FHI Study 10015: FEM-PrEP

Phase 3, multi-center, double-blind, randomized, placebo-controlled effectiveness and safety study to assess the role of Truvada® in preventing HIV acquisition in women

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Family Health International

Family Health International

FEM-PrEP – Science

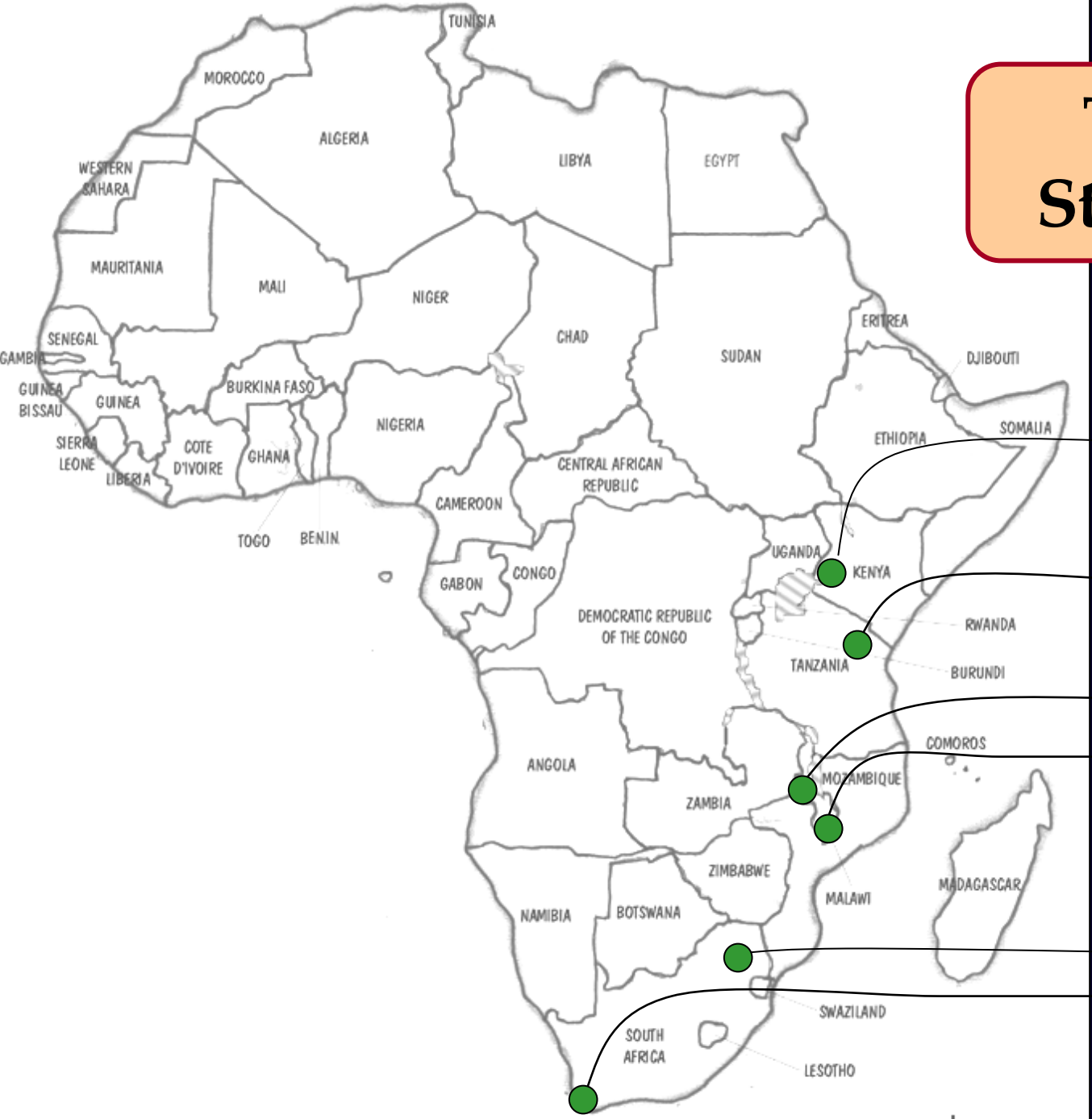
- **Three Protocols:**
  - **Socio-behavioral and ongoing community (SBC) preparedness activities**
  - **Randomized clinical trial of Truvada**
  - **Pilot intervention planning study for using Truvada, if found to be safe and effective**

Clinical Protocol

Design

- Phase III, randomized (1:1), placebo-controlled, blinded trial
- Sample size: 3900 women
- HIV negative women at higher risk of infection
- Follow-up for one year on study drug and short period after stopping drug

Truvada Study Sites



Bondo, Kenya

Arusha, Tanzania

Lilongwe, Malawi

Blantyre, Malawi

Pretoria, South Africa

Cape Town, South Africa

Primary Objective

To determine the effectiveness and safety of daily Truvada compared with placebo for HIV prevention among HIV-uninfected women who are at higher risk of becoming HIV infected through sexual intercourse

Secondary Objectives (1 of 3)

1. **PROGNOSIS** - To compare viral load, viral set point and CD4+ T cell counts among participants who HIV seroconvert while receiving Truvada versus placebo.

2. **RESISTANCE** - To compare frequency of FTC and tenofovir phenotypic and genotypic drug resistance among participants who HIV seroconvert while receiving Truvada versus placebo.

Secondary Objectives (2 of 3)

3. **BONE DENSITY** - To determine, in a subset of participants (N=200), the effects of co-administration of Truvada and depot medroxyprogesterone acetate (DMPA) on bone mineral density over time and compare to the effects of DMPA in the placebo group

4. **PREGNANCY** - To evaluate the effects of administration of Truvada versus placebo during early pregnancy on pregnancy outcome

Secondary Objectives (3 of 3)

5. **ADHERENCE** - To assess adherence to once-daily pill taking

6. **DISINHIBITION** - To describe the effect of potential pre-exposure prophylaxis on risk disinhibition

7. **BEHAVIOR** - To compare sexual behaviors before and after seroconversion

Study Procedures (1 of 6)

- **Always**
  - Risk reduction counseling
  - HIV testing with counseling
  - Male partner referral
  - Pregnancy testing
  - Contraception provision with counseling
  - Condom provision (male and female where available)
  - Sexual behavior data collection
  - Contact information collection

Study Procedures (2 of 6)

- **Screening, additional procedures:**
  - Informed consent with assessment
  - Physical (incl. pelvic) exam
  - STI testing and treatment
  - Renal and hepatic function tests
  - Hepatitis B test
  - Medical history assessment
  - Vitamin provision

Study Procedures (3 of 6)

- **Enrollment, additional procedures:**
  - Informed consent with assessment
  - Vitamin ingestion
  - Clinical exams and testing as indicated
  - Hepatitis B vaccination (for negative participants)
  - Adherence counseling
  - Medical history and medication assessment
  - Randomization
  - Study product distribution
  - DEXA in subset

Study Procedures (4 of 6)

- **Follow-up visits:**
  - Clinical exams and testing as indicated
  - Pill counts and adherence counseling
  - Adverse event and concomitant medication assessment
  - Study product distribution
  - Renal and hepatic function tests*
  - Informed consent questionnaire*
  - DEXA in a subset of participants*
  - Qualitative interviews among 5% of randomly selected participants*

* Periodically, not at every follow-up visit.

Study Procedures (5 of 6)

- Drug Interruptions:
  - Pregnancy
    - Infant outcome
  - HIV seroconversion
    - Resistance
    - Set points
  - Toxicities
  - Other as determined by site investigator
- Post study and drug discontinuation
  - 1 month follow-up of all participants
  - 3 month follow-up of all participants at risk of hepatitis flare
  - 12 month follow-up of all HIV seroconverters

Study Procedures (6 of 6)

- Care
  - Physical exams as indicated
  - STI treatment as indicated
  - Treatment of drug-related adverse events
  - Referral to care and treatment (for seroconverters)
  - Referral to PMTCT
  - Gilead will provide drug for a limited time to all participants if Truvada is found to be safe and effective for HIV prevention

Socio-Behavioral & Community Activities (SBC)

Overview of the Socio-Behavioral & Community (SBC) Approach

- Preparedness data
- Qualitative interviews during clinical trial implementation
- Community engagement program
- Qualitative protocol to inform site-specific pilot prevention interventions

SBC Preparedness Data

Purpose: Inform the community about the trial, engage in communication about trial procedures and community perceptions, identify recruitment areas

Method: In-depth interviews (IDIs), focus group discussions (FGDs), & community mapping interviews

Participants: Women at higher risk of HIV exposure, Community stakeholders, Men who are sexually active

Outcome: Gauge community support of the trial, develop recommendations for clinical trial study procedures

SBC Qualitative Interviews During Clinical Trial Implementation

Trial Participants:

Quarterly qualitative in-depth interviews with a randomly selected 5% of all enrolled study participants:

- to assess factors affecting adherence
- to describe possible risk disinhibition
- to explore positive and negatives of trial participation

Community Stakeholders:

Regular meetings to:

- provide updates on the clinical trial
- explore potential issues with the clinical trial
- learn community reaction to the clinical trial

SBC Community Engagement Program

Purpose:

- to foster community-researcher partnerships
- to improve understanding and trust in clinical research
- to build research literacy/community capacity

Current Activities:

- building partnerships with community advisory boards
- building relationships with civil society stakeholders
- research ethics training for community advisory boards

Upcoming Activities:

- training CABs on clinical research practices
- input from CABs on informed consent procedures
- ongoing communication about rumors and concerns

SBC Qualitative Protocol to Inform Site-Specific Pilot Prevention Interventions

Research: Conduct IDIs and FGs to identify

- country priorities for PrEP
- target populations for PrEP
- constraints and requisitions for integration with local HIV prevention programs

Community Planning: To conduct workshops and *facilitate* a community planning process

Output: To produce country-specific pilot intervention plans based on research and community planning results

Overall Timeline

- Jun 2007 – Initiation of non-research community activities (i.e. CABs)
- Aug 2007 – Initiation of site preparedness activities
- Oct 2007 – Investigators' Meeting (Nairobi)
- Jan 2008 – Finalization of protocol
- Feb 2008 – FDA pre-IND submission
- Jan-March 2008 – Finalization of study documents and procedures
- March 2008 – FHI PHSC approval
- Mar-May 2008 – Local IRB and regulatory submissions
- Aug 2008 – 1st candidate screened - Bondo, Kenya

Questions & Comments