



Welcome to the Microbicide Trials Network

Regional Meeting
October 29, 2013

R4P 2014

- Separate meetings for HIV vaccines, microbicides, and treatment for prevention will not be supported by NIH and the BMGF
- Why a combined meeting?
 - funding constraints
 - need to create more synergy across the HIV prevention research field
- Research for Prevention Conference 2014: AIDS Vaccine, Microbicide & ARV-based Prevention Science
 - 28-31 October 2014 Cape Town International Conference Centre
- **MTN Regional Meeting is scheduled just prior to the R4P meeting from Saturday Oct 25 through Monday Oct 27**
 - **Shorter meeting with few plenary sessions and focus on team meetings**

R4P Conference

- Enterprise Board Conference Committee and Program Organizing Committee convened
- 3.5 days long
- ~1,500 participants
- Estimated 700 abstract submissions
- 200 full and 100 partial scholarships
- Daily plenaries; concurrent abstract-driven sessions, invited symposia and roundtables
- HIV R4P abstract and scholarship deadline will be May 9, 2014.

The MTN Year in Review: Oct 2012 to Today

- VOICE: Completed all cleanup of data and resolution of endpoints, drug level testing and efficacy review (September to December) and announcement of results (March 2013)
- ASPIRE: opening of sites in S Africa, Zimbabwe, Uganda and Malawi and enrollment of 1832 participants at 15 sites
- Completion of MTN-005, 008, 013
- Launch of first phase 2 rectal microbicide study, MTN-017
- Sites and network went through recompetition

How is microbicide research like farming?

“Farming is a profession of hope.”

Brian Brett



How else is microbicide research like farming?

- Every planting season will not yield a good crop because of things outside of one's control: rainfall, heat, natural disasters, insects
- Every HIV prevention will not yield the desired outcome because the intervention may not work, or it may not be used often enough to be effective

VOICE Product Adherence from 3 Different Measures

	Truvada Tablet	Tenofovir Tablet	Tenofovir Gel
Returned Pill or Applicator Counts	92%	87%	86%
Self Report	91%	90%	90%
Drug Detected in Blood	29%	28%	23%
Percentage of women with no drug detected in <i>any</i> sample	50%	58%	55%

Reflections on VOICE.....



Dr. Judith D. Auerbach: :What I find most interesting is how the field talks about what went on in this trial and what the problems or issues are. We heard that women in the trial who *said* they were taking the oral drug (although the gel was also problematic) were not actually taking the pill, so the issue becomes cast as an adherence problem: Women didn't take the drug as prescribed.

Reflections on VOICE



“The other way people talk about the trial is to say that the product didn’t work, or the trial didn’t work. And neither of those is true.

What we know is that the product works, in an efficacy sense, when it’s in the body—you know, “the right drug, at the right dose, in the right place, at the right time.”

Reflections on VOICE



“So the issue is not that the drug doesn’t work, and the issue isn’t even that the trial didn’t work—because the trial did everything it was designed to do. The issue is really that **certain** women don’t take drugs, period.”

Judy Auerbach

In an interview March 4, 2013

What is VOICE C teaching us?

“VOICE participants misrepresented their adherence behaviour, not only to continue to benefit from the trial, but also to sustain their new found identities as HIV negative, healthy and empowered. Admitting to being faulty with regard to adherence threatened to undermine these subjectivities.”

Jonathan Stadler

What is VOICE D teaching us?

“Participants spoke widely of ‘other women’ not adhering.....Participants demonstrated poor understanding of adherence questions, rating scale and response categories”

Zoe Duby

How else is microbicide research like farming?

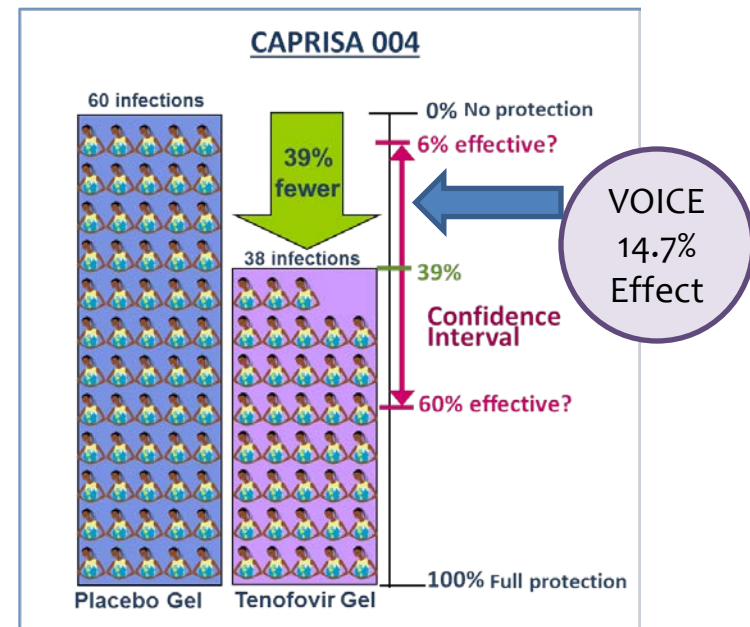
- A farmer has a limited number of “planting seasons” in his or her life to try new approaches- perhaps 30-40 seasons in a lifetime
- There will be a limited number of trials which can be conducted to evaluate an approach due to limitations in
 - Funding
 - Support from the communities



“Seasons” of Microbicide Research



- Surfactants: N-9, Savvy (C31G)
- Nonspecific microbicides:
 - BufferGel
 - PRO2000
 - Cellulose sulfate
- Tenofovir gel daily or coitally
 - CAPRISA-004: 39% effective
 - VOICE: 14.7% effective
 - FACTS-001: ??
- Dapivirine sustained delivery ring
 - IPM-027 RING study
 - ASPIRE
- No effect or slightly harmful
- PRO 2000 30% decrease in HPTN-035, not confirmed in MDP-301



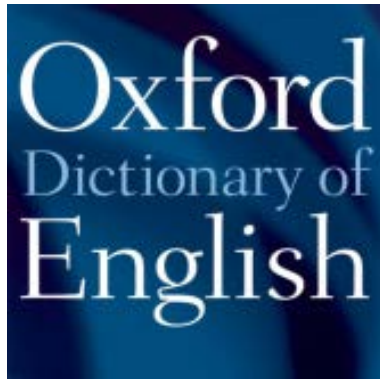
Getting the most out of the studies we have completed

- VOICE B- still need to complete drug levels to assess impact of oral PrEP on bone density
- VOICE C- community views (Plenary 3)
- VOICE D- in depth interviews (Plenary 3)
- Secondary analyses of HSV-2 (Plenary 3)

Long Acting Reversible Prevention

- **LARC= Long Acting Reversible Contraception**
 - Contraceptive Action Team has been working to increase contraceptive mix to more effective family planning methods (plenary 4)
 - Greatest transition has been from OCs to IUCDs and implantable devices
 - Pregnancy rate among women in MTN studies has been reduced to 3% in ASPIRE!
- **LARP= Long Acting Reversible Prevention**
 - Sustained delivery of ARVs for prevention of HIV

What does ASPIRE mean?



aspire(as·pire)

Pronunciation: /ə'spī(ə)r/

Verb [no object]

direct one's hopes or ambitions toward achieving something

MTN noun:

1. A Phase III study that seeks to determine whether a woman's use of a vaginal ring containing the antiretroviral (ARV) drug dapivirine is a safe and effective method for protecting against HIV infection.

verb:

1. **To seek to end the HIV epidemic** < We *aspire* to prevent HIV >

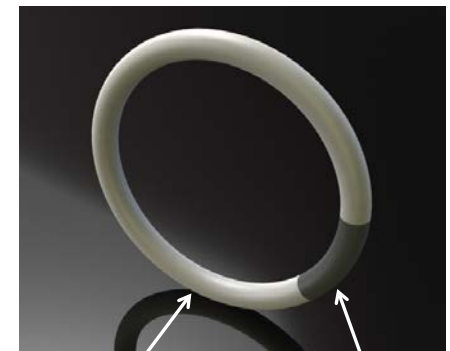
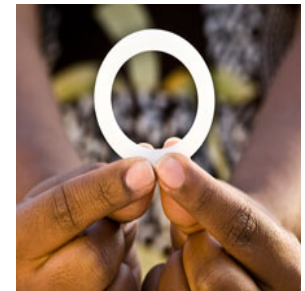


What is ASPIRE Teaching Us About Rings for Sustained Delivery?

- Rings are new for many women, but women get better at using rings over time (Plenary session 5)
- They deliver drugs effectively to the vagina and cervix, but drug disappears rapidly when rings are removed (MTN-013)
- Most women report that the ring cannot be felt during sex and that it is comfortable but it is not for everyone
- Based on drug levels, adherence to study product is greater when drug is delivered via ring vs. daily use products

Next Generation MPT Rings

- HIV, Contraception
 - Dapivirine + HC Vaginal Ring (IPM)
 - 60 day use
 - Preclinical formulation ongoing
- HIV, STI, Contraception
 - TNF/LNG 90 day IVR (CONRAD)
 - HIV, HSV, pregnancy protection
 - Segmented design; co-extruded reservoir LNG segment
 - Sheep vaginal tissue: > 1% TFV gel over 90 days; Target trial date: Q1, 2014



TNF

LNG

Contraceptive Rings with ARVs

- Group discussion with 40 contraceptive providers (physicians and nurses) from Zimbabwe, Uganda and S Africa in January '13
 - Women do not want others to know that they are using HIV prevention products because of stigma associated with HIV: **90%**
 - Women would be more likely to use an ARV for prevention if combined with HC: **78%**
 - Continuous use of an ARV/HC ring would be acceptable to African women even if it meant that they would not have monthly menses: **93%**

Stealth HIV Prevention in a Contraceptive Ring?

- May reduce stigma associated with use of ARVs for prevention
- Could increase “desirability” of product
 - Many more women will say that they want a contraceptive than to acknowledge that they are at risk of HIV



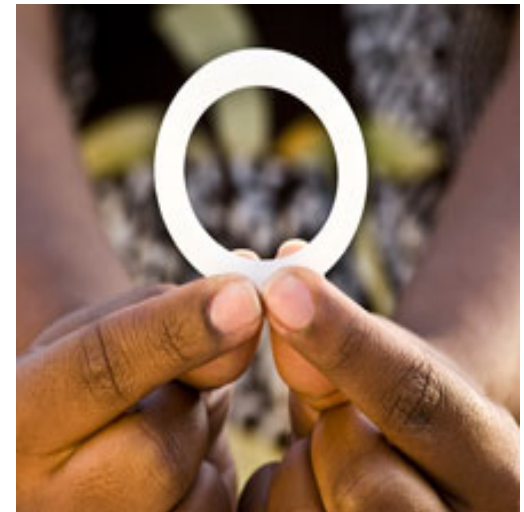
Partnerships for the Next Generation of Products



- Several new products in development
 - Different, smaller more flexible rings
 - Different ARVs
 - Combinations of contraceptives and ARVs
 - Combination products active against STIs/ HIV
- Will need to make tough decisions on which products will represent the “next season” of microbicides
- Partnership with NIH and BMGF

How else is microbicide research like farming?

- Both can contribute to healthier and longer lives for men and women everywhere
- And farmers and microbicide researchers work very hard, and they never, never lose hope.





Welcome to the 2013 MTN Regional Meeting
