



MTN 034/IPM 045: African Adolescents

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On behalf of MTN 034 protocol team

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Presentation Outline

- Rationale for evaluating new prevention options amongst adolescents
- Description of MTN 034: design/study regimen/objectives
- Contribution of MTN 034 to adolescent PrEP research
- Behavioral Assessments

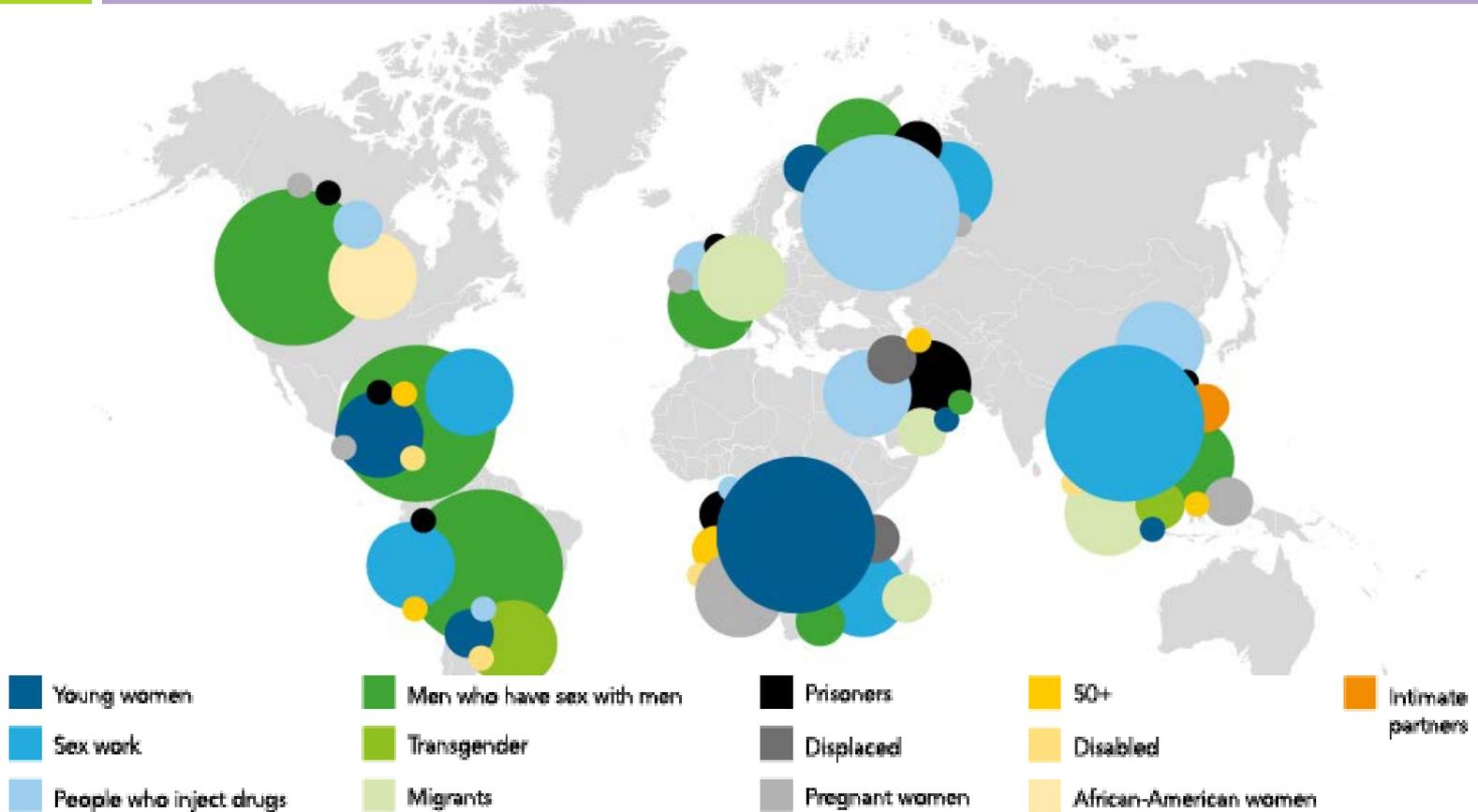
MTN 034

Safety and Adherence Study of the DPV (25 mg) VR and TDF/FTC Tablet in an Adolescent Female Population

- VR safety data will be provided by MTN 020, MTN 023 and other studies
- MTN 034: safety and tolerability amongst African adolescent women



Rationale: One third of new HIV infections occur in young African women



- In context of ART scale up with 40% of HIV+ persons on ART & 6 million medical male circumcisions performed by end of 2013
- Need to implement effective primary prevention strategies

MTN 034 Rationale:

Need HIV prevention & new prevention modalities for African adolescents

Risk of HIV acquisition amongst adolescent females in Africa

- 2.1 million adolescents infected globally (2012)
- 85% reside in SSA
- 56% are female 
- In 2012, 82% of incident adolescent infections in SA were amongst girls
- Only age group with increasing mortality between 2001- 2010

for the 1st time PEPFAR focuses on decreasing HIV incidence amongst adolescents in 10 high burdened countries in SSA



D.R.E.A.M.S.

WORKING TOGETHER FOR AN AIDS-FREE FUTURE FOR GIRLS



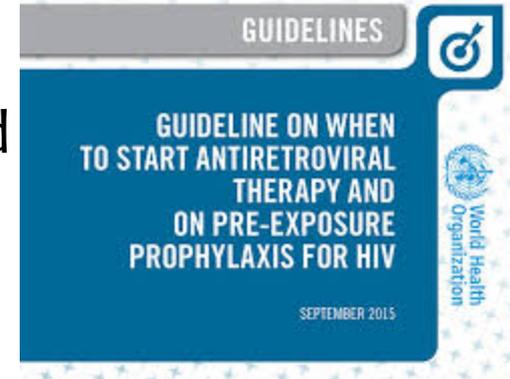
BILL & MELINDA GATES foundation

Nike Foundation

MTN 034

Background - Assumptions

- Understanding uptake, adherence and safety of new HIV prevention technologies amongst adolescent females in SSA relevant:
 - If ASPIRE shows efficacy
 - In light of WHO guidelines (Sep 2015) for PrEP: - “oral PrEP containing TDF should be offered as an additional choice for people at substantial risk of HIV as part of a combination prevention package.”



Background-

Relevant findings about Contraceptive VR and Oral PrEP in young women

- Contraceptive ring studies among adolescents
 - Being comfortable with appearance, hygiene and functions of genitals significantly associated with willingness to try the vaginal ring.¹
 - Liking the ring was associated with having had prior pelvic exam and experience with vaginal product use.²
- Oral PrEP dosing strategies: ADAPT/HPTN067
 - Median age 26
 - HPTN 067: evidence that daily dosing of TDF/FTC is acceptable amongst women in Cape Town
 - Daily oral TDF/FTC PrEP resulted in better coverage of sex acts and increasing adherence associated with higher drug levels
 - Perceived benefit to community (“Ubuntu” – reciprocity) influenced adherence

1. Terrell LR et al: [J Pediatr Adolesc Gynecol](#). 2011 Aug;24(4):204-10

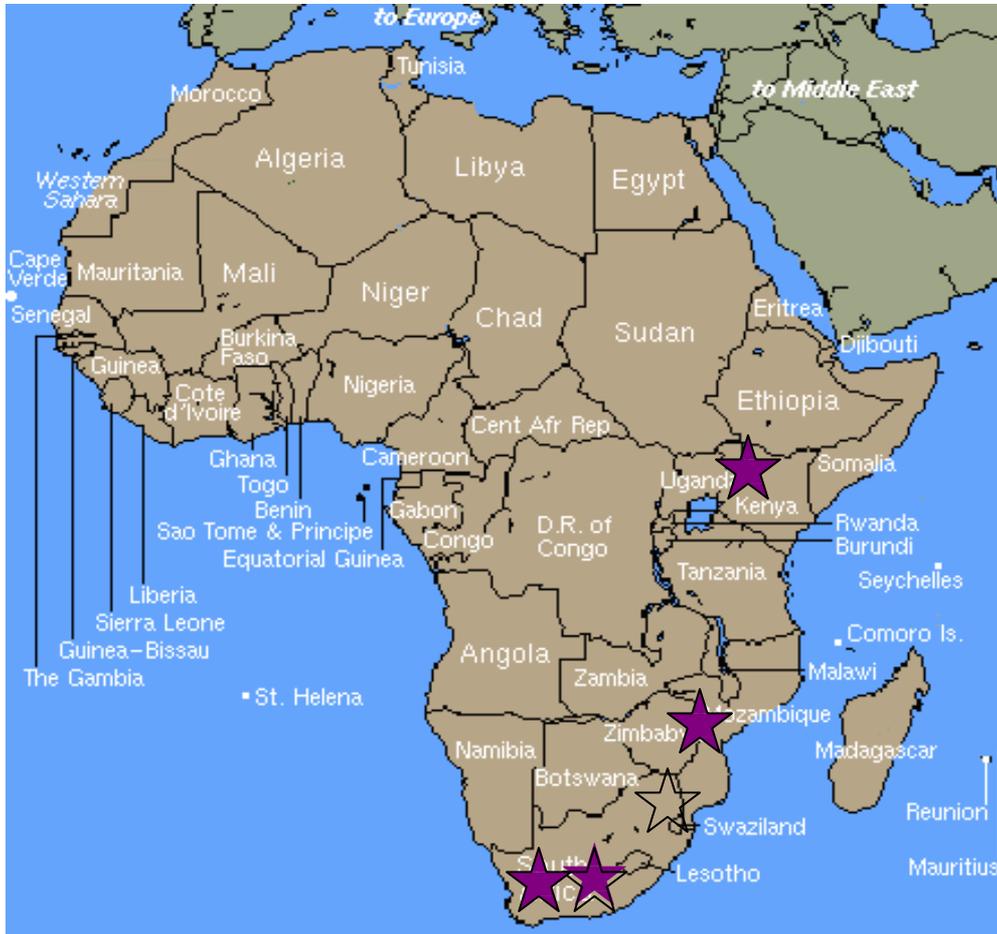
2. Carey AS et al: [Contraception](#). 2007 Dec;76(6):444-50. Epub 2007 Nov 9

MTN 034: Design

- **Sample Size:** Approximately 300 participants
- **Study Population:** Healthy, HIV-uninfected, adolescent females, 16 - 17 years old, on effective contraception
- **Study Duration:** Approximately 12 months of follow-up per participant with a projected accrual period of approximately 10 months at each site .

MTN 034:

4 Sites in 3 countries



MU-JHU Research
Uganda

Zengeza
Zimbabwe

eThekwini

Vurulum CRS

South Africa

MTN 034: Study Design

	N	Period 1 (24 Weeks)	Off-Product	Period 2 (24 Weeks)	Exit
Sequence A	150	Vaginal ring (dapivirine 25 mg VR)	~1 week	Oral PrEP (Daily FTC/ TDF tablet)	
Sequence B	150	Oral PrEP (Daily FTC/ TDF tablet)	~1 week	Vaginal ring (dapivirine 25 mg VR)	

Rationale for Study Design

- Cross over design:
 - allows for quick study with small sample size – implications for licensure
 - Direct comparison of user acceptability and preferences
 - Short interval of product use – informs on immediate side effects (GIT, vaginal bleeding)
 - May predict long term adherence: high initial adherence translates to long term adherence
- Simultaneous evaluation of 2 effective prevention interventions:
 - Ethical issues with use of placebo in current landscape

Primary objectives

- Safety: to describe the safety of Truvada and Dapivirine VR simultaneously
 - Grade 2 or higher AEs related to intervention
 - All grade 3 and 4 AEs
- To compare adherence to TDF/FTC and the dapivirine VR by:
 - Self report
 - Drug concentrations: blood/vaginal fluid/vaginal ring

Secondary Objectives=Behavioral Assessments



Summary about MTN 034

Behavioral Assessments

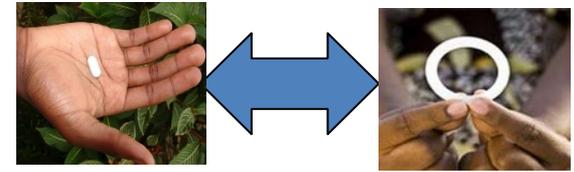
- Methods - how?
 - Design
 - Data collection
 - Interventions
- Measures - what?
 - Acceptability
 - User preferences
 - Use experiences

MTN 034 Methods – how?

- **Design** - Prospective from baseline to exit
- **Data collection** - Quantitative & Qualitative
- **Interventions**
 - ❑ **Daily** oral TDF/FTC PrEP
 - ❑ **Monthly** dapivirine IVR
- **Assessments:** Baseline, Monthly/Quarterly and exit

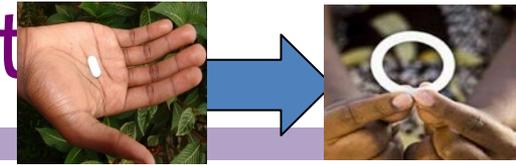


MTN 034 – Acceptability measures



- Uptake and time to discontinuation
- Facilitators and barriers to use
- Acceptability during sex and menses
- Correlates of acceptability
 - Behavioral risk and risk perception
 - Understanding of relative & partial effectiveness of oral TDF/FTC PrEP and dapivirine IVR
 - Familiarity
 - Stigma associated with oral ARVs
- Product use concerns (baseline as during use)
 - Partner's reaction
 - Side effects (e.g., GI vs vaginal symptoms)
 - Concerns systemic vs topical exposure to ARVs

MTN 034 – User experience assessment



- Reports of product use
- Ring insertion, removal ease
- Frequency & context of IVR expulsion incidents
- Disclosure to partner, family, and friends
- Product storage
- Vaginal hygiene practices: Baseline and follow-up
- Condom use
- Assess FP method during use of oral PrEP and dapivirine IVR

MTN 034 – User Preference Measures



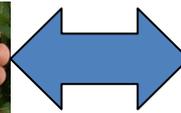
**Daily oral
TDF/FTC
PrEP**



**Monthly
dapivirine IVR**

- Preference at beginning of study (after counseling & being shown TDF/FTC pill & dapivirine ring)
- Change in preference over 6 months of each phase of oral PrEP or dapivirine IVR
- Preferences for future use at end of study after experience with oral PrEP and dapivirine IVR

Summary behavioral questions



Topic	Sample Questions
Acceptability	What did adolescents experience ? Initiation and (dis)continuation rates?
Preferences	Which method do adolescents prefer?
Adherence	Do they use the methods often enough? Correlates, barriers & facilitators
User experiences	Use as relates to sexual behavior? Condom use? Contraceptive use? Vaginal hygiene practices?

MTN 034: Conclusions

- If ASPIRE shows efficacy, need safety data on dapivirine IVR and TDF/FTC for regulatory approvals for African adolescents
- Assess IVR and daily TDF/FTC adherence and continuation among adolescent women who use both for 6 months each
 - Acceptability of and adherence to IVR and daily pill taking may differ from older women
- Characterize and probe user experiences
- Assess adolescent preferences for PrEP choices after experiencing dapivirine VR & oral PrEP

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