

Microbicide Trials Network: State of the Network

MTN Annual Meeting

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March 16, 2010



Who Is Here Today?

- 283 people registered
- 128 site investigators, staff and community members
- 68 people from the NIH or other US government agencies
- 55 people from MTN CORE, lab and SCHARP
- 12 people from collaborating partner organizations (CONRAD, IPM, Gilead)
- 5 people from advocacy organizations (GCM, IRMA, AVAC)
- A few people I don't know yet who marked "other" when they registered



Who Is Here Today?

- 283 people registered
 - 128 site investigators, staff and community members
 - 63 people from NIH and other US government agencies
 - 55 registrants from MTN CORE, lab and SCHARP
 - 42 people from collaborating partner organizations (CONRAD, IPM, Gilead, Population Council)
 - 5 people from advocacy organizations (GCM, IRMA, AVAC)
 - A few people I didn't know who said that were "other"
- We welcome you all to the 4th annual MTN meeting!**

Time for a Mid Course Evaluation

- MTN was funded in July 2006 for 7 years
- We are now completing the 4th year of our 7 years of funding
- We can anticipate that we will submit an application for continued funding in 2012
- 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's Original Research Questions

- Can a chemoprophylactic agent applied topically or orally at least partially prevent HIV infection?
- How can we best measure safety?
- How acceptable are these products, and how can we best measure adherence and its impact on effectiveness?
- How can we move into other high risk populations including pregnant women and adolescents
- Which strategy makes more sense for antiretroviral prophylaxis in women: oral or topical?

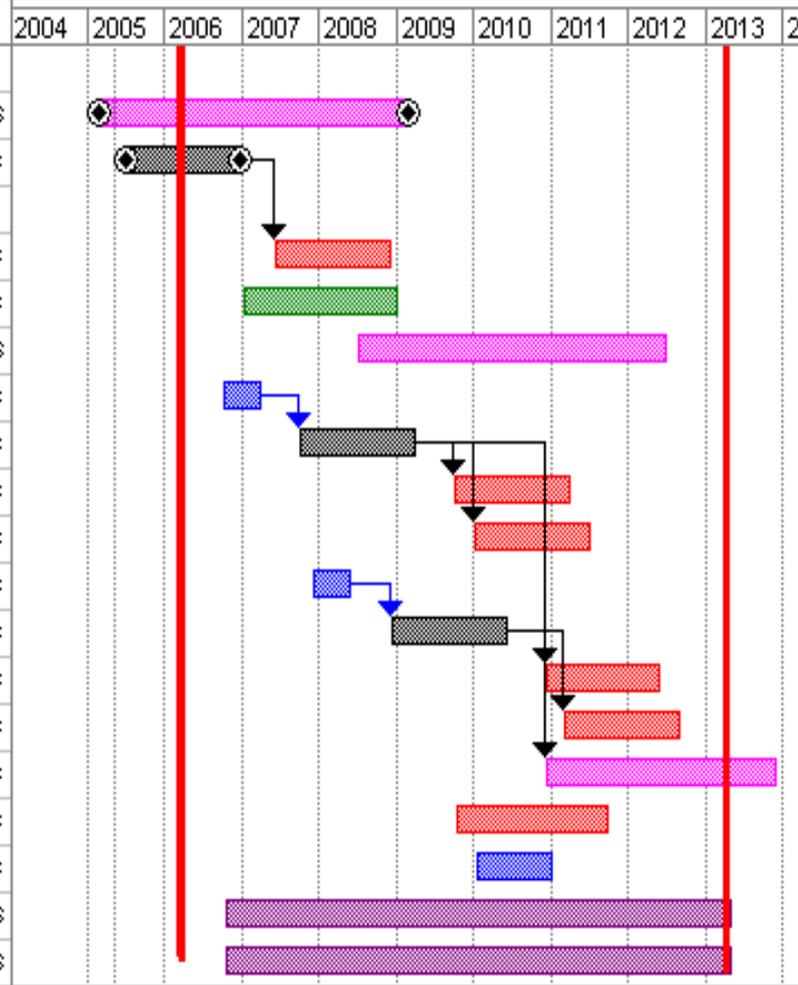


A Network with a Drug Development Focus

- Research under IND of drug agents in support of NDA
- Goal of moving prevention products forward to licensure
- Development of network structures in support of a drug development team
 - Preclinical evaluation
 - Industry relationships to develop access to new products
 - Pharmacovigilance teams to detect emerging AE reporting differences across sites, and emergence of safety signals within studies
- Tight, timeline driven management of network operations

What Did We Promise to Do in 2005?

Task Name	Product (s)	Population	Phase	N	Duration	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
HPTN-035	BG, Pro2000	HIV Neg	2B	3220	1040 days											
HPTN-059	PMPA	HIV Neg	2	200	390 days											
MTN-001	PMPA	HIV Pos	1	45	390 days											
MTN-002	N/A	HIV Neg	Prep	1500	520 days											
MTN-003	TDF, PMPA	HIV Neg	2B	3000	1040 days											
MTN-004	CCR5	HIV Neg	1	30	130 days											
MTN-005	FI, CCR5	HIV Neg	2	300	390 days											
MTN-006	FI	HIV Pos	1	45	390 days											
MTN-007	CCR5	HIV Pos	1	45	390 days											
MTN-008	RTI ring	HIV Neg	1	30	130 days											
MTN-009	RTI, RTI ring	HIV Neg	2	300	390 days											
MTN-010	RTI	HIV Pos	1	45	390 days											
MTN-011	RTI ring	HIV Pos	1	45	390 days											
MTN-012	RTI, FI, CCR5	HIV Neg	2B	4900	780 days											
MTN-013	RTI	HIV Neg + HIV Pos	1	60	520 days											
MTN-014	Rectal TBD	HIV Neg	1	30	260 days											
MTN-015	N/A	HIV Pos	Seroconverter	300	1712 days											
MTN-016	N/A	HIV Pos	Registry	225	1712 days											



And How Did We Do?

Goals in 2005

Complete HPTN 035

Complete HPTN 059

Have 10 new protocols underway or completed

Rectal Phase 1 to start in 2010

Start Phase 2B study of oral vs. topical tenofovir in 2008

Actual Activity as of Q1 2010

Completed in August 2008 (within one month of timeline projected in 2005)

Completed on time and \$500K under budget

6 protocols underway
4 completed
5 more completed PSRC review

MTN-006 started in 2009 and MTN-007 will start in 2010

Started in 2009, but scheduled to complete within 6 months of the 2005 plan of mid-2012

What Questions Will We Answer by 2013?

- Can a chemoprophylactic agent applied topically or orally at least partially prevent HIV infection?
 - VOICE
- How can we best measure safety?
 - 001, 006, 007, 010
- How acceptable are these products, and how can we best measure adherence and its impact on effectiveness?
 - VOICE, MTN-001
- How can we move into other high risk populations:
 - Pregnant women (MTN-002, 008, 016)
 - Adolescents (MTN-004)
 - MSM (MTN-006, 007)
- Which strategy makes more sense for antiretroviral prophylaxis in women: oral or topical?
 - VOICE, MTN-001



What Did the NIH External Advisors Say After the Review of MTN in January 2010?

- “The External Experts commended the MTN’s efforts in achieving the goals originally set out in their grant application, for their collaboration with other networks, and demonstrating flexibility and innovation regarding leveraged resources.”



Getting to the Best Prevention Science

- Protocol concepts are provided to a broad range of people for input and suggestions
 - Sites
 - Funder
 - Network Lab, CORE and SCHARP
 - Three working groups: Community, Biomedical Science and Behavioral Research
- Input continues throughout protocol development process

Biomedical Science Working Group

- Provide scientific advice on protocol design and implementation
- Translate results obtained in the lab to protocol design
 - Translate clinical trial results **back to the lab**
 - Recommend & implement sub-studies



Building MTN Sample Repository

- ❑ HPTN 035 Swab Repository: collaboration with Gates Foundation. Total of 3,524 genital swabs from 2,031 women collected
- ❑ MTN-001 (TFV PK)
 - Collect CVL for vaginal flora proteomics and markers of inflammation
- ❑ MTN-003/VOICE
 - Vaginal and endocervical swabs for biomarkers every six months
- ❑ MTN-004 (Vivagel)
 - Swabs for flora, cytokines & endogenous antimicrobial activity

Behavioral Research Working Group

- Participate in the process of study design from the concept stage forward
- Identify best quantitative and qualitative approaches for behavioral assessment
- Collaborate with SDMC staff in designing and pre-testing behavioral questionnaires (both electronic and paper)
- Plan analysis of behavioral data from each trial
- Research agenda supported by NIMH and implementation supported jointly by NIMH, DAIDS and NICHD

BRWG – New Directions

- Develop and expand behavioral research into pregnant and lactating women (MTN-008)
- Assess acceptability of rectal microbicides (MTN-006 and MTN-007)
- Conduct mixed-methods (quantitative/qualitative) behavioral research on adherence and product sharing (MTN-001)
- Scale up and implement pictorial ACASI in VOICE trial (5 countries/9 languages)
- Implement innovative ethnographic/qualitative research – ancillary protocol to support/expand adherence research in VOICE-C

CWG Addressing Challenges

- Identifying new leadership for a rapidly growing working group
- Creating discussion time for numerous topics, relevant to US and non-US sites
- Telecommunication
- Male involvement



CWGW Future Directions

- Solicit opinions on potential outcomes of ongoing prevention trials
- Grow partnership between VOICE sites and surrounding communities
- Capacity-building to meet the needs of site communities and the network agenda





Most Important Accomplishments 2009

- First study directly assessing PK and acceptability of an oral vs topical antiretroviral (MTN-001)
- First study of microbicide gel in pregnant women (MTN-002)
- Initiation of flagship topical and oral PrEP protocol, VOICE, in 2009 (MTN-003)
- First joint IPCP-MTN protocol evaluating rectal microbicides (MTN-006)
- Launch of seroconverter protocol (MTN-015) and pregnancy registry (MTN-016)

VOICE and Related Studies

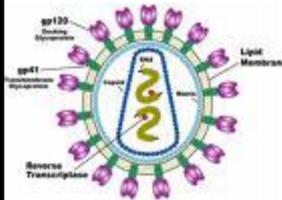
VOICE Study

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 (p27)
3. Negative control
4. Indeterminate profile (p24/p27 negative)

MTN-015

Drug toxicity



VOICE-B

Community Perceptions



VOICE-C

The PrEP Landscape

	2009	2010	2011	2012	2013	
Bangkok IDU						
iPrEx						
CAPRISA 004						
Partners PrEP						
FEM-PrEP						
VOICE						

Current MTN Portfolio

	Phase	Product (s)	08	09	10	11	12	13
MTN-001	2	TDF/Tenofovir						
MTN-003	2B	TVD/TDF/Tenofovir						
MTN-005	1	Placebo ring						
MTN-006	1	Tenofovir						
MTN-007	1	Tenofovir/HEC/N-9						
MTN-008	1	Tenofovir						
MTN-009	Resistance	N/A						
MTN-010	2	UC781						
MTN-015	Seroconversion	N/A						
MTN-016	Pregnancy	N/A						

What Are the Opportunities?

- Expansion of biomedical prevention research into MSM:
 - Expanded rectal microbicide safety; effectiveness study
- New products:
 - NNRTIs, integrase inhibitors, CCR5, combinations
- New delivery methods:
 - Rings, injectables, films
- New and expanded collaborations:
 - CONRAD, Gilead, IPM, Population Council

Potential New Products

- Reverse transcriptase inhibitors
 - Dapivirine ring or gel (IPM)
 - TMC-278 LA injectable (IPM and BMGF)
 - UC-781 (CONRAD)
 - Tenofovir + UC781 (CONRAD)

- Entry Inhibitors with RTI's
 - Maraviroc plus dapivirine (IPM)



What are our Challenges?

- Predicted and *unpredicted* closures of prevention trials
- Development of alternative strategies for future trial design once a placebo control is no longer ethically feasible
- High costs and complexity of prevention trials- the need to maintain our pipeline of products while conducting VOICE- in a flat NIH budget

So Why Are We Smiling?

- We are happy to seeing each other in person instead of talking by conference call
- We like to have fun even though we are efficient and timeline driven (be sure to come to the reception tonight!)
- We have strong partnerships with sites, community and funders
- There are multiple opportunities to develop and evaluate new products and approaches which can be implemented as part of combination prevention in the future

For HIV Prevention....

- The road is never straight
- There are always more mountains to climb
- There are always people willing to tell you how much better they could direct the climb up the mountain if they were in charge

- But in the MTN family, we can *lean* on each other and *learn* from each other
- If we remember to *love* each other and *laugh* as we go.....we will find a way
- HIV prevention is in our hands