

HPTN 052 Study Monitoring Committee Review

Review Date: 26 May 2006

10:00am – 12:00pm ET

DRAFT SUMMARY OF COMMENTS AND RECOMMENDATIONS

Participating SMC Reviewers:

Tom Fleming, SMC Chair, University of Washington
Jim Hughes, SMC Co-Chair, University of Washington
Ward Cates, HPTN CORE, Family Health International (FHI)
Mary Fanning, Division of AIDS (DAIDS), National Institutes of Health
Chuck Hicks, Duke University

HPTN 052 Protocol Chairs/Site Representatives:

Mike Cohen, University of North Carolina
David Celentano, Johns Hopkins University/RIHES, Baltimore MD
Sheela Godbole, National AIDS Research Institute, Pune, India
Mina Hosseinipour, UNC Project, Lilongwe, Malawi
Kenneth Mayer, Fenway Community Health, Boston, MA, U.S.A.
Taha Taha, Johns Hopkins/Malawi College of Medicine Project, Blantyre, Malawi
James Hakim, University of Zimbabwe Clinical Research Center, Harare, Zimbabwe
Breno Santos, Hospital Nossa Senhora da Conceição, Porto Alegre, Brazil

Observers:

David Burns, DAIDS
Mary Fanning, DAIDS
Estelle Piwowar-Manning, HPTN CL
Drew Edwards, SCHARP
Ben Masse, SCHARP
Ying Chen, SCHARP
Geetha Beauchamp, SCHARP

Lei Wang, SCHARP
Missie Allen, HPTN CORE, FHI
Nirupama Sista, HPTN CORE, FHI
Marybeth McCauley, HPTN CORE, FHI
Carolyn Yanavich, HPTN CORE, FHI
Theresa Gamble, HPTN CORE, FHI
Jackie Talley, HPTN CORE, FHI

Formatted: German (Germany)

Formatted: Italian (Italy)

SUMMARY OF COMMENTS AND RECOMMENDATIONS:

The following are comments and recommendations from the Study Monitoring Committee:

- **The PIs and team members have achieved significant success in the run-in period of HPTN 052.**
- **All international sites have completed enrollment.**
 - It was noted that some sites (*e.g.* Blantyre and Porto Alegre) took longer than the intended 3 months for full accrual and that other sites achieved enrollment targets in much less than 3 months. Some of this diversity in accrual may be reflective of a site's ability to pre-screen couples for enrollment. Sites are encouraged to continue to identify couples as appropriate in preparation for the full study.
- **Fenway Community Health Center (located in Boston, MA, USA) has had difficulty fully enrolling into the run-in period due to the unwillingness of potential participants to be randomized to immediate or delayed treatment (lack of equipoise).**

- The SMC strongly encourages the site to continue with all reasonable efforts to fully enroll participants into the run-in period.
- The SMC encourages the team to seek clarification from DAIDS regarding whether the site will be allowed to initiate its enrollment into the full study at the time the international sites begin.
- **It is important to enroll a population with the intended risk level so that the study will be adequately powered to meet its primary objectives.**
 - Early data reflect that, at some sites, the Index Case and Partners are somewhat older than anticipated and, in some cases, the couples are reporting less sexual activity and higher condom use than expected.
 - It appears that sites are identifying cohorts that will achieve the targeted levels of risk over the full duration of the trial.
- **The data show some discrepancies between screening and enrollment CD4+ cell count values for some Index Cases, with all meeting the eligibility criteria of 300-500 cells/mm³ at screening, followed by a higher or lower value at enrollment.**
 - Two to three of the sites are more heterogeneous in their enrollment CD4+ cell count values than others, which may be due to cofactors such as malaria.
 - CD4 cell counts can be highly variable, and this kind of fluctuation is not necessarily reflective of a true difference in values.
 - The SMC encourages the team to continue monitoring this issue so that proper accommodations can be made, if necessary, to ensure that there is an adequate time difference between ART initiation in the two groups.
- **The retention rates are as expected at this early point in the study, with some sites experiencing a 100% retention rate.**
 - It is important for the sites to achieve the protocol target of 2-4% lost-to-follow-up on an annual basis.
 - There is some early indication that the targeted level of retention might not be achieved for individual clinic visits; however, in most of cases, the couples are facing temporary difficulties that have been subsequently resolved. The site-specific teams expect to recover the participants at future visits.
 - The SMC reiterates the importance of high levels of retention of both the Index Cases and the Partners.
- **The most recent data indicates a very high adherence to study drug (ART).**
- **The team has achieved significant successes since the time of the last meeting in the area of drug procurement.**

- It appears now that Efavirenz will be available and that, while Kaletra is still being pursued, all drugs required for the full study will be available.
- **The team intends to initiate the full study by late summer 2006.**
- **Two sites (Blantyre and Harare) have experienced on-going laboratory-related issues; however, efforts are underway at both sites to implement corrective action measures in order to resolve the issues.**