

FEM-PrEP – Update, June 2011

Components

- Randomized clinical trial
- Socio-behavioral and community (SBC) activities
- Seroconverter sub-study



Orderly Closure of FEM-PrEP

- **Following a meeting of the Independent Data Monitoring Committee (IDMC) on April 14, 2011, FHI decided to proceed with an orderly closure of the trial. The IDMC reviewed data through February 18, 2011.**
- **FEM-PrEP will be highly unlikely to be able to demonstrate the effectiveness of Truvada for prevention of HIV infection in the study population.**
- **At this time, it cannot be determined whether or not Truvada works to prevent HIV infection in women.**

FEM-PrEP Design

- **Phase III, randomized (1:1), placebo-controlled, blinded, multi-center trial of daily, oral tenofovir disoproxil fumarate - emtricitabine (TDF-FTC, Truvada)**
- **Sample size: ~3900 women**
- **Target: 72 HIV endpoints**
- **Women who are HIV-negative at higher risk of infection**
- **Follow-up for one year on study drug**
- **Seroconverters followed for one year after diagnosis**

FEM-PrEP Objectives

- **Primary**
 - safety
 - effectiveness
- **Secondary**
 - impact on infection (VL, CD4, ARV resistance)
 - adherence
 - risk compensation
 - pregnancies

FEM-PrEP Clinical Trial Sites



Bondo, Kenya
Arusha/Moshi,
Tanzania

Harare, Zimbabwe
Pretoria, South Africa
Bloemfontein,
South Africa



Socio-Behavioral Research

- **Preparatory and during study**
 - Inform and support trial
 - Assess adherence and risk compensation
- **Interviews with trial participants**
 - HIV-negative participants: Adherence, retention, understanding of clinical trial, trial experiences and sexual behaviors, including risk compensation
 - Seroconverters: access to care, coping, sexual behaviors and adherence
- **Focus groups with community stakeholders**
 - Community reactions to trial, concerns and rumors
 - Provide updates on trial progress
- **Behavioral monitoring**
 - Recruitment, adherence and informed consent

Recruitment

- **High-risk, priority areas identified by socio-behavioral and community (SBC) preparedness research and mapped/clustered using GIS**
- **Staff systematically recruited from priority areas during the trial, focusing on social establishments, VCT centers and STI clinics**
- **Monthly decisions were made on where to recruit (current priority area or next) based on staff experience and review of data**

Adherence

- **SBC data on potential barriers and facilitators integrated into adherence program**
- **Participant-centered and goal-oriented counseling**
 - Incorporated adherence messages and checklists
 - Participants created their own individual adherence plans
 - Encouraged use of adherence reminders: cell phone alarms, pill holder, calendars
- **Vitamin run-in period**
- **Regular monitoring of adherence; data used to enhance counseling**
 - Periodic interviews with trial participants
 - Monthly adherence CRF

FEM-PrEP Status

- **Screened:** 3752 (21% HIV-positive)
- **Enrolled:** 1951 (50%)
 - Bondo, Kenya 739
 - Pretoria, SA 764
 - Bloemfontein, SA 432
 - Arusha, Tanzania 16
- **Retention:** ~90%
- **Person-years of follow-up:** 1100

Data through Feb 18, 2011

FEM-PrEP Data

- **Mean age of participants:** 24 years
- **Sex acts past week:** mean 3.7
- **Self-reported adherence:** ~95%
 - (for week before a visit when study drug available)
- **Contraceptive use at enrollment:**
 - Injectables: 66%
 - OCs: 30%
- **Adverse events (hepatic, renal, etc.):**
 - Consistent with Truvada use

Data through Feb 18, 2011

FEM-PrEP Main Findings

- **HIV incidence:** 5.1 per 100 person years
- **HIV infection endpoints:** 56 (78% of 72)
 - Truvada arm: 28
 - Placebo arm: 28
- **Pregnancies:** 9 per 100 person years
 - Higher among women in Truvada arm compared with placebo arm

Data through Feb 18, 2011

Hypotheses for HIV Outcome

- **Adherence too low to show effectiveness**
- **Biological (next slide)**
- **Product sharing**
- **Chance**
- **Combination of factors**

Possible Biological Explanations

- **Penetration of tenofovir and/or emtricitabine in female genital tract inadequate to provide protection**
 - Differential distribution to rectum and the female genital track
- **High drug levels required at site of HIV entry**
 - These levels may not be achieved in female genital tract with a single daily dose
- **Contraceptive hormones**
 - May interfere with effectiveness of Truvada (TDF-FTC)
- **Truvada side effects**
 - May have resulted in decreased adherence to study drug

Hypotheses for Pregnancy Finding

- **Previously unknown interactions** between Truvada (TDF-FTC) and contraceptive hormones
- **Differential adherence to oral contraceptives** between women on Truvada and women on placebo
 - Possibly due to Truvada side effects
- **Chance observation**

Samples Available for Analyses

- **Per participant prior to seroconversion**
 - At each monthly visit:
 - up to 4 mL plasma
 - 1 mL upper layer packed cells (ULPC)
 - Quarterly:
 - 1 mL serum
- **Last visit on study product**
 - Cervico-vaginal fluid from a sub-set of women (Pretoria) after the study closure announcement

Sample Testing to be Performed

- 1. HIV endpoint (seroconverters)**
 - Confirmation of HIV testing
 - Determination of time of infection
- 2. ARV resistance (seroconverters)**
- 3. Tenofovir and emtricitabine levels**
- 4. Contraceptive hormone levels**

Anticipated Timeline - I

- **Complete follow-up of HIV-negative cohort:** end Aug 2011
- **Data cleaning:** end Oct 2011
- **Results of drug level testing:** Q3-Q4 2011
- **Primary data analysis:** Nov 2011
- **Publication of main findings and dissemination in the communities:** Q4 2011-Q1 2012

Anticipated Timeline - II

- **Secondary analyses and paper writing:** continue while follow-up of HIV-positive cohort continues
- **FDA study report:** finalize after follow-up of seroconverters is complete
- **End of follow-up for seroconverters:** end Aug 2012
- **Final completion FEM-PrEP:** Q4 2012