

Welcome & State of the Network

MTN Annual Meeting

Sharon Hillier PhD

Ian McGowan MD PhD FRCP

March 28, 2011



2010

The year that change the face
of HIV prevention research



CAPRISA 004



iPrEx

The MTN in 2011

- MTN was funded in July 2006 for 7 years
- We are now completing the 5th year of funding
- We can anticipate that we will submit an application for continued funding next year
- It is a good time to reflect on where we have been, where we are today, and where we are going to in the years ahead



MTN Study Updates

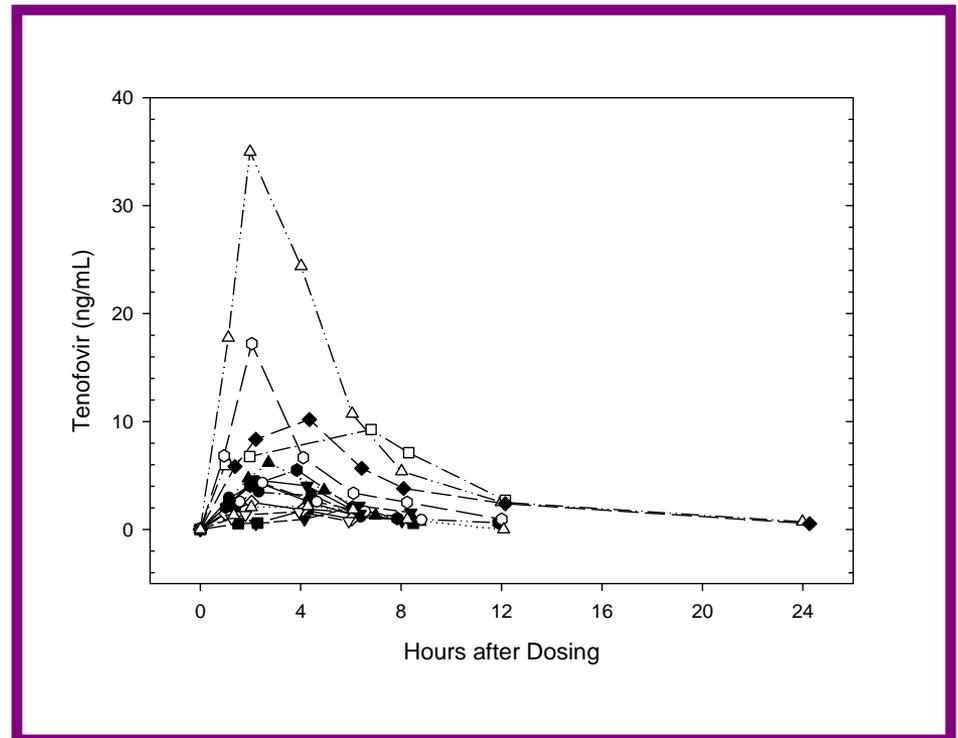
MTN-001

- First cross-over study oral and vaginal preparations of tenofovir for PK and acceptability
- Study completed in USA, Uganda, S Africa
- Data presented at CROI 2011 as a latebreaker
- Manuscript in preparation



MTN-002

- Maternal pharmacokinetics and placental transfer of tenofovir 1% vaginal gel
- Study completed
 - Pittsburgh, PA
- Data presented at Microbicides 2010
- Manuscript completed and under review at the MTN MRC



Maternal tenofovir PK



The VOICE Study

- Currently enrolling
- South Africa, Zimbabwe, and Uganda
- Total accrual: 3800 (80%) of 5,000 participants enrolled
- MTN-003B – Bone density substudy
 - Target enrollment: 329
 - Total accrual as of 18th March, 2011: 428
 - Will provide critical bridging data on bone toxicity in women

VOICE Related Studies

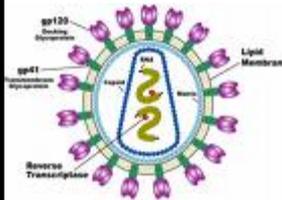
VOICE Study

Pregnancy



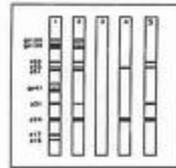
MTN-016

Resistance



MTN-009

HIV
Seroconverters



Figures:
Images of positive by an HIV-1 Western blot:
1. Positive control (p24)
2. Positive control (anti-p24)
3. Negative control
4. Test sample
5. Test sample (anti-p24 negative)

MTN-015

Bone health



VOICE-B

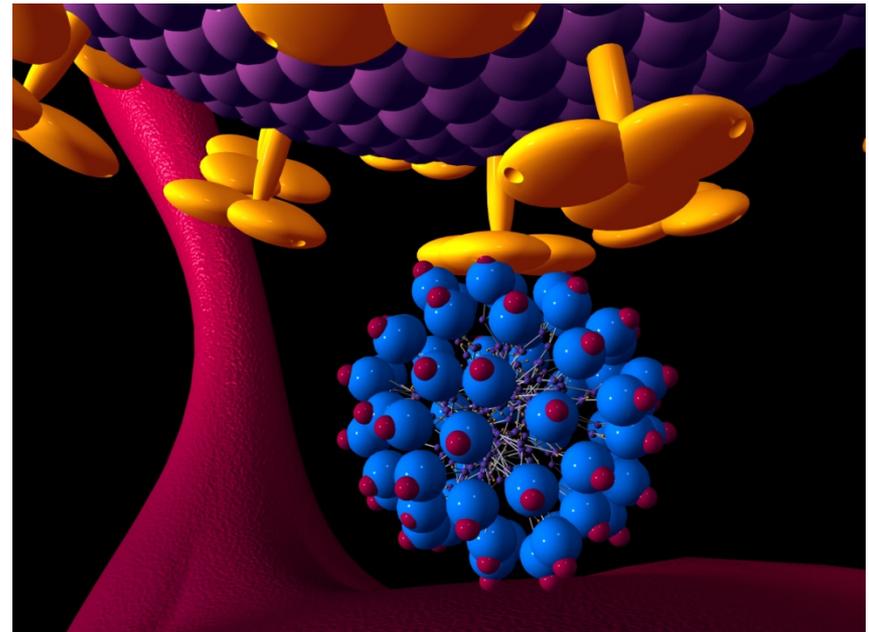
Community
Perceptions



VOICE-C

MTN-004

- Safety and acceptability of SPL7013 VivaGel Gel in sexually active women
- Study completed
 - Pittsburgh, PA
 - San Juan, PR,
 - Tampa, FL
- Data presented at Microbicides 2010; provided data which changed the development pathway
- Manuscript accepted by AIDS



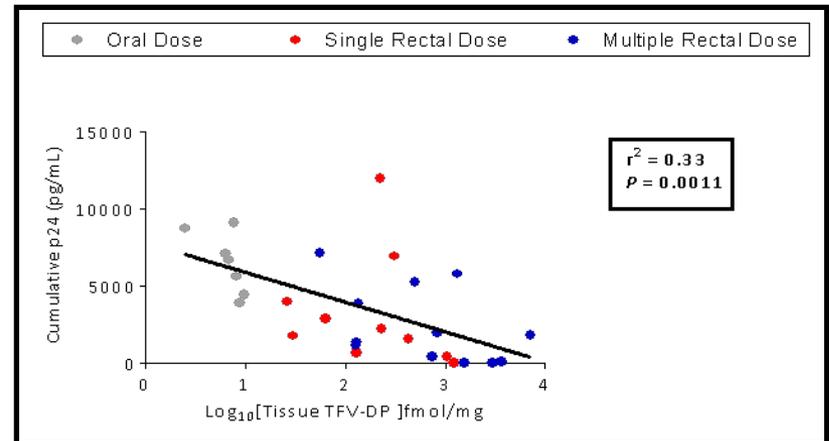
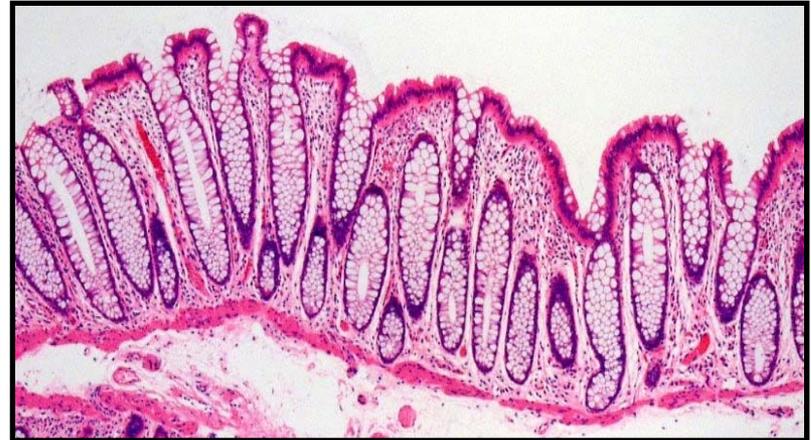


MTN-005

- Safety and acceptability of a non-medicated intravaginal ring
 - Bronx-Lebanon, NY
 - Birmingham, AL
 - Pune, India
- Study specific training ongoing; estimated start date Q2 2011
- Will provide acceptability and safety data

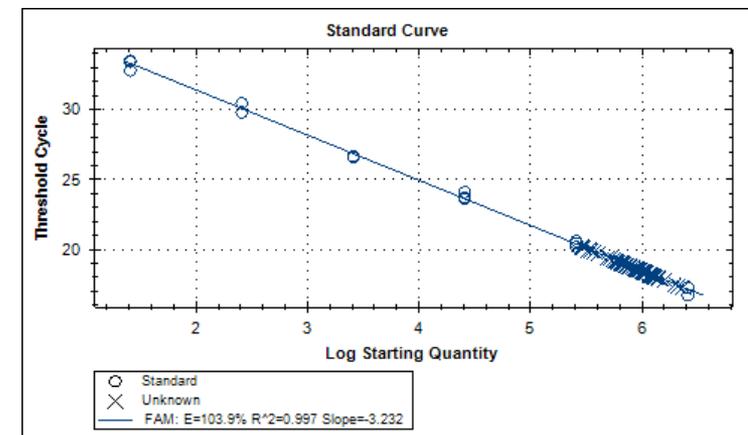
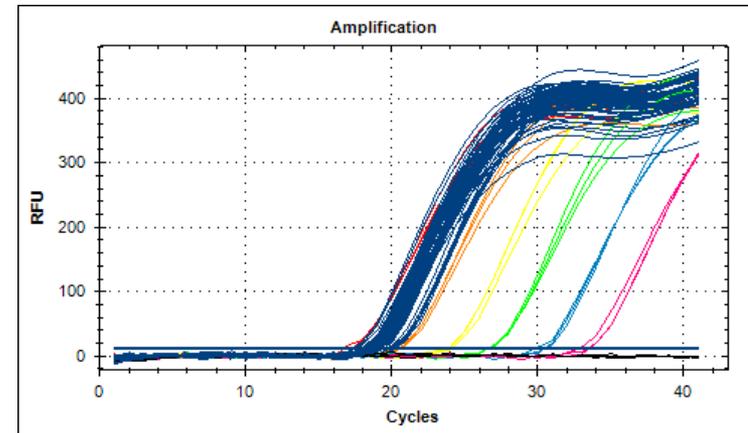
RMP-02 / MTN-006

- Rectal safety, acceptability and PK/PD of tenofovir 1% gel
- IPCP collaboration
- Study completed
 - Los Angeles, CA
 - Pittsburgh, PA
- Data presented at CROI 2011 as latebreaker
- Manuscript in preparation



MTN-007

- Rectal safety and acceptability tenofovir 1% gel (low glycerin)
- Accrual
 - Pittsburgh: 20/20
 - Birmingham: 15/20
 - Boston: 11/20



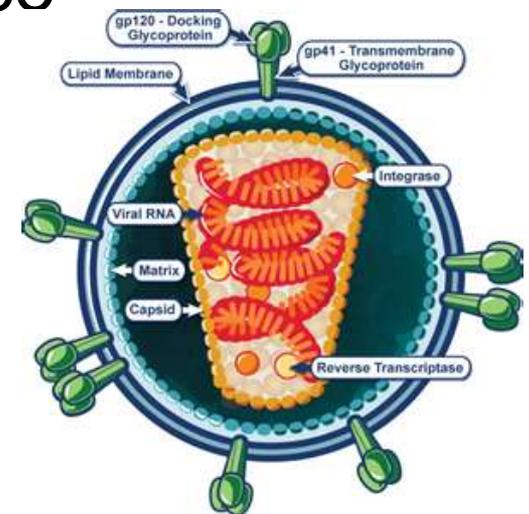
MTN-008

- Expanded safety of tenofovir 1% gel in pregnancy and lactating women
- Study sites
 - Pittsburgh, PA
 - Birmingham, AL
- Study activated in Pittsburgh
- Will fill licensing gap in pregnant & breastfeeding women



MTN-009

- HIV resistance at screening for HIV prevention trials at MRC sites
- Fully enrolled
- Will provide critical data on the background rate of ARV resistance among HIV isolates in the communities in Durban where VOICE participants are being enrolled



MTN-011

- Post-coital PK/PD of tenofovir 1% gel
- 32 couples
- Sites
 - Cleveland, OH
 - Pittsburgh, PA
- Protocol development meeting scheduled for April 21st, 2011
- Will sex change drug absorption?



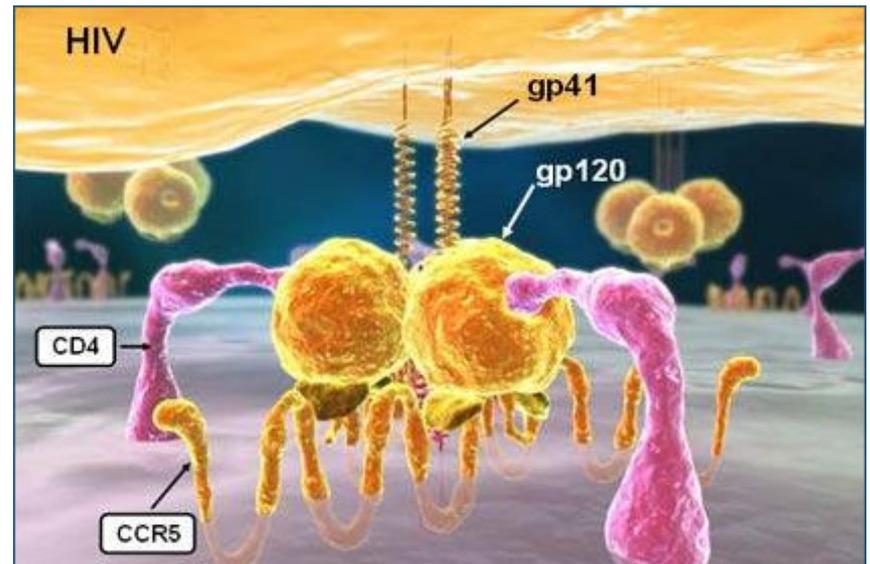
MTN-012

- Male tolerance of dapivirine gel
- Sample size: 48
- Will provide critical safety data for dapivirine phase 3 program
- Study Status
 - Birmingham, AL: activated
 - Pittsburgh, PA: pending



MTN-013

- Phase 1 safety and PK/PD of dapivirine/maraviroc intravaginal ring
- Sites
 - Pittsburgh, PA
 - Boston, MA
 - Birmingham, AL
- Study protocol completed PSRC & regulatory review completed





2010-2011

3/10

Annual Meeting

7/10

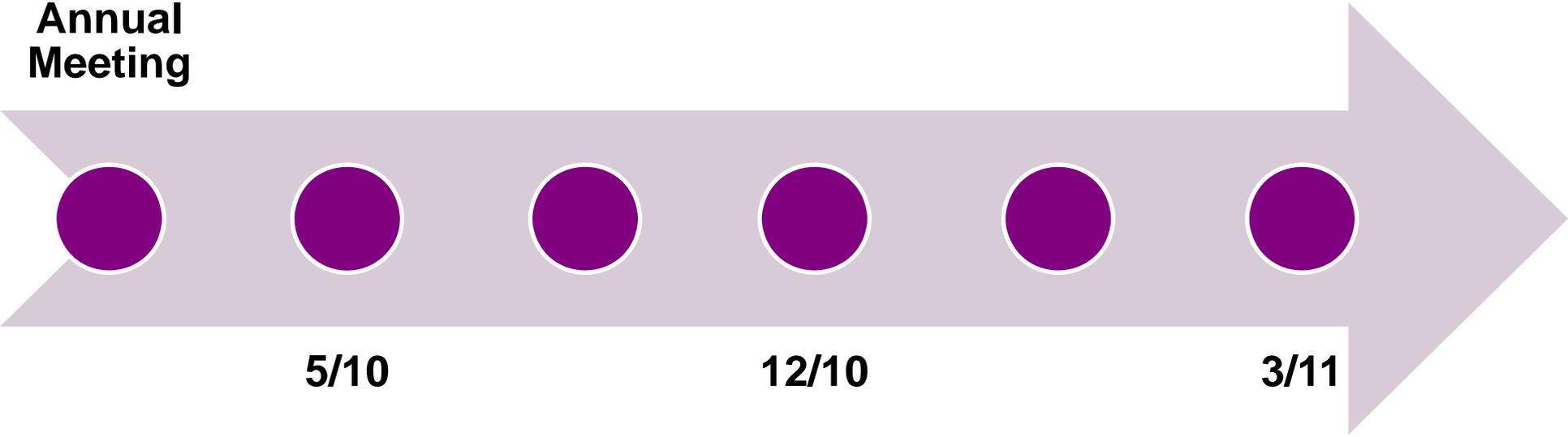
2/11



5/10

12/10

3/11





2010-2011

3/10

Annual
Meeting

7/10

2/11

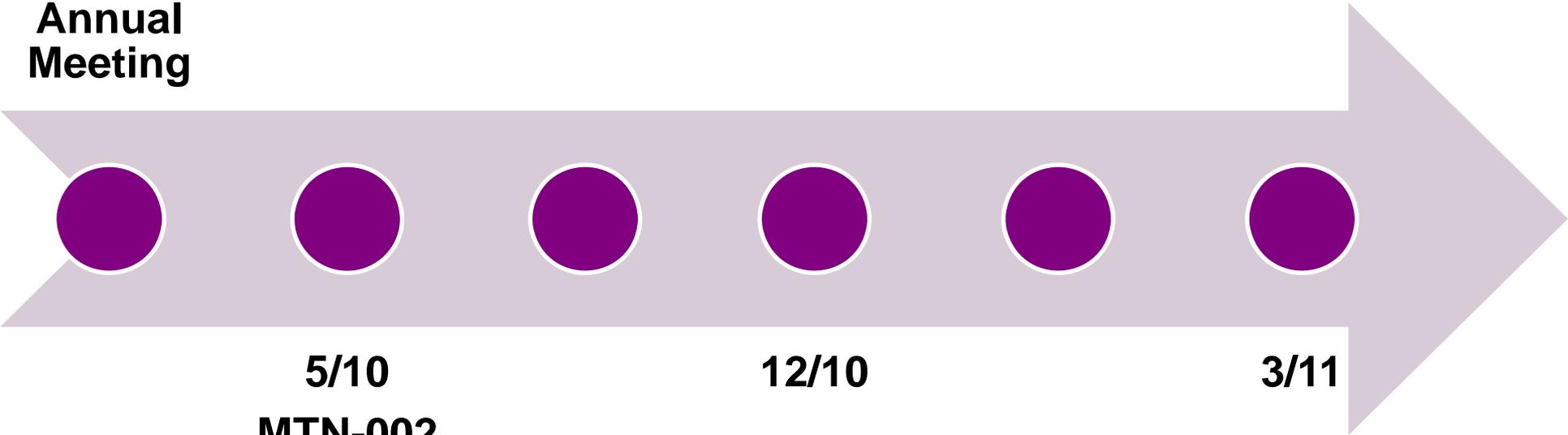


5/10

MTN-002
& MTN-
004 at
M2010

12/10

3/11





2010-2011

3/10
Annual Meeting

7/10
VOICE
25%

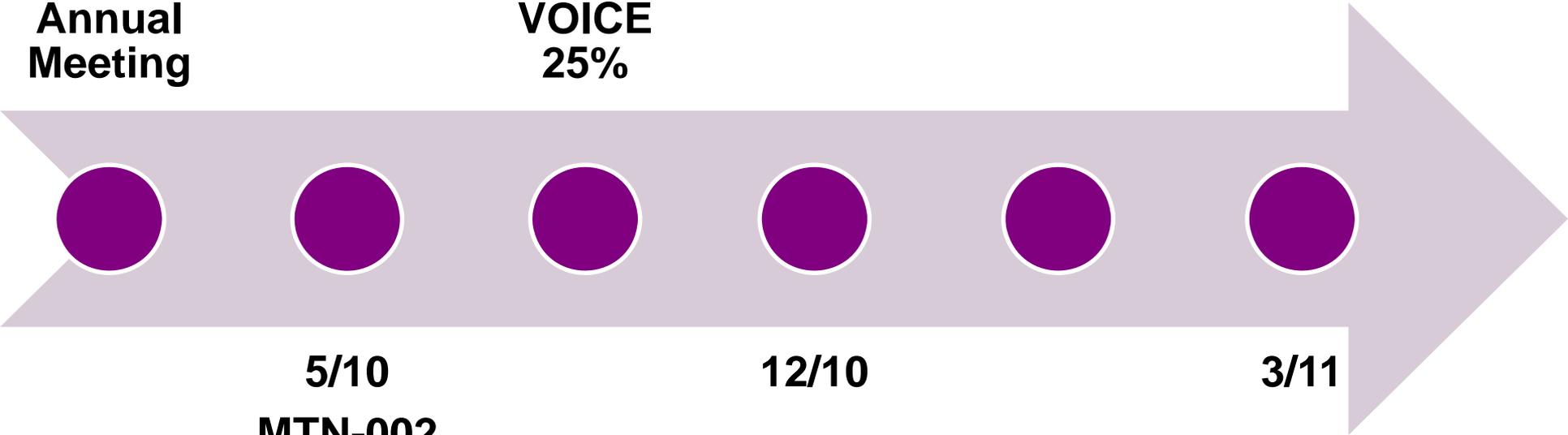
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5/10
MTN-002
& MTN-
004 at
M2010

12/10

3/11





2010-2011

3/10
Annual Meeting

7/10
VOICE
25%

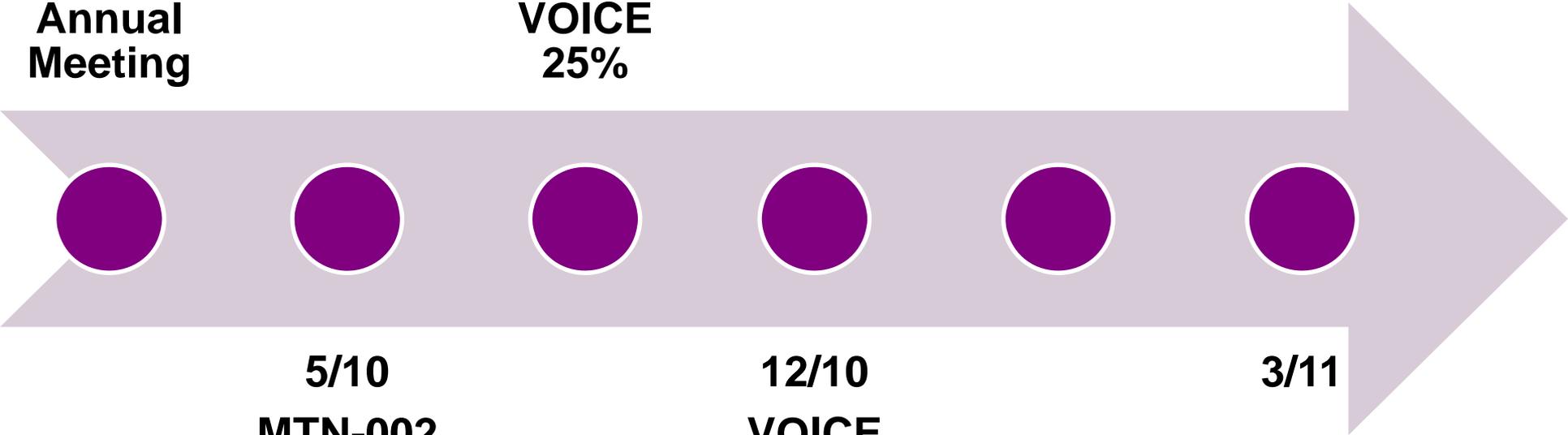
2/11



5/10
MTN-002
& MTN-
004 at
M2010

12/10
VOICE
50%

3/11





2010-2011

3/10
Annual Meeting

7/10
VOICE
25%

2/11
MTN-001
& MTN-
006 at
CROI

5/10
MTN-002
& MTN-
004 at
M2010

12/10
VOICE
50%

3/11





2010-2011

3/10
Annual Meeting

7/10
VOICE
25%

2/11
MTN-001
& MTN-
006 at
CROI

5/10
MTN-
002 &
MTN-
004 at
M2010

12/10
VOICE
50%

3/11
MTN-009
100%,
MTN-008
& MTN-
012 open,
VOICE
80%



MTN-002 - USA



MONDAY, MAY 24, 2010

Study is Step toward Preventing HIV Transmission to Pregnant Women

Young women of reproductive age are among those at the greatest risk of acquiring HIV. A new study on microbicides--medications that prevent the heterosexual spread of HIV--could help establish a safe way to curb the transmission of HIV to pregnant women.

Doctor Richard Beigi at Magee-Womens Hospital of the University of Pittsburgh Medical Center and lead researcher on the study says there is a void when it comes to data on the safety of medications taken by pregnant women. This study involved sixteen healthy, HIV-negative women who had a single dose of tenofovir applied to the vagina hours before giving birth by cesarean section. Beigi says for the first trial of the drug it was applied almost immediately before birth to minimize risk to the mothers and infants. Researchers found that only a small amount of the drug was absorbed into the womens' bloodstream, amniotic fluid and the umbilical cord. Now a larger study is in the works that will include more women, begin slightly earlier in the pregnancy and include two doses of the medication. Beigi says the collective trials will hopefully prove that the microbicides are safe for use pregnant women.

MTN-002 - South Africa



Microbicides safe during pregnancy - study

24.05.2010 Lungi Langa

■ Pittsburgh – A microbicide that researchers are pinning their hopes on is safe for use in pregnant women, according to a study presented at the Microbicide 2010 conference taking place in the United States this week.

Study participants applied a single dose of tenofovir gel two hours before birth by cesarean section.

Dr Richard Beigi of the University Pittsburgh and Magee-Women's Hospital, who headed the study for the Microbicide Trials Network (MTN), said microbicides could be an integral part in the prevention arsenal since there was evidence that condom use decreased during pregnancy.



MTN-001 - USA

HIV and Hepatitis.com Coverage of the 18th Conference on Retroviruses and Opportunistic Infections (CROI 2011)

February 27 - March 2, 2011, Boston, MA



Safety and Acceptability of Tenofovir Gel and Tablets for Pre-exposure Prevention

By Paul Dalton

An experimental vaginal gel containing a 1% concentration of tenofovir is being studied to prevent HIV transmission. Tenofovir (included in the [Truvada](#) and [Atripla](#) coformulations) is widely used as part of combination antiretroviral therapy for the treatment of [HIV infection](#).

In an oral presentation at CROI, Craig Hendrix from Johns Hopkins University described an open-label crossover study comparing the 1% vaginal gel versus oral tenofovir in 144 HIV negative women in Africa and the U.S.

Women in the study used the pill alone, the gel alone, and the pill and gel together (dual regimen) each for 6 weeks. The women served as their own controls in the study, using the 3 regimens in a randomized order.

The researchers looked at pharmacokinetic parameters (drug levels), markers of adherence, and product acceptability of the 3 regimens.



PrEP researchers Walid Heneine,
Gerardo Garcia-Lerma,
Peter Anton, and Craig Hendrix
(Photo: Liz Highleyman)

MTN-001 - Uganda



HIV drug trial promising

Publication date: Friday, 11th March, 2011

By Hilary Bainemigisha

THE results from an HIV prevention trial that was concluded at Mulago are promising. According to the results released recently, the HIV study drug used was well tolerated by the women in the trial.

The study, known as MTN-001, was testing how women would respond to the use of a drug formulation, Tenofovir, when applied as a gel (or cream) into the vagina or swallowed as a tablet.

MTN-001 - UK



HIV & AIDS - sharing knowledge, changing lives

First pills-versus-gel trial finds US women prefer oral PrEP

Gus Cairns

Published: 02 March 2011



(Image: Microbicide Trials Network, University of Pittsburgh and Magee-Womens Research Institute)

The first head-to-head trial directly comparing the acceptability of tenofovir pills and tenofovir microbicide gel amongst HIV-negative women has found that, while African women liked both products equally, three-quarters of US women preferred a pill.

MTN-001 - Nigeria



HIV prevention preferences Differ among U.S. African Women, study finds

Thursday, 03 March 2011 00:00 By
Ben Ukwuoma [Features](#) - [Science](#)

WHAT do women prefer for HIV prevention: pill or gel, was the thrust of two promising approaches for preventing HIV in women presented on Monday at the International conference on Retroviruses and Opportunistic Infections (CROI), which ended in Bolton.

In the first study to make head-to-head comparisons between tenofovir gel and oral tenofovir – two promising approaches for preventing HIV in women – researchers found that daily use of the vaginal gel achieved a more than 100-times higher concentration of active drug in vaginal tissue than did the oral tablet, while compared to the gel, the tablet used daily was associated with a 20-times higher active drug concentration in blood.

But the Phase II trial, which examined differences in drug absorption as well as women's preferences for each daily regimen, claimed that most of the women in the United States favoured the oral tablet over the vaginal gel, while African women who participated in the study favoured the gel and tablet equally.

MTN-006 - USA

Bloomberg Businessweek

Executive Health February 28, 2011, 12:00 EST

Rectal Gel Could Help Ward Off HIV: Study

But more research needed before treatment can be released to the public, experts say



MONDAY, Feb. 28 (HealthDay News) – Preliminary research suggests that an HIV-fighting gel has the potential to become

another weapon in the fight against AIDS when applied to the rectum before anal intercourse.

This is the first time scientists have found evidence that people would tolerate using a gel form of the commonly used AIDS drug tenofovir (Viread) in the rectum. However, there are caveats. The volunteers who tried the gel weren't exposed to HIV and they didn't like the treatment very much. There were side effects in some people, and there's still more research needed to figure out whether the treatment is ready for release to the public.

MTN-006 - USA

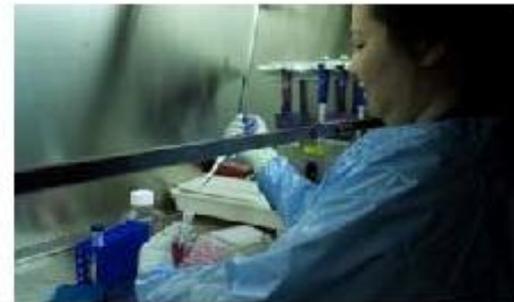
TIME Partners with **ON** **TIME Healthland**

An Anti-HIV Gel Shows Some Promise for Prevention

By [MEREDITH MELNICK](#) Monday, February 28, 2011

A new study presented Monday at the annual Conference on Retroviruses and Opportunistic Infections (CROI) in Boston suggested the potential of an anti-HIV gel in protecting rectal tissue cells from infection with the virus that causes AIDS.

For the new study, researchers from the Microbicide Trials Network, University of Pittsburgh and Magee-Womens Research Institute recruited 18 sexually abstinent HIV-negative men and women to participate. The volunteers were first asked either to apply the anti-HIV gel to the rectum once or to take an oral tenofovir pill once. Then, the patients followed up by applying either tenofovir gel or placebo gel every day for six days at home; a final, seventh dose was applied in the lab.



MTN-006 - USA



AIDS gel shown to protect anal tissue from HIV

Mon, Feb 28 2011

LOS ANGELES (Reuters) - An experimental gel containing a prescription HIV drug has been shown for the first time to protect rectal tissue against the virus that causes AIDS, according to new research.

The gel, containing Gilead Sciences Inc's AIDS drug tenofovir, has previously been shown to sharply reduce HIV infections in women when applied inside the vagina.

The latest study, which involved rectal tissue biopsies taken from HIV-negative men and women who used the product daily for one week, provides the first evidence that tenofovir gel could help reduce the risk of HIV from anal sex.



MTN-006 - South Africa



Rectal gel shows promise in HIV fight

2011-02-28 16:56

Washington - A gel that has been shown to reduce the risk of HIV infection in women during vaginal sex has also shown promise toward preventing transmission during anal sex, US researchers said on Monday.

"HIV was significantly inhibited in tissue samples from participants who used tenofovir gel daily for one week compared to tissue from participants who used the placebo gel," the study said.



Moving Forward



The MTN Research Portfolio

- Expansion of rectal microbicide agenda
 - MTN-017
- Development of peri-approval trial for tenofovir 1% gel
 - MTN-018
- Expansion of pregnancy agenda
 - MTN-019
- Sustained delivery of an NNRTI ring
 - MTN-020
- Safety data in adolescents
 - MTN-021



MTN-017

- Phase 2 rectal safety study
- International sites
 - United States
 - Thailand
 - South Africa
 - Peru
- Design: Crossover
- Endpoints
 - Safety
 - Adherence
 - Self report
 - Objective measures
 - Acceptability
 - PK/PD

MTN-017 Preliminary Design

| | | | | |
|---|---------|--------------|---------|--|
| Topical RGF tenofovir 1% gel | Washout | Oral Truvada | Washout | Oral Truvada + Topical RGF tenofovir 1% gel |
| 4-6 weeks | 2 weeks | 4-6 weeks | 2 weeks | 4-6 weeks |
| N = ~ 100 - 120 | | | | |
| Safety and acceptability (All sites) | | | | |
| Objective measures of adherence (All sites) | | | | |
| Mucosal safety (Domestic site[s]) | | | | |
| PK/PD (Domestic site[s]) | | | | |





MTN-018

Committed to **H**aving **O**ptions for
Interventions to **C**ontrol the
Epidemic:
a Follow-up Study to MTN-003

Committed to **H**aving **O**ptions for
Interventions to **C**ontrol the **E**pidemic

CHOICE

MTN-018 – A Phase 3B Study

- Phase 3B studies conducted just before or during regulatory filing
- Provides better understanding of benefit/risk ratio
- Safety and efficacy in real world settings
 - Open label study
 - Reduced frequency and intensity of trial monitoring
 - Introduces “choice”

MTN-018 Timelines

□ January 2011

■ Advocates' Consultation: Johannesburg

□ January 17-18, 2010

■ Protocol Development Meeting: Durban

□ January 19-21, 2010

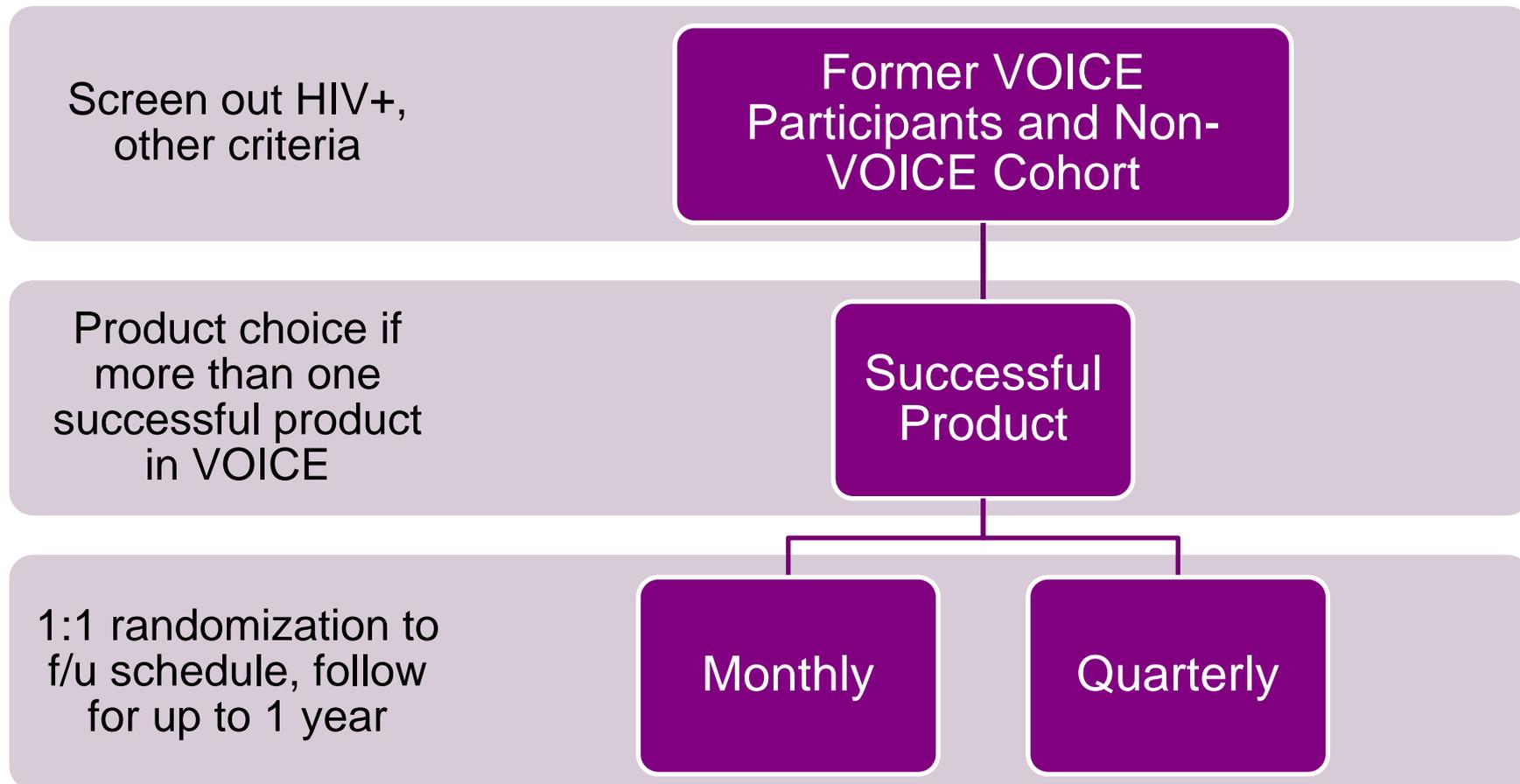
□ March - May 2011

■ DAIDS PSRC review of MTN-018 protocol

■ Protocol received MO sign-off

■ Will be presented to DAIDS SWG in May 2011

Draft design of MTN-018



Currently anticipate only one oral drug for this protocol.

MTN-018 – Next Steps

2011

- PSRC Review 15 March 2011
- Develop and finalize MTN-018
- Complete accrual in VOICE

2012

- Complete f/u in VOICE
- Pre-implementation of and local approvals for MTN-018

2013

- Announce VOICE results
- Offer MTN-018 to VOICE ppts.

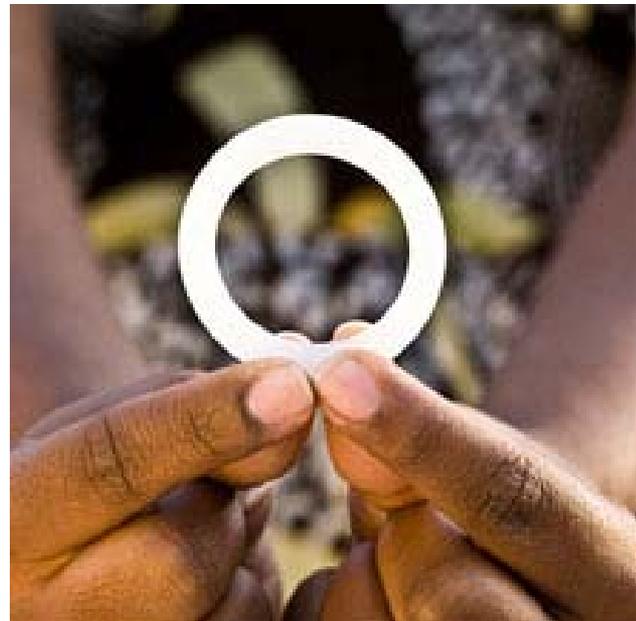
MTN-019

- ❑ Extended safety of tenofovir 1% gel in pregnancy
- ❑ Stepwise progression of pregnancy safety data including second trimester
- ❑ Concept approved for protocol development
- ❑ Protocol development meeting March 2011



MTN-020

- Safety and effectiveness study of dapivirine ring
- Silicone elastomer vaginal matrix ring
- Target sample size approximately 3,000
- Concept approved
- Protocol discussion at MTN Annual Meeting



MTN-021

- Safety and tolerability of tenofovir 1% gel in adolescent females
- Protocol being developed in response to FDA request for additional safety data in this population
- Participants will be enrolled at NICHD ATN and IMPAACT clinical sites
- Study concept approved for protocol development



National Institutes of Health
Eunice Kennedy Shriver
National Institute of Child Health & Human Development





The Extended MTN Family

Tenofovir 1% Gel

- MTN-001
- MTN-002
- MTN-003
- RMP-02 / MTN-006
- MTN-007
- MTN-008
- MTN-011
- MTN-017
- MTN-018
- MTN-019
- MTN-021



- MTN-005
 - Placebo ring
- Preclinical comparative studies
 - MIV-150, zinc, Carraguard gel



- MTN-017



- MTN-012
 - Dapivirine gel
- MTN-013
 - Dapivirine/maraviroc gel
- MTN-020
 - Dapivirine ring

BILL & MELINDA
GATES *foundation*

The National Institutes of Health



NIAID



National Institutes of Health

Eunice Kennedy Shriver

National Institute of Child Health & Human Development

Current MTN Portfolio

| | Phase | Product (s) | Route | 11 | 12 | 13 | 14 |
|------------|----------------------------|---------------------------|-------|----|----|----|----|
| MTN-003 | 2B | TVD/TDF/Tenofovir | O, V | | | | |
| MTN-005 | 2 | Placebo ring | V | | | | |
| MTN-007 | 1 | Tenofovir/HEC/N-9 | R | | | | |
| MTN-008 | 2 | Tenofovir | V | | | | |
| MTN-009 | Resistance | N/A | | | | | |
| MTN-011 | 2 | Tenofovir | V | | | | |
| MTN-012 | 1 | Dapivirine | P | | | | |
| MTN-013 | 1 | Dapivirine/maraviroc ring | V | | | | |
| MTN-015/16 | Seroconversion / Pregnancy | | | | | | |
| MTN-017 | 2 | TVD/Tenofovir | O, R | | | | |
| MTN-018 | 3B | TVD or TDF/Tenofovir | R | | | | |
| MTN-019 | 2 | Tenofovir | V | | | | |
| MTN-020 | 2B/3 | Dapivirine | V | | | | |
| MTN-021 | 2 | Tenofovir | V | | | | |



Meeting Highlights

- Plenary sessions today and tomorrow morning
- Special screening of “We Were Here” tonight from 5:00 to 6:30
- Welcome reception and poster session highlighting work from the network lab from 7:00 to 9:00 PM

Enjoy the Meeting!

