MTN-001
Phase 2 Adherence and Pharmacokinetic Study of Oral and Vaginal Preparations of Tenofovir

Dr. Clemensia Nakabiito MBChB, MMED
Makerere University-Johns Hopkins University
Research Collaboration
Kampala
Uganda

MTN Regional Meeting
Cape Town, South Africa
September 8-11, 2008

Outline

This presentation will highlight:

- Protocol Information
  - Rationale, design & objectives
- Site Information
  - Location, accrual update and other trial milestones achieved thus far

Background

- Microbicides are being developed for prevention of HIV and/other STIs when applied topically
- In vitro body, animal, and preliminary clinical data suggests tenofovir to be a safe and effective vaginal microbicide
- While vaginal use may confer less systemic toxicity, oral use is less closely linked to sexual practices, and possibly could be administered by the woman without knowledge of her partner

MTN
microbicide trials network

Primary Objectives

- To compare adherence to and acceptability of three daily regimens of tenofovir (oral, vaginal, and dual use)
- To compare systemic and local PK among three regimens of tenofovir (oral, vaginal, and dual use) in a subset of participants

Secondary Objectives

- To identify factors associated with product adherence
- To examine whether sexual activity or male condom use varies with use of different regimens
- To assess the timing of product use with sexual intercourse
- To determine the level of sharing of study products
- To characterize the differential safety profiles of three daily regimens

Rationale in Relation to the VOICE Study

- Compare oral v. vaginal product adherence
- Examine impact of second product on adherence
- Compare oral v. vaginal PK
- Integrated multi-compartment PK model after oral dosing (blood cells, tissue, lumen)
- Examine additive effect of dual route dosing
- Compare observed vs. unobserved PK to assess adherence

Study Design

- Phase 2
- Multi-site
- Randomized
- Six sequence, three period
- Open label crossover study

Study Population

- Sexually active
- HIV-uninfected women
- Age 18-45 years

Sample Size

- 144 participants
  - This includes 48 for intensive pharmacokinetic sub-study at US sites
- Each site will enroll up to 24 fully evaluable participants

Study Duration

- Approximately 21 weeks per participant, with projected six calendar months of accrual

Study Regimen

- **Period 1: 6 WKS then 1 WK Wash-out**
- **Period 2: 6 WKS then 1 WK Wash-out**
- **Period 3: 6 WKS then 1 WK Wash-out**
- **Sequence A 24** Oral, Vaginal, Oral + Vaginal
- **Sequence B 24** Vaginal, Oral ,Oral + Vaginal
- **Sequence C 24** Oral + Vaginal, Oral ,Vaginal
- **Sequence D 24** Oral + Vaginal, Vaginal, Oral
- **Sequence E 24** Oral, Oral + Vaginal, Vaginal
- **Sequence F 24** Vaginal, Oral + Vaginal Oral

MTN
microbicide trials network

Participating Sites

- South Africa
  - Umkomaas , Durban
  - Botha's Hill , Durban
- Uganda
  - Makerere University - JHU Research Collaboration (MU-JHU CARE Ltd), Kampala, Uganda
- United States
  - Case Western (CWRU), Cleveland
  - Pittsburgh, PA
  - Bronx-Lebanon, New York
  - University of Alabama, Birmingham, Alabama

MTN
microbicide trials network

MTN 001 Milestones

- Protocol version 1.0, 12 NOV 2007
- Protocol version 2.0, 29 August 2008
- FDA IND approval was received (IND # 55690)
- IRB Approvals
  - Pitt approved 6 MAR 08; Registration submitted 31 MAR 08
  - CWRU approved 28 MAR 08; Registration submitted 3 APR 08
  - Durban approved 01 Sep 08, Awaiting approval by MCC
  - MUJHU approved 01 Sep 08, Awaiting approval by UNCST

MTN
microbicide trials network

MTN 001 Milestones Cont'd

Study-Specific Training

- Pitt: 8 –10 April 2008
- Cleveland: 29 April –1 May 2008
- Kampala planned for 15th -19th Sept 2008
- Other sites are expected to be trained in Oct/Nov

Site Activation

- Pittsburgh: 18 June, 2008
- CWRU: 07 July, 2008

MTN 001 Milestones Cont'd

Screening and Enrollment (as of 04 Sep 08)

Site	Screened	Enrolled
CWRU	2 (1st: 04/Aug/08)	1 (1st: 18/Aug/08)
Pittsburgh	4 (1st: 27/Jun/08)	3 (1st: 18/Jul/08)
Total	**6**	**4**

Acknowledgements

- Sponsors: NIAID (5U01AI068633), NICHD and NIMH, NIH
- CONRAD
- MTN Core in Pittsburgh
- FHI
- SCHARP
- MTN EC
- All Participating sites
- MTN Community Team

Thank You