Anticipated Modifications to VOICE: Version 2.0

VOICE Team Meeting
Cape Town, South Africa
4 October 2010

Modifications in 2.0

- Previous modifications
  - CM #01 (May 2009)
  - CM #02 (August 2009)
  - LoA #01 (March 2009)
  - LoA #02 (March 2010)
- Of the above changes, not all to be retained in Version 2.0
- New modifications

Section 2: Introduction

- Results of completed effectiveness trials
  - HPTN 035
  - MDP 301
  - CAPRISA 004
- New data on TFV in pregnancy
  - MTN-002
  - Interim data from HPTN 057
  - Antiretroviral Pregnancy Registry (treatment)

Section 4: Study Design

	Version 1.0	Version 2.0
Number of participants	4200	Approximately 5000
Duration of f/u on product	12 – 33 months	12 – 36 months
Time to complete accrual	Approximately 21 mos.	Approximately 24 mos.
Weeks of f/u off product	8 additional	8 additional
Minimum study follow-up	14 months	14 months
Maximum study follow-up	35 months	38 months
Average duration product use	22.5 months	24 months

MTN
microbicide trials network

Section 5: Study Population

- Suggested change:
  - "Thorough explanation of the study visit schedule and procedural requirements during the informed consent process, and re-emphasis at each study visit. Also as part of the informed consent process, encouragement of participants to discuss potential study participation **including family planning requirements** with their husbands/partners and other influential family members."

Section 5: Study Population

- Existing clarifications re location of HIV testing algorithms, non-exclusionary non-menstrual bleeding
- Suggested change from MU-JHU
  - Allow expansion of upper limit of age range
    - New recruitment population, but will HIV incidence be adequate?
  - What are your thoughts?

Section 6: Study Product

- Previous changes related to retrieval of temporarily held or permanently discontinued study product
- Currently no new changes requested

Section 7: Study Procedures

- As previously modified, omit PBMC archive
- Moving enrollment consent to prior to final confirmation of eligibility would allow for:
  - Single blood draw on day of enrollment
  - Participants to return if run out of time
- What are your thoughts?

Section 7: Study Procedures

- Clarify procedures for HIV-infected participants who continue VOICE visits
  - Decrease ACASI (under discussion)
  - Omit gram stains
  - Omit dipstick urinalysis
  - CBC, AST, ALT, creatinine, phosphate at 8 weeks post-seroconversion, and then STOP those labs

Section 8: Assessment of Safety

- Mostly updates related to changes at NIH/DAIDS
  - Include updates to DSMB name and policy, frequency of meetings
  - Adverse event reporting requirements
  - Changes mandated by new EAE manual

Section 9: Clinical Management

- General guidelines for temporary product hold/permanent discontinuation
- Adds PSRT consultation before permanent product discontinuation
- 9.5.6 – Hypophosphatemia mgmt will be based on absolute values
- 9.6 – Proteinuria – clarification of product hold guidelines

Section 9: Clinical Management

- 9.14 Criteria for Early Termination of Study Participation
  - Clarify how eligibility to restart study product will be assessed and/or captured

Section 10: Statistical Considerations

- Number of participants
- Maximum months of study product use
- Expected person-years of f/u
- Anticipated average HIV rates
- Tables

Section 11: Data Handling and Recordkeeping

- Update references to DAIDS policies

Section 12: Clinical Site Monitoring

- Minor updates to language in bullet points

Section 13: Human Subjects Protections

- 13.2 – update protocol registration instructions
- 13.4 – Risk Benefit Statement
  - Modify to reflect content in current DAIDS risk lists and results of CAPRISA 004
  - Comment on DMC reviews to date, and lack of significant safety concerns

Section 15: Appendices

- Appendix I
  - Previous modification: omit PBMC archive
- Schedule of Post-HIV-1 Seroconversion Laboratory Procedures
  - Clarification of HBsAb following HBV vaccine series

Informed Consent: Screening

- Number of participants
- Length of screening procedures (leave blank for site-specific estimates)

Informed Consent: Enrollment

- # of participants, length of participation
- Summarize CAPRISA 004 results
- HBsAb after HBV vaccination for HIV+
- Risk lists for tablet and gel
  - Omit anxiety, add depression for oral
  - Add diarrhea for gel
- Emphasize frequent and temporary nature of mild to moderate symptoms

Enrollment Consent (cont.)

- Clarify testing done on Sample 2 blood draw
- If consensus, modify language to reflect final confirmation of eligibility following signing of enrollment consent

Informed Consent: Storage and Future Testing

- Currently no requests for modification

Miscellaneous Minor

- Roster
- Acronyms
- Formatting
- Web links

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