

Protocol

Version 1.0

HVTN 130/HPTN 089

A phase 1 clinical trial to evaluate the safety, tolerability, pharmacokinetics, and antiviral activity of combinations of monoclonal antibodies PGT121, PGDM1400, 10-1074, and VRC07-523LS administered via intravenous infusion in healthy, HIV-uninfected adult participants

DAIDS-ES ID 38531

[IND #143616—HELD BY DAIDS]

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

The following information impacts the HVTN 130/HPTN 089 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.

List of changes

The changes described herein will be incorporated in the next version of Protocol HVTN 130/HPTN 089 if it undergoes full protocol amendment at a later time.

Item 1 Laboratory staff blinding removed in Section 6.3, *Blinding*

In planning laboratory assays for protocol HVTN 130/HPTN 089, it was recognized that requiring Laboratory program staff to remain blinded during sample analysis in this otherwise open label trial would necessitate performance of multiple redundant and meaningless assays. Since many assays are study product specific and lab program staff were not to know which study products participants had received, the labs would have to perform all assays for all study product combinations on samples from all participants. Given the consequent delays and expense, it was determined that the costs of maintaining this blind vastly outweighed any potential benefits. Accordingly, Section 6.3 has been revised to indicate that laboratory program staff, like study participants and site staff, will be unblinded to participant group assignments. In addition, since this study is now entirely open label, a reference to unblinding in Section 12 has been removed. These changes are shown below (deletions shown by ~~strikethrough~~; added text in **bold underline**).

A Revised in Section 6.3

Revised:

6.3 Blinding

Participants**,** ~~and~~ CRS staff**, and laboratory program staff** will be unblinded to participant group assignments. ~~Laboratory program staff will remain blinded during sample analysis.~~

B Revised in Section 12

Revised:

This protocol and all actions and activities connected with it will be conducted in compliance with the principles of GCP (ICHe6), and according to DAIDS, HVTN and HPTN policies and procedures as specified in the network-specific Manuals of Operations, DAIDS Clinical Research Policies, and Standard Procedures Documents including procedures for the following:

…

- ~~Unblinding of staff and participants;~~

Item 2 Updated in Section 1.1, *Protocol Team*: DAIDS Medical Officer

Section 1.1 has been updated to reflect a change in one of the Medical Officers for this protocol.

Previous:

DAIDS Medical officer	David Burns DAIDS, NIAID 301-435-8896 david.burns@nih.gov

Revised:

DAIDS Medical officer	Wairimu Chege DAIDS, NIAID 240-292-4786 wairimu.chege@nih.gov

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 130/HPTN 089 are described below.

Date: November 26, 2019

Protocol version: Version 1.0
Protocol modification: Letter of Amendment 1

Item 1 Laboratory staff blinding removed in Section 6.3, *Blinding*

Item 2 Updated in Section 1.1, *Protocol Team*: DAIDS Medical Officer

Date: June 17, 2019

Protocol version: Version 1.0
Protocol modification: Clarification Memo 2

Item 1 Clarified in Sections 4.3 and 11.3.3: Enrollment in Group 4 restricted to one participant per day across all CRSs for first 6 participants

Date: May 22, 2019

Protocol version: Version 1.0
Protocol modification: Clarification Memo 1

Item 1 Corrected in Section 8.3.1.2, *PGT121 intravenous infusion preparation,* Section 8.3.4.2, *VRC07-523LS intravenous infusion preparation,* and Section 8.5, *Acquisition of study products*: Typographical errors related to Sodium Chloride for Injection, 0.9% USP

Item 2 Added to Title page: IND number

Date: April 04, 2019

Protocol version: Version 1.0
Protocol modification: NA

Original protocol

Protocol Signature Page

A phase 1 clinical trial to evaluate the safety, tolerability, pharmacokinetics, and antiviral activity of combinations of monoclonal antibodies PGT121, PGDM1400, 10-1074, and VRC07-523LS administered via intravenous infusion in healthy, HIV-uninfected adult participants

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 130/HPTN 089

DAIDS Protocol Version: Version 1.0

Protocol Date: April 4, 2019