

CONRAD

Phase III Clinical Trials

Phase III Trial Product

- ◆ Cellulose sulfate, a viral entry inhibitor
- ◆ CS inhibits HIV-1 type X4 and R5, HIV-2, *N. gonorrhoeae*, *C. trachomatis*, HSV-1, HSV-2 and *T. vaginalis in vitro*.
- ◆ In previous safety trials, CS was as safe, well tolerated and accepted as KY[®] Jelly and Conceptrol[®].
- ◆ CS has a contraceptive effect *in vitro* and in animal models. Two Phase II effectiveness trials are ongoing in the US.
- ◆ Two HIV prevention trials will be implemented

CONRAD's Trial

- ◆ Start end of 2004
- ◆ Projet Sida 3, Cotonou, Benin,
Prof. Michel Alary
- ◆ Centre Muraz, Bobo Dioulasso, Burkina Faso,
Dr. Nicolas Nagot
- ◆ YRG Care, Chennai, India,
Dr. Suniti Solomon
- ◆ African Center for Clinical Trials, Nairobi, Kenya,
Prof. Gilbert Kokwaro
- ◆ Medical Research Council, Durban, SA,
Dr. Gita Ramjee
- ◆ Makerere University, Kampala, Uganda,
Prof. Florence Mirembe

Design and study population

- ◆ Randomized, triple-blinded, placebo-controlled, two-arms
- ◆ Sample Size = 2,574 HIV-negative women
- ◆ Participants = HIV-negative women at risk of HIV infection through sex defined as: average of at least three vaginal acts per week **PLUS** at least three different partners in the last three months and expected to continue this behavior.

Gel allocation and delivery

- ◆ Placebo = HEC-based “universal” placebo
- ◆ 1:1 allocation
- ◆ Gels: single use opaque applicators, 3.5 ml delivery; 6 groups in the field

Why not a no-treatment arm?

- ◆ Advantage of no-treatment arm:
 - ▶ Incidence among women not using any product
- ◆ Disadvantages:
 - ▶ Differential behavior change between gel arm(s) and no-gel arm
 - ▶ Trial sample size ↑↑
 - ▶ Potential product sharing
 - ▶ Impact on recruitment and loss-to-follow-up

Assumptions for sample size

- ◆ HIV-incidence in control arm = 4%
- ◆ 50% effectiveness of CS
- ◆ 2-sided significance level of 0.05
- ◆ 80% power
- ◆ 80% of participants completing 12-month follow up

Objectives and Endpoints

◆ **Primary:**

- ▶ Effectiveness in preventing male-to-female transmission of HIV-infection through vaginal intercourse by comparing HIV incidence in both arms (ITT)

◆ **Secondary:**

- ▶ Effectiveness in preventing male-to-female transmission of NG and CT through vaginal intercourse by comparing the incidence in both arms (ITT – time to first event)

Study Procedures

- ◆ **Screening**: consent; interview; pelvic exam with samples for NG and CT; HIV testing and counseling; condoms
- ◆ **Enrollment**: consent; HIV testing and counseling; gels and condoms; pelvic exam and samples
- ◆ **Follow-up**: questionnaire; HIV testing and counseling; gels and condoms; monthly self-collected swabs and every 3 months a pelvic exam

Study Procedures, cont.

- ◆ Colposcopy will not be performed
- ◆ No diaries
- ◆ Consent will not be obtained from male partners, nor data collected

Background data

◆ Benin

- ▶ HIV-incidence 5 - 10%
- ▶ NG and CT prevalence \pm 4%

◆ Burkina Faso

- ▶ HIV incidence \pm 3 - 4%
- ▶ NG and CT prevalence very low
- ▶ HSV-2 prevalence 69% +

Background data, cont.

Kenya

- ◆ Condom use with non-paying partner
 - ▶ Last act 50%
 - ▶ Consistent 34%
- ◆ Condom use with paying partner
 - ▶ Last act 87%
 - ▶ Consistent 67%
- ◆ HIV prevalence
 - ▶ General 15%
 - ▶ High risk population 70%

Background data, cont.

India

- ◆ HIV prevalence 9.2%
- ◆ NG prevalence 1.4%
- ◆ Syphilis 16.0%

COLLABORATORS

- ◆ Centers
- ◆ Family Health International (NC, USA)
(training, data management/analysis and monitoring)
- ◆ Institute of Tropical Medicine (Antwerp, Belgium) (lab evaluation, training and QC)