MTN Annual Meeting Welcome and Introduction of HPTN 035

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MTN
microbicide trials network

Major Accomplishments of the MTN Since Our Last Meeting

- Initiation of new protocols:

  -MTN-001 (first crossover study of oral and vaginal tenofovir pharmacokinetics and acceptability): Pittsburgh, Cleveland and Birmingham

  -MTN-002 (first study of topical microbicides to be conducted among pregnant women): Pittsburgh

  -MTN-015 Seroconverter study: 035 sites
- Development to Version 1.0 of two new rectal microbicide protocols: MTN-006 and MTN-007
- Development of the MTN-016 Pregnancy Registry
- Meeting materials include synopses of all protocols

Major Accomplishments of the MTN Since Our Last Meeting

- Completion of HPTN-035 within one month of the timeline projected in May 2005
- Presentation of the HPTN 035 data at CROI and dissemination of findings at the sites in February
- Press coverage highlighted during the reception Monday night!

Travel Back in Time: 10 Years Ago

- 1999: HIVNET was planning a study of N-9 gel for prevention of HIV; COL1492 study was underway
- DAIDS network recompetition leading to the formation of the VTN and HIV Prevention Trials Network
- HPTN application included a formal microbicide plan to perform studies including a phase 2B intermediate size trial of 2-3 microbicide products
- HPTN funded in 2000

It is Time to Travel Back in Time

- COL1492 study of N-9 completed. Women randomized to N-9 had an *increased* risk of HIV compared to women in the Replens control group (Durban 2000)

  - Was Replens really a placebo or might it have had some protective effect?

  - Would any gel negatively impact the vaginal ecosystem and increase risk of HIV?

The New Age of Microbicides in 2001

- Several products in development: BufferGel, PRO2000/5, SAVVY (C31G), Ushercell (cellulose sulfate), Carraguard
- No clear regulatory pathway for approval of a microbicide; no broadly accepted standard protocol for evaluation of microbicide effectiveness

The New Age of Microbicides in HPTN

- Step 1: Select products (Fall 2000)
- Step 2: Concept approval by the HPTN EC (Feb 2001)
- Step 3: Develop the study design
  - Placebo control? Which one? Design of a new placebo!
  - No gel comparison arm?
  - Phase 3 or 2B?
  - FDA consultation on study design and endpoints (2001)
- Step 4: Develop seroincidence data for new sites (HPTN 055)

This took several years…….

Timelines

- March 19, 2002: Initial PSRC review
- December 2, 2002: FDA Advisory Panel on Microbicide Study Design
- May 15, 2003: External review of HPTN 035 by NIH. Outcome:

  - Study products selected appropriate
  - Reduce study size from phase 3 to 2B
- August 2004: Protocol approved for implementation
- February 2005: First participants enrolled in Durban, South Africa and Philadelphia, USA
- July 2007: Last participants enrolled
- September 2008: Follow-up completed

Today's Presentation: the Outcome of a Decade of Hard work and Commitment

- Study Overview
- Self-reported behavioral data
- Product safety and pregnancy
- STI endpoints
- HIV endpoints
- What we learned about BufferGel and PRO2000
- What we learned about the placebo gel
- A chance to hear from you