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April 15, 2020

Clarification Memorandum # 2 to HIVTR-CCR5 Protocol Version 4.0 (2.28.19)

To: HIVTR-CCR5 Principal Investigators
HIVTR-CCR5 Study Coordinators

From: Rodney Rogers, Project Manager, UCSF

Protocol Title: Impact of CCR5 Blockade in HIV+ Kidney Transplant Recipients

Protocol ID# DAIDS-ES 20730

Principal Investigator: Peter Stock, MD, PhD

RE: COVID-19 Related Guidelines and Clarifications (Revision of March 19th Standard Memo)

This clarification memo does not result in a change in the protocol informed consent document. The Division of AIDS does not require you to forward it to your IRB; however, as always, you must follow your IRB's policies and procedures. If IRB review of clarification memos is required at your site, please submit this document for review. Each site should file a copy of this clarification memo with the protocol for reference. The protocol clarifications contained in this memo should be implemented immediately. These updates will be included in the next version of the protocol if it is amended at a future date.

AE REPORTING

Report all cases of COVID-19 as a Serious Adverse Event regardless of grade. If no other serious criteria are met, the event should be considered of medical importance and reported in the Emmes IDES as well as the DAERS. Also, complete an Infection Form.

Include the following information in the SAE report:

- Indicate the source of the sample used for SARS CoV2 PCR – such as nasopharyngeal swab or wash, saliva bronchoalveolar lavage, blood.
- Findings from Chest x-ray, CT scan or other imaging studies.
- Nadir O2 saturation and current O2 saturation.
- Suspected exposures such as dialysis or recent travel.
- Therapy for COVID-19 including supportive care and experimental therapy e.g. hydroxychloroquine.

COVID-19 RELATED PROTOCOL DEVIATIONS AND EMMES IDES REQUIREMENTS

All COVID-19 related protocol deviations must be documented in the source documents as well as the Emmes IDES. It is critical that sites include that the deviation is related to COVID-19 so that the sponsor, data center, and your institution can satisfy FDA recommendations for documentation during the COVID-19 outbreak and to ensure you are following GCP standards. Examples of COVID-19 related protocol deviations include (but are not limited to):

- Study visit conducted remotely (phone/video) and not in person (***Visit Form – Comments***)
- Missed visit due to COVID-19 travel restrictions and inability to conduct remotely (***Visit Form – Specify reason for visit not occurring***)
- A missed essential test that impacts the ability to evaluate the protocol endpoints. (***Protocol Deviation Form plus Missing Value Exemption Request Reason***) Please obtain even if out of window when possible, but be sure to document appropriately
    - 6 month protocol biopsy
    - Cystatin C sample send outs to Covance
    - eGFR
    - Iohexol study at week 52
- Any other missed reporting or test deviation outlined in section "13.2 Protocol Deviations" of the Manual of Procedures ***(Protocol Deviation Form)***
- Note that missed important tests collected for primary/secondary endpoint assessments (such as iohexol clearance at year 1, protocol biopsy at 6 months, measures of kidney function (Cystatin C and eGFR) at months 3, 6, 9, years 1, 2, 3) should be attempted to be subsequently collected whenever possible, despite being out of visit window.

NEW ENROLLMENTS

Enrollment may continue in the HIVTR-CCR5 trial. Sites should consider site COVID-19 specific guidelines and policies during the COVID-19 outbreak, which may introduce barriers to accrual. However, the sponsor is not specifically halting accrual and defers to sites to follow all federal, local and institutional safety guidelines when considering new enrollments.

If you are not able to obtain the baseline research recipient blood, urine, lymph or donor spleen sample(s) for new enrollments during COVID-19 site restrictions, this will be a COVID-19 related major deviation but will not prohibit enrollment into the trial, and future post-transplant research sample collections should continue as possible even in the absence of the pre-transplant research baseline sample(s).

STUDY PRODUCT

For rare instances or emergency cases, the *Pharmacy Guidelines and Instructions for DAIDS Clinical Trials Networks*, which your HIVTR-CCR5 Pharmacist of Record (PoR) has on file, permits shipment or courier of study product from the site directly to participants. This method should only be used on a short-term basis and only if permissible by the site's institution. If this

method is to be implemented, each site's PoR must develop appropriate procedures for the shipment or courier of study product to identified participants in accordance with these guidelines and document chain of custody. Prior to implementation, the site PoR must coordinate with site clinic staff to determine the appropriateness of this method for HIVTR-CCR5 protocol and participants.

Any protocol-specific, study product-related queries should be directed to the DAIDS PAB Protocol Pharmacist, Katherine Shin at (240) 627-3047 or kashin@niaid.nih.gov.

Any changes to site pharmacy processes or procedures in response to the COVID-19 pandemic should be clearly documented and maintained in site pharmacy files.