MTN 016

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MTN
microbicide trials network

Introduction

- HIV Prevention (Microbicide/PrEP) trials recruit reproductive age women

- Pregnancy is a natural consequence
  - 85% per year in non-contraceptive users
  - 0.5-15% per year in typical users of all different methods

Rationale for investigation

- Sexual activity is common in pregnancy and the early post partum period
- Pregnancy may be a risk factor for HIV acquisition
- If microbicides are available, pregnant women will use them
- Anti-HIV microbicides may potentially have a role in preventing vertical transmission of HIV

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MTN approach

- MTN: Proactively evaluate microbicides and other prevention tools in pregnancy
- MTN-002:
  - Phase 1, open label, pharmacokinetic, placental transfer and safety evaluation
- MTN-016
  - HIV Prevention Agent Pregnancy Exposure Registry
    - Protocol development in progress

MTN-016

- HIV Prevention Agent Pregnancy Exposure Registry
  - Prospective observational cohort
  - 500 pregnant women and 300 live infants
    - Inadvertent exposure to microbicides and/or PrEP agents during HIV prevention trials
    - Planned exposures (MTN-002)
    - Controls = Placebo exposed
  - Planned through May 31st, 2013

Exposures

- Tenofovir gel
- Oral tenofovir disoproxil fumarate (TDF)
- Oral emtricitabine/TDF
- UC-781 gel
- Placebo products

Objectives

- Primary Objectives
  - To compare the prevalence of spontaneous pregnancy loss and structural abnormalities in fetuses
    - Mothers exposed to active agent vs. placebo
  - Evaluate fetuses, newborns and infants for unique patterns of malformations

Objectives

- Secondary Objectives
  - To monitor for adverse pregnancy outcomes
  - To compare growth parameters in the first year of life
  - To provide a cohort of unexposed newborns and infants
    - This cohort will represent the background incidence of major birth defects and abnormalities in HIV prevention trials

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Objectives

- Exploratory Objectives
  - To monitor for select risks of agents identified in preclinical studies by trimester of exposure
  - To evaluate the prevalence of HIV drug resistance mutations in HIV-infected infants
  - To compare developmental screening results during the first year of life

Participants

- Parent trial participants will be offered enrollment whenever it is determined that there has been an exposure to a study agent during pregnancy
- Sites are encouraged to enroll participants as early in pregnancy as possible
- Open to participants from other HIV prevention trials not part of the MTN

Study visits

- Mother
  - Screening and Enrollment
  - Quarterly
  - Pregnancy outcome
- Infant
  - Newborn visit
  - Month 1
  - Month 6
  - Month 12

Screening and enrollment

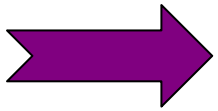
- Administrative
  - Obtain written informed consent
  - Locator information
  - Reimbursement
- Clinical
  - Obtain medical history
  - Obtain medication history
  - Obtain pregnancy history
- Radiology
  - Dating obstetrical ultrasound

Quarterly visits

- Administrative
  - Locator information
  - Reimbursement
- Clinical
  - Update medical history
  - Update medication history
  - Update pregnancy course
- Radiology
  - Anatomy ultrasound

Pregnancy outcome visit- mother

- Administrative
  - Locator information
  - Reimbursement
- Clinical
  - Update medical history
  - Update medication history
  - Update pregnancy history
  - Obtain pregnancy outcome



Pregnancy outcome visit- mother

- Outcomes of interest
  - Pregnancy-related morbidities
    - Hypertensive disorders
    - Premature rupture of membranes
    - Abnormal placentation
  - Type of delivery
  - Gestational age
  - Delivery complications
    - Chorioamnionitis
    - Intrapartum hemorrhage

Newborn visit (up to 10 days of life)

- Administrative - informed consent
- Clinical
  - Medical history
  - Medication history
  - Weight
  - Length
  - Head circumference
  - Abdominal circumference
  - Physical exam
  - Photographic documentation of suspected or confirmed anomalies

Newborn visit (up to 10 days of life)

- Laboratory
  - HIV tests for infants born to mothers identified as HIV-infected

Infant follow-up

- Performed at 1, 6, and 12 months
- Administrative- locator information
- Clinical
  - Update medical history
  - Update medication history
  - Weight
  - Length
  - Head circumference
  - Physical Exam
  - Development assessment (6 and 12 mos)
- Laboratory as needed

HIV infected newborns

- Quarterly testing
  - HIV-1 RNA
  - Standard genotypic testing
  - Plasma for storage
  - Additional resistance testing as needed

Update

- Currently under protocol revision
- Anticipate DAIDS approval 10/08
- Begin enrollment early 2009