



Microbicide Trials Network

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Annual Meeting Welcome

11 February 2013

Overview

- What has the MTN been doing over the past year?
- Why is doing HIV prevention research so complicated?
- Our major themes?
 - Responding to change
 - Embracing new technology
 - Reaching out to new populations
 - Seeking community perspectives
 - Creating a vision for the future
- What to expect at this meeting

Our Major Activities-A Snapshot

- Completion of VOICE in August 2012, data clean-up and preparation for presentation at CROI on March 5, 2013
 - 1 million case report forms, thousands of vaginal fluid and plasma samples
- Launch of MTN-011- first MTN study to incorporate timed intercourse to evaluate the impact of sex on drug pharmacokinetics
- Enrollment of the first study of a microbicide in lactating women (MTN-008)
- Completion of first vaginal ring phase 1 studies: MTN-005 and MTN-013
- Launch of ASPIRE (MTN-020)- phase 3 study of the dapivirine ring

It seems so simple

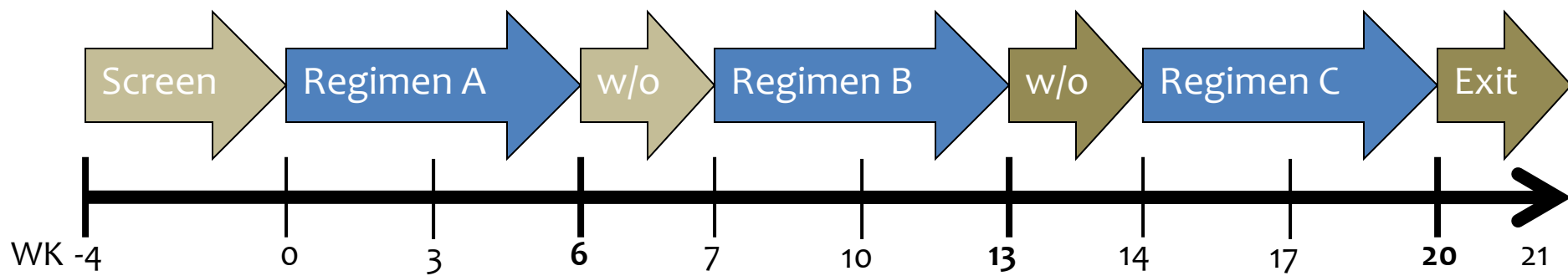


But It is Much More Complicated



MTN-001 Study Design

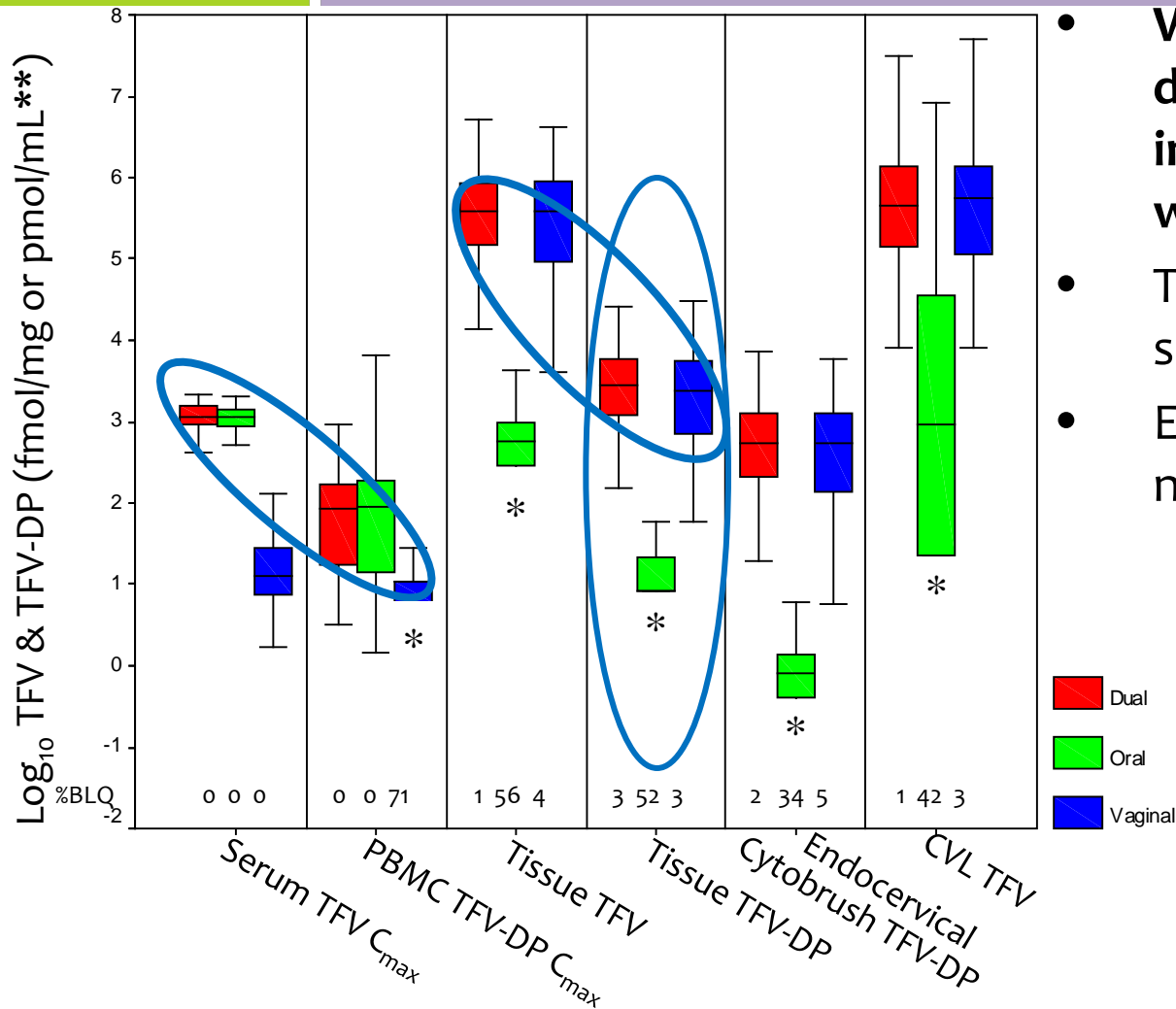
- Three period, open label crossover study
- All receive oral, vaginal, dual – sequence randomized
 - Tenofovir disoproxil fumarate (TDF) 300 mg oral tablet daily
 - Tenofovir 1% (TFV, 40 mg) vaginal gel daily
- 144 sexually active, HIV- women, 18-45 y.o., 7 sites
- 21 weeks (3, 6-week periods; 1 week washout)



- Safety, adherence, acceptability, PK each visit

MTN-001

TFV & TFV-DP by Route & Site



- Vaginal dosing achieves active drug (TFV-DP) concentrations in tissue >100x higher than with oral dosing
- TFV-DP ~5-15% of TFV in the same compartment
- Effective concentrations have not been established

Hendrix, et al, PLoS One 2013

*Median <LLOQ, assigned BLQ/2 for median; value **Molar equivalent units assumptions: gm = mL, 10⁶ cells = 0.2uL

Self-Reported Product Adherence

	Overall	Vaginal Gel	Oral Tablets	Dual
	N=851‡	N=285	N=282	N=284
	%	%	%	%
Adherence Measures				
% daily doses taken (mean, SD)†	94.0 (10.8)	94.4 (12.2)	93.9 (10.1)	93.8 (10.2)
>=90% doses taken	81	85	79	79

†p=0.8 (mixed effect model with Gaussian link and fixed effects for treatment, period, sequence; random effect of participant within sequence).

‡N=visits among 144 participants; maximum of 864 possible visits.

No differences in among regimens or across study sites.
 BUT- only about 50% of women used their drug

Adherence and HIV protection in oral PrEP trials evaluating FTC/TDF

	% of blood samples with tenofovir detected	HIV protection efficacy in randomized comparison
Partners PrEP FTC/TDF arm	81%	75%
TDF₂	79%	62%
FEM-PrEP	26%	6%

**There is a clear dose-response
between evidence of PrEP use & efficacy**

Lessons Learned

- To quote Connie Celum, “Adherence is the Achilles heel of ARV-based prevention”
- The same intervention used in a different population (different age, different risk perception can yield very different results)



A convergence of factors



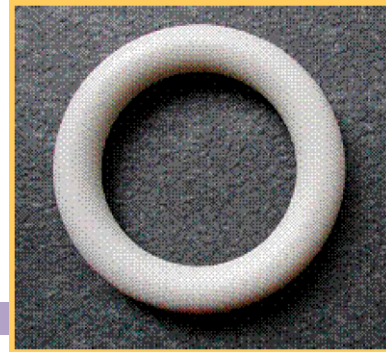
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Responding to Change



- VOICE D- new study developed after the closure of the oral and topical tenofovir arms in VOICE; completed in Uganda and Zimbabwe, ongoing in Durban
- Incorporation of real-time PK measurement in MTN-017, expanded safety study of tenofovir gel as a rectal microbicide
- Changing the design of MTN-011 (coital study of tenofovir PK) after the closure of the tenofovir gel arm in VOICE for futility

Embracing new technology



- Evaluation of vaginal rings for sustained delivery of ARVs
 - MTN-005- placebo ring collaboration with the Population Council
 - MTN-013- first combination dapivirine plus maraviroc ring, 4 arm study; first time maraviroc evaluated intravaginally
 - MTN-020-pivotal phase 3 study of the dapivirine ring for prevention of HIV

Reaching out to diverse populations

US, African and Indian Women



Pregnant and breastfeeding women



MTN-002, 008 and 016

Across the lifespan



Adolescent girls: MTN-023

Post-menopausal women:
MTN-024



MSMs and Transgender Women



RMP-02/MTN-006, MTN-007 and
MTN-017

Transgender women
in MTN-017



Seeking community perspectives

- VOICE-C: protocol developed in collaboration between the Community Working Group and the Behavioral Research Working Group.
- Multiple community consultations
 - African women and MSM
 - Advocates and key stakeholders in Africa
 - Black MSM in the US
 - Thai and Peruvian MSM
- Partnership with Be The Bridge (welcome!)

Creating a vision for the future

- MTN application for 2013 to 2020 submitted in September 2012
- CTU applications just submitted in January 2013
- Stay tuned for Ian McGowan's presentation tomorrow..... Much exciting science ahead

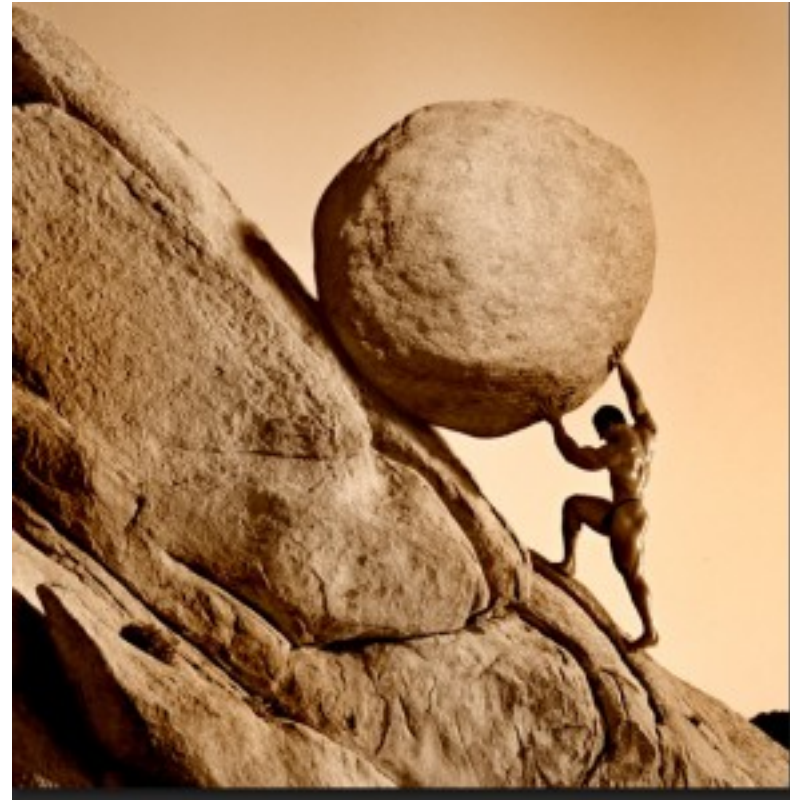
Keeping an eye on the horizon

- US budget crisis is placing great pressure on research
- NIH budget is flat and may get worse
- We have to do the best science as efficiently as possible



For this meeting

- Work hard
- Thank our funders for their support of our work
- Have fun-Join us for the reception tonight
- Meet someone new
- Tell us how we can do better
- Help us find creative solutions



Acknowledgements

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