

Clarification Memo # 1 to:

HPTN 077: A Phase IIa Study to Evaluate the Safety, Tolerability and Pharmacokinetics of the Investigational Injectable HIV Integrase Inhibitor, GSK1265744, in HIV-uninfected Men and Women, Version 1.0, May 1, 2014, DAIDS Document ID: 11964, IND # 122,744

Final Version of Clarification Memo # 1: 05 August 2014

Summary of Revisions and Rationale

This memorandum clarifies that the randomization process will stratify participants by gender and by region (US sites vs. non US sites). The protocol inadvertently did not specify that stratification will occur by region in addition to gender.

Implementation

The procedures clarified in this memorandum have been approved by the Division of AIDS (DAIDS) Medical Officer and are to be implemented immediately upon issuance. IRB/EC approval of HPTN 077 Protocol Clarification Memo # 1 to HPTN 077 V. 1.0 is not required by DAIDS; however, sites may submit the clarification memo to the responsible IRBs/ECs for their information.

No change in the informed consent forms is necessitated by or included in this Clarification Memo.

The modifications included in this Clarification Memo will be incorporated into the next full protocol amendment. Text noted below by strikethrough will be deleted; text appearing below in **bold** will be added. The modifications are also highlighted in yellow for ease of reference.

Revision 1 Section 7.1 – Review of Study Design

This is a Phase IIa, randomized, multi-site, two-arm, double-blinded study of the safety, tolerability, pharmacokinetics and acceptability of 744LA. Eligible participants will be randomized 3:1, stratified by gender **and region (US and non US sites)**, to receive GSK1265744 or matching placebo. Participants will receive daily 30 mg oral 744 tablets or matching placebo for 4 weeks, followed by a one week washout period, to assess for safety and tolerability prior to receiving injections. Following clinical review of safety lab assessments from the oral regimen phase, participants will enter the injection phase and receive IM injections of 744LA or placebo at three time points at 12 week intervals. IM injections will consist of 800 mg of 744LA or a matching vehicle control, and administered as two 400 mg injections. Participants in the active drug arm will be followed for 52 weeks following their last injection. Participants in the placebo arm will be followed until 52 weeks after their last injection or until the last participant in the active study product arm completes their Week 41 visit, whichever comes first, at which time the study will be unblinded to assess the primary endpoint. When all procedures related to unblinding are completed, participants in the placebo arm will no longer be followed.

176 participants will be randomized 3:1, stratified by gender **and region (US and non US)**, as follows:

Revision 2 Section 7.4 – Random Assignment

Enrolled participants will be **randomized to one of two study arms with an active GSK1265744 to placebo ratio of assigned 3:1. The arm randomization will be at random to one of two study arms** stratified by gender **and region (US and non-US sites) and done in blocks to ensure balanced treatment assignments within each gender and region.** The randomization scheme will be generated, operationalized and maintained by the HPTN SDMC. Additional details regarding the process of randomization will be included in the SSP Manual.