MTN 015:
An Observational Cohort Study of Women following HIV-1 Seroconversion in Microbicide Trials

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Rationale

- Many potential compounds, with and without specific HIV-1 inhibitory activity administered topically and orally, will be studied by the MTN
- Only limited data are available describing clinical outcomes of women following HIV-1 seroconversion during preventative microbicide trials
- It is critical to assess the short and long term impact of microbicide use in participants who become infected during product use – especially in regard to the potential for HIV-1 drug resistance

MTN 015 Hypothesis

Exposure to study agents in MTN clinical trials will not impact the natural history of HIV-1 infection as measured by the virologic, immunologic and clinical outcomes of participants with HIV-1 seroconversion during microbicide trials.

Goals and Objectives

- Overall Goal: Evaluate and monitor the virologic, immunologic and clinical outcomes of participants with HIV-1 seroconversion during microbicide trials

- Primary Objective: To compare the plasma HIV-1 RNA level 12 months after HIV-1 seroconversion among ART naïve participants assigned to an active microbicidal or chemoprophylactic agent compared to control participants

Secondary Objectives

- Many additional important comparisons:
  - HIV viral load over time
  - CD4 cell counts over time
  - HIV-related and AIDS-defining clinical events
  - HIV drug resistance
    - Plasma and cervical lavage
    - Standard and investigational assays
  - Sexual behaviors

Secondary Objectives

- Establish a repository of biological specimens for future analyses
  - Plasma
  - PBMCs
  - Vaginal swabs
  - Cervicovaginal lavage

Study Design

- **Study Population:**
  - Women who have HIV-1 seroconversion during participation in microbicide trials, including HPTN 035 (and HPTN 059)
- **Sample Size:**
  - Approximately 500 (estimated minimum 165, with 138 available for the primary objective)
- **Study Design:**
  - Prospective observational cohort

Study Visits

- Screening and Enrollment
  - As soon as possible after identification of seroconversion but anytime acceptable
- Follow-up
  - Non-ART visit schedule
    - 1, 3, 6 months and every 6 mo
  - ART visit schedule
    - 2 w, 1, 3, 6 months and every 6 mo

Evaluations

- Clinical: medical history, physical exam
- Laboratory (real-time): CD4, HIV RNA, ‘safety’ labs (CBC, LFT, creatinine), STI testing, baseline HIV drug resistance
- Behavioral questionnaires
- Repository: Plasma, PBMC, cervical lavage for future studies including resistance, HIV-specific immunity

Supportive Services

- Active referral for HIV care
  - ART
  - PMTCT
- Secondary prevention counseling
- Treatment and prevention counseling for STI for participants and partners
- Provision of condoms
- HIV counseling and testing for partners
- Contraceptive counseling; direct provision or with-in site referral for contraception

Protocol sites

- Currently opening at African 035 sites
  - Lilongwe, Malawi
  - Blantyre, Malawi
  - Harare, Zimbabwe
  - Lusaka, Zambia
  - Durban, SA
- Planned to open concurrently with MTN 001 at new African sites
  - Durban, SA
  - Kampala, Uganda

MTN 015 Study Update

- Current protocol status: Version 1.0
- Study specific training Jan 2008 (Durban)
  - Included laboratory training for PBMC
- First site activated July 08: Lilongwe
- First enrollment Aug 08: Lilongwe
- Second site with protocol registration: Zimbabwe
- Other site IRB/EC approvals ongoing
- Laboratory certifications nearly complete
- Monthly site-team calls