

# MTN Welcome

# State of the Network

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MTN LOC

**MTN Meeting**

March 20, 2017



# State of Biomedical HIV Prevention in 2017

1. Oral PrEP (Truvada)- approved and rolling out
2. Potential licensure of dapivirine IVR; OLEs enrolling
3. Long acting injectables in clinical trials
  - a. Cabotegravir; rilpivirine
  - b. Phase 3 trial in men to launched (HPTN 083) and protocol for women nearing launch (HPTN-084)
4. Broadly neutralizing antibodies : Antibody Mediated Prevention (AMP) trials (HVTN/HPTN) over 50% enrolled
5. HVTN 702 vaccine trial launched

# The Prevention Landscape



- There have been tremendous changes in the HIV epidemic in the US and internationally
- Scale up of treatment of prevention and circumcision leading to 60% reductions in new infections among men and 30% among women (CROI 2017)
- PrEP programs rolling out domestically and in Africa
  - Challenges in youth
  - Even with uptake, sustained use difficult

# State of the MTN

- First funded in 2006, and has now been in existence for a decade. Our mission: to evaluate and bring to licensure more prevention tools for the toolbox!
- *Have enrolled over 11,000 study participants into IND studies of investigational drugs*
- *Partners: Gilead, CONRAD, IPM, Pop Council, Merck*
- Scientific contributions:
  - Since our renewal December 1, 2013
    - 69 manuscripts published or accepted
    - 180 scientific presentations at professional meeting



# What Have We Accomplished with Dapivrine Rings Since 2013?



- Completed ASPIRE, published primary data, working toward submission of the clinical study report and supporting IPM in the submission of the regulatory dossier.
- Completed MTN-023: safety study in 15-17 year olds
- Completed MTN-024: safety study in post-menopausal women
- Launched MTN-025 (HOPE)
- Completed MTN-029: lactation study in US women
- MTN-034: Developed protocol for African adolescents

# What Have We Accomplished Since 2013?

- Merck vaginal ring containing vicriviroc and the integrase inhibitor MK-2048: completed MTN-027 and 028 phase 1 studies.
- Tenofovir gel studies (vaginal):
  - MTN-011: vaginal sex decreases drug levels (Herold, published 2015)
  - MTN-014: cross- compartment drug inadequate to provide protection (manuscript in preparation)

# What Have We Accomplished Since 2013 for Rectal Microbicides?

- Completed MTN-017 (oral Truvada and tenofovir gel), published primary paper (2016)
  - Use of an applicator was not acceptable rectally
  - Gel applied rectally did not provide sufficient lube such that MSM still had to use additional lube for anal sex
- MTN-026 and 033: dapivirine gel, pending activation
  - Will address whether using a gel as a lube without an applicator can provide adequate drug for protection

# What's Next for Rectal Microbicides?

- MTN-035: Acceptability study of the rectal insert vs douche as a delivery system
- MTN-037: MIV 150 gel escalation to assess volume of gel impact on drug distribution (Population Council)
- MTN-039: PK/PD study of the elvitegravir (integrase inhibitor) rectal insert (CONRAD)

# What are the Highest Priorities for the Next 3.5 Years?

- Support the completion of the dapivirine ring dossier for regulatory approval
- Generate new data on high priority populations
  - Generate data on adolescents (MTN-034)
  - Data for pregnant and breastfeeding women
    - Protocol concept for evaluation of safety of dapivirine ring in pregnant and breastfeeding women in a “de-escalation” of gestational age model
    - To be discussed at the Executive Committee meeting on Wednesday

# Why Pregnancy?



- Pregnant women at high risk of HIV
- No regulatory approval for use of PrEP in pregnant and breastfeeding women
- WHO recommendation for use but S Africa advises against its use.
- Lesson learned: need to anticipate need for these data so that pregnant and breastfeeding women are not excluded from benefits of new prevention products

# High Priority: Development of an MPT

- Move forward on the development of the MPT next generation rings
- Tenofovir 90 day ring (MTN-038)
- Higher dose dapivirine rings with and without levonorgestrol
  - MTN-030 set to launch in Pittsburgh and Birmingham next month
  - MTN-036 in development: 100 and 200 mg rings intended for 3 months of use
- How can we expedite MPT development?

# Why Microbicides?



- Proof of concept established that vaginal products can provide substantial reduction in HIV with high adherence
- Low level of systemic drug= better safety profile
- Less “medicalized” than use of systemic drug for protection
- Increases number of options, thereby increasing uptake
- Platform for development of MPTs

# Why NOT Microbicides?



- Oral PrEP is available and very effective if used
- Ceiling of efficacy for dapivirine ring may be lower than oral PrEP
- Topicals do not provide protection for all sexual risk exposures (anal and vaginal)
- Topicals are user dependent and therefore will always have adherence challenges
- Injectable cabotegravir or implants could have higher adherence

# How We View New Technology: Something Like Royalty



# No Technology is Perfect All Will Have Challenges

- A pill a day?
- Perfect for some, but
  - Have to monitor kidney function
  - Need to remember to use it
  - Takes many days to achieve protective levels in women
  - Pills are big and not discreet
  - Since the tablets look just like treatment, can make people think that you may be HIV infected



# No Technology is Perfect All Will Have Challenges



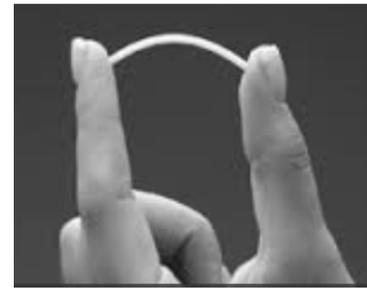
- The Dapivirine ring- just insert it once a month, starts working right away and gets good drug levels in hours after insertion, low levels of drug so very safe
- Perfect for some, but
  - Some women do not like a ring in the vagina
  - Partners can sometimes feel it so you might have to explain what it is
  - May not be as effective as oral PrEP used daily, especially for women who have anal sex

# No Technology is Perfect All Will Have Challenges



- An injection every 8 weeks may be proven to be effective
- Perfect for some, but
  - The drug may persist at nontherapeutic levels for more than a year after the last injection so you may have to take oral PrEP for a year or more
  - You have to come back to the clinic every 2 months for another injection
  - You may have injection site reactions

# No Technology is Perfect All Will Have Challenges



- Implantable rods containing long acting ARVs. We don't know yet whether they work, but wouldn't they be perfect if they did? Great adherence; no drug tail like injectables
- Perfect for some, but
  - Some people will not want a foreign body
  - Insertion and removal requires trained personnel

# Prevention Toolbox

- The prevention toolbox is real and like contraception should provide options
- All HIV prevention strategies will have strengths and weaknesses
- Rings appears to be an attractive option with respect to safety, scale up and implementation
- Next generation microbicides will focus on MPTS, rectal products and extended release non-coital products for women



**HIV prevention is a complicated problem: No tools should be discarded until we figure out which tools will work best where they need to be used.**

# Choice Matters



Pill

Vaginal ring

Injectable

Vaginal/rectal  
inserts

Vaginal films

Vaccine

- Products must be used to be effective
- People's preferences and needs are not all the same
  - Analogy: for contraception, women regularly weigh side effects, efficacy, life burden, and “medicalization” when making choices
- People want options so they can make choices

*We are naïve if we think one option will work for all, or that people will use something just because we made it*

# Enjoy the Meeting!

- Meet someone new
- Enjoy the plenary sessions
- Come to the reception tonight and see some great posters and chat with the MTN Friends and Family
- Think about how we can change the face of prevention

