



March 26, 2020

Clarification Memo 3

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 DOCUMENT ID 38531

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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

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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 Clarified in Section 9.9, *Visit windows and missed visits: Allowable visit windows*

In order to address the impact of the current COVID-19 pandemic on clinical site operations and to enhance site flexibility to follow public health guidelines aimed at maximizing participant and staff safety, allowable visit windows have been expanded, as shown below (revised text shown in **bold**).

Previous

9.9 Visit windows and missed visits

Target visit windows for follow-up visits have been chosen to ensure the viability of robust PK calculations and cross-protocol comparison. As such, Visits 3 and 4 should be done on Day 3 and 6 on target days; target windows for Visit 5 through visits 24 weeks after the final infusion (ie, Visit 11 for Groups 1-3 and Visit 13 for Group 4) are ± 3 days. The target window expands to ± 7 days for all remaining follow-up visits. The target window for the second infusion visit in Group 4 (Visit 9) is ± 7 days. Broader allowable visit windows are shown below:

- For Groups 1-3: Visit 3 (-2, +1 day(s)), Visit 4 (± 2 days), Visits 5, 6, 7, 9, and 11 (± 7 days), and Visits 12, 13, and 14 (± 14 days)
- For Group 4: Visit 3 (-2, +1 day(s)), Visit 4 (± 2 days), Visits 5, 6, 7, 8, 10, 11, 12, and 13 (± 7 days), and Visits 9, 14, 15, and 16 (± 14 days)

All follow-up visits should take place within the target visit windows. The expanded allowable visit windows may be utilized only if the visit cannot be scheduled within the target visit window. Visits scheduled outside the allowable visit windows are considered protocol deviations. Visit windows are defined in greater detail in the HVTN 130/HPTN 089 SSP.

If a participant misses a scheduled visit, the CRS staff should attempt to bring the participant in as soon as possible to complete the required safety assessments and other procedures. The procedures for documenting missed visits and out of window visits are described in the HVTN 130/HPTN 089 SSP.

If a missed visit required study product administration or if study product administration must be permanently discontinued, please refer to Section 7.3.2 for resolution.

Revised:**9.9 Visit windows and missed visits**

Target visit windows for follow-up visits have been chosen to ensure the viability of robust PK calculations and cross-protocol comparison. As such, Visits 3 and 4 should be done on Day 3 and 6 on target days; target windows for Visit 5 through visits 24 weeks after the final infusion (ie, Visit 11 for Groups 1-3 and Visit 13 for Group 4) are ± 3 days. The target window expands to ± 7 days for all remaining follow-up visits. The target window for the second infusion visit in Group 4 (Visit 9) is ± 7 days. Broader allowable visit windows are shown below:

- For Groups 1-3: Visit 3 (-2, +1 day(s)), Visit 4 (± 2 days), Visits 5, 6, 7, and 9 (± 7 days), **Visit 11 (± 21 days)**, and Visits 12, 13, and 14 (± 28 days)
- For Group 4: Visit 3 (-2, +1 day(s)), Visit 4 (± 2 days), Visits 5, 6, 7, and 8 (± 7 days), **Visits 9, 10, 11, 12, and 13 (± 21 days)**, and Visits 14, 15, and 16 (± 28 days)

All follow-up visits should take place within the target visit windows. The expanded allowable visit windows may be utilized only if the visit cannot be scheduled within the target visit window. Visits scheduled outside the allowable visit windows are considered protocol deviations. Visit windows are defined in greater detail in the HVTN 130/HPTN 089 SSP.

If a participant misses a scheduled visit, the CRS staff should attempt to bring the participant in as soon as possible to complete the required safety assessments and other procedures. The procedures for documenting missed visits and out of window visits are described in the HVTN 130/HPTN 089 SSP.

If a missed visit required study product administration or if study product administration must be permanently discontinued, please refer to Section 7.3.2 for resolution.

Item 2 Clarified throughout protocol: “Clinic visits”

Throughout the protocol, “clinic visits” for data collection and procedures (scheduled and ad hoc) may be conducted by phone, text message, email, or other electronic means. An in-person clinic visit is required only for physical exam, point-of-care testing, collecting biological samples, or administering study agents.

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: March 26, 2020

Protocol version: Version 1.0

Protocol modification: Clarification Memo 3

- Item 1 Clarified in Section 9.9, *Visit windows and missed visits*: Allowable visit windows
- Item 2 Clarified throughout protocol: “Clinic visits”

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