

MTN Welcome

State of the Network

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MTN LOC

MTN Meeting

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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



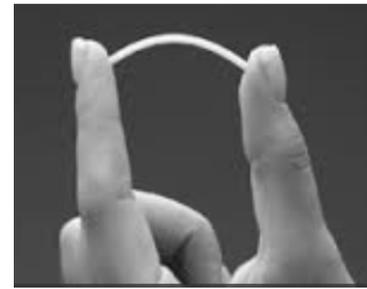
- The Dapivirine ring- just insert it once a month, starts working right away and gets good drug levels in hours after insertion, low levels of drug so very safe
- Perfect for some, but
 - Some women do not like a ring in the vagina
 - Partners can sometimes feel it so you might have to explain what 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

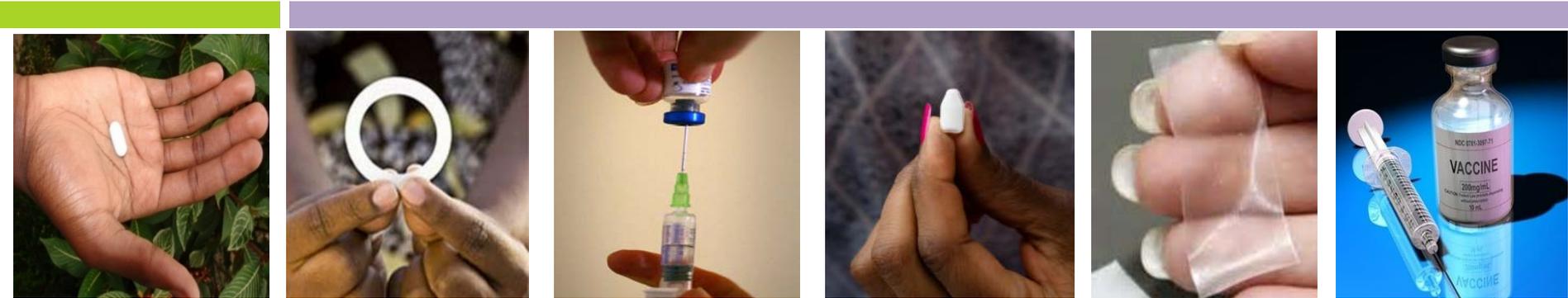
Prevention Toolbox

- 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

