



Moving the MTN Rectal Microbicide Agenda Forward

MTN Annual Meeting
March 15th, 2016

Rectal Microbicide Studies

- **Phase 1**

- Nonoxynol-9
 - HIVNET-008
- UC781
 - RMP-01
- Tenofovir 1% gel
 - RMP-02/MTN-006
 - MTN-007
 - Project Gel
 - CHARM-01 & CHARM-02
- Maraviroc
 - CHARM-03

- **Phase 2**

- MTN-017

- **Planned Phase 1 Studies**

- MTN-026
- MTN-033
- MTN-037
- DREAM-01
- PREVENT-01

Where to Next?



Some Questions

- Could a rectal microbicide work?
- Do we need rectal microbicides?
- Do women need rectal microbicides?
- Do we need to use applicators to deliver rectal microbicides?
- What is the best product to move into an effectiveness study?
- How would we design a rectal microbicide Phase 3 study?

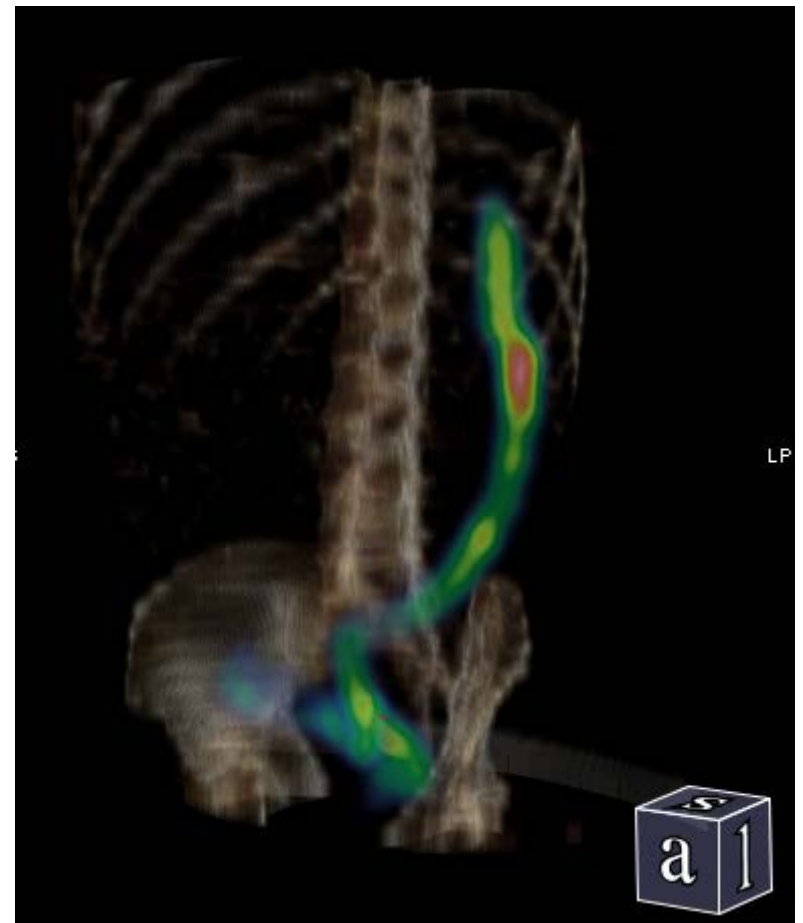
Could a Rectal Microbicide Work?



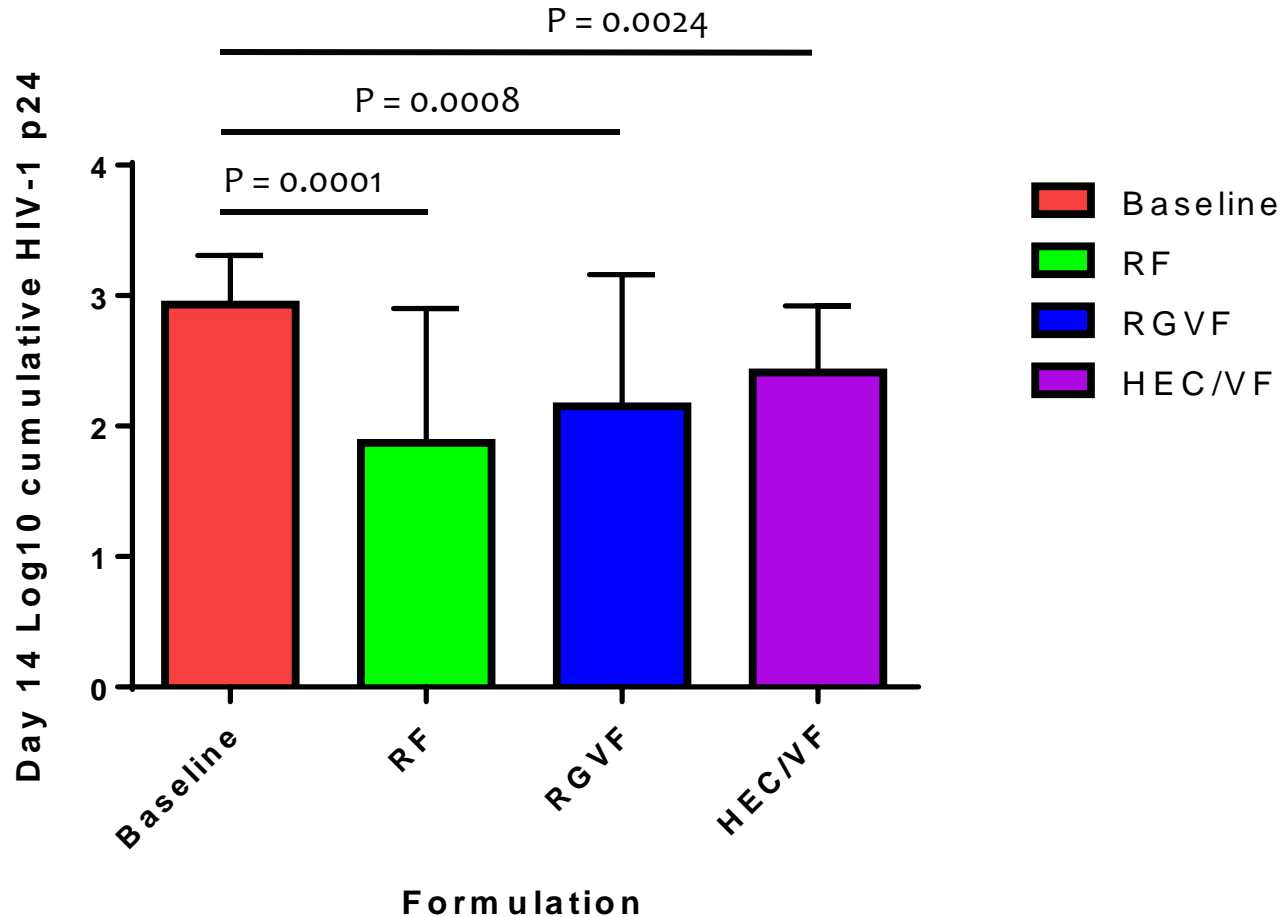
Rectal Microbicide Distribution

“HIV” ($^{99m}\text{Tc-SC}$) in Ejaculate

“Microbicide” ($^{111}\text{In-DTPA}$)



CHARM-01 Explant Data



Do We Need Rectal Microbicides?



Oral PrEP Trials in MSM

Effect Size



44%



86%



86%

PrEP Challenges / Questions

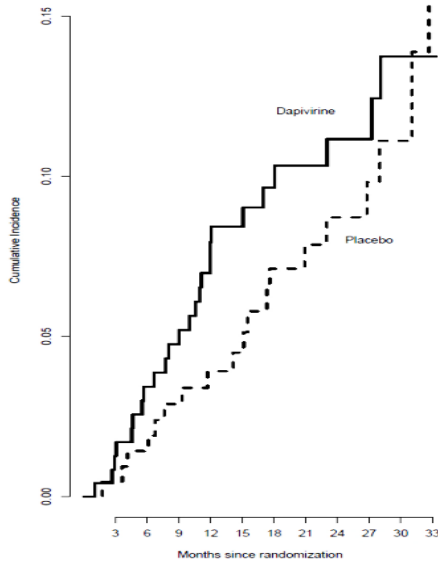
- Access
- Uptake
- Adherence
- Dosing requirements
- Toxicity
- Consumer preference

Do Women Need Rectal Microbicides?

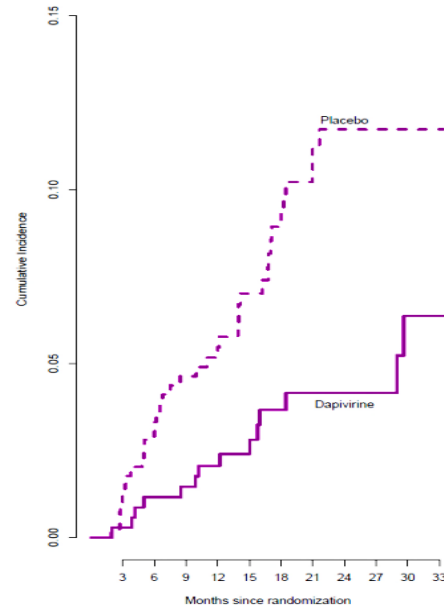
Age and HIV-1 Protection

- HIV-1 protection effectiveness was explored in additional age-stratified categories, and lack of HIV-1 protection was limited to those ≤ 21 years of age:

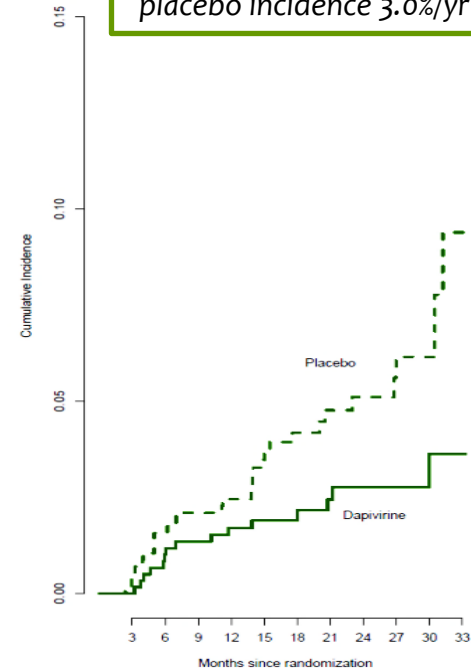
Age 18-21
-27% (-133,31)
placebo incidence 5.4%/yr



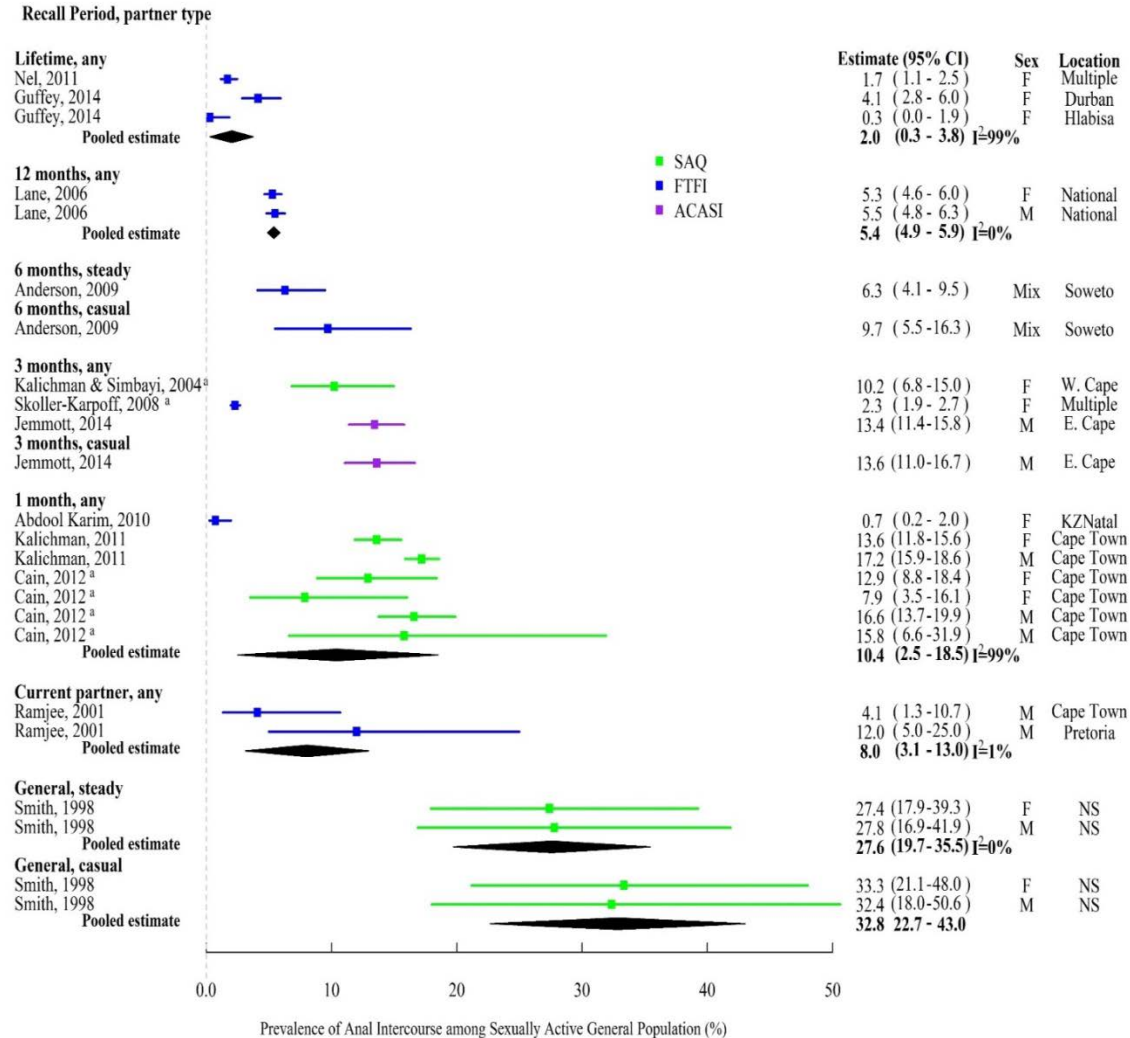
Age 22-26
56% (19,76)
placebo incidence 6.1%/yr



Age 27-45
51% (8,74)
placebo incidence 3.0%/yr

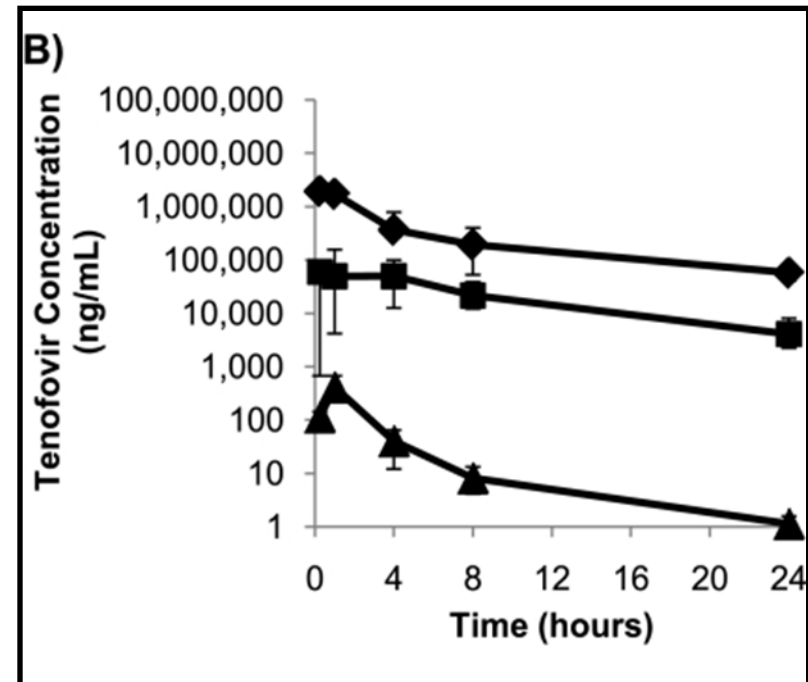


Rates of RAI in Women



Microbicide Protection for RAI

- Would a vaginal microbicide protect against RAI-associated HIV infection?
 - Non-human primate data
 - Nuttall J et al. 2012
 - Human data
 - MTN-001
 - MTN-014
 - Vaginal ring?



SAVE THE DATE!

Workshop Announcement

**Modeling HIV Transmission
Does Anal Intercourse contribute to
Heterosexual HIV Transmission?**

**September 15-16, 2016
National Institutes of Health**

Do We Need Applicators to Deliver Rectal Microbicides?



What the Consumers Want

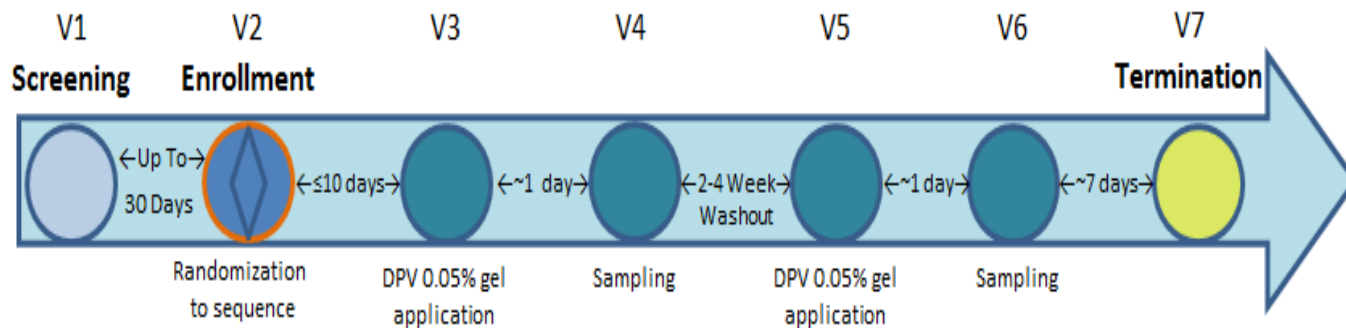


What They Get



MTN-033

- Phase 1 evaluation of dapivirine gel to determine whether digital / phallic insertion equivalent to applicator insertion of microbicide
- HIV-uninfected men who have sex with men (MSM) and transgender females who have sex with men, 18 years or older (N=16)



What Is the Best Product to
Move Into a Phase 3 Study?



Rectal Microbicides in Development

- Tenofovir: Phase 2
- Maraviroc: Phase 1
- Dapivirine: Preclinical
- Griffithsin: Preclinical
- MIV-150/Carageenan/Zinc: Preclinical
- 5P12 RANTES: Preclinical
- NOV-1003: Preclinical

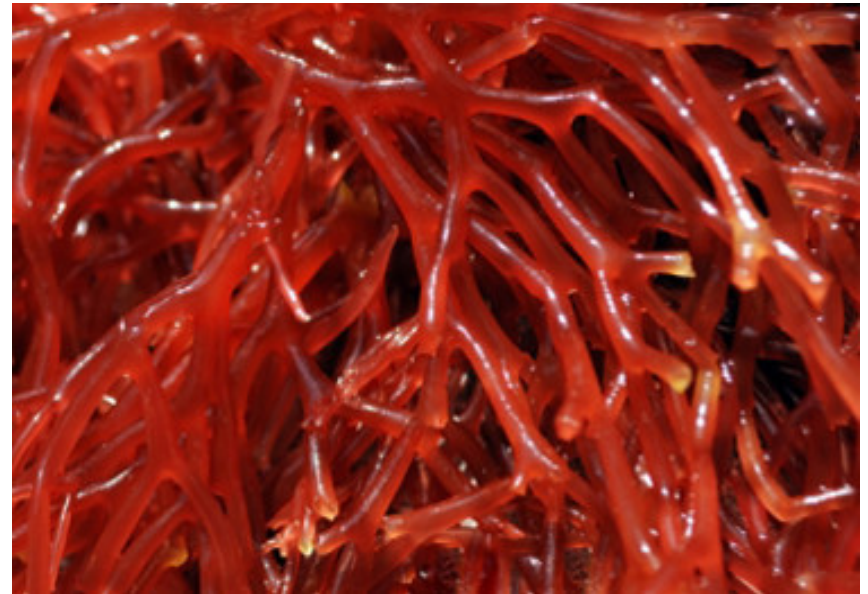
DREAM and PREVENT Programs

DREAM Program



Tenofovir
prodrug enemas
PI: Craig Hendrix, JHU

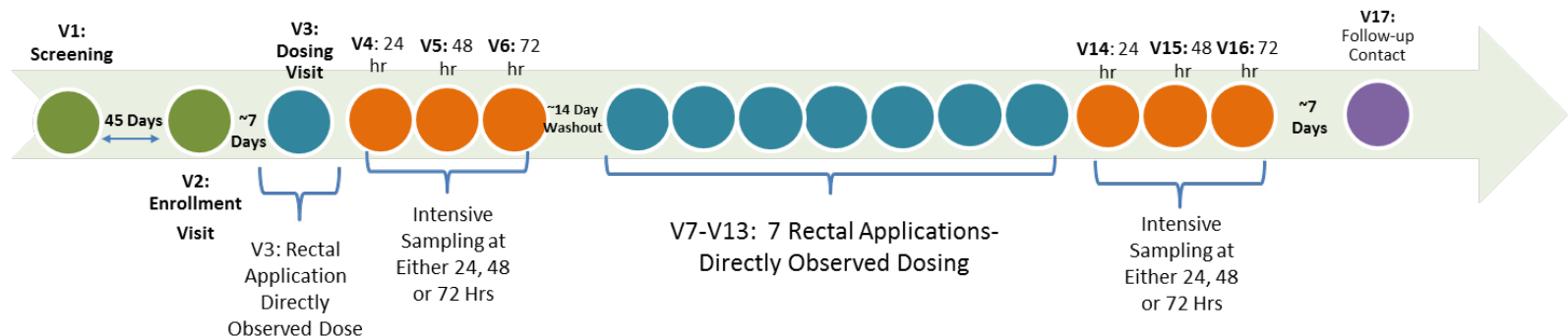
PREVENT Program



Griffithsin rectal gel
PI: Kenneth Palmer,
University of Louisville

MTN-026

- Phase 1 rectal safety, acceptability, and PK/PD evaluation of dapivirine gel
- N = 27
- Clinical sites
 - Pittsburgh, Birmingham, and Bangkok

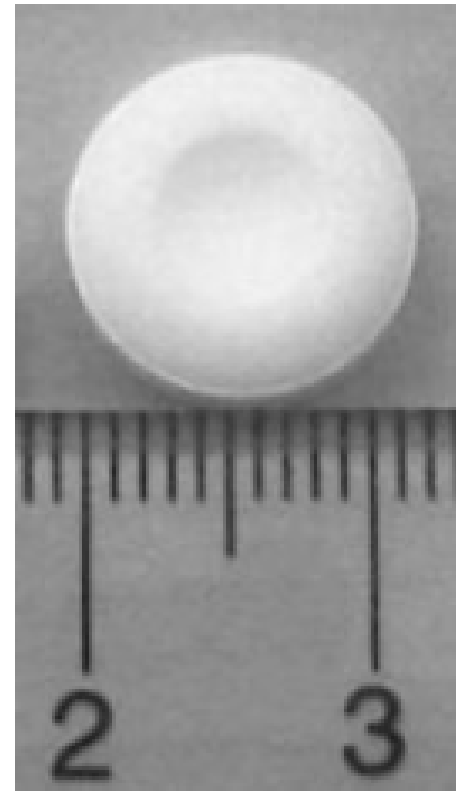


MTN-037

- Collaboration with the Population Council
- Phase 1 dose escalation of MIV-150/Carageenan/Zinc gel
- Safety, acceptability, and PK/PD
 - Group 1: 4 mL of gel
 - Group 2: 8 mL of gel
 - Group 3: 16 mL of gel
 - Group 4: 32 mL of gel
- Status: In protocol development

MTN-OXX

- Phase 1 rectal safety, acceptability, and PK/PD assessment of a combination fast dissolving ‘insert’ or suppository
- Possible combination APIs
 - TFV and Elvitegravir
 - Tenofovir alafenamide
- Concept timeline
 - Q2 2016



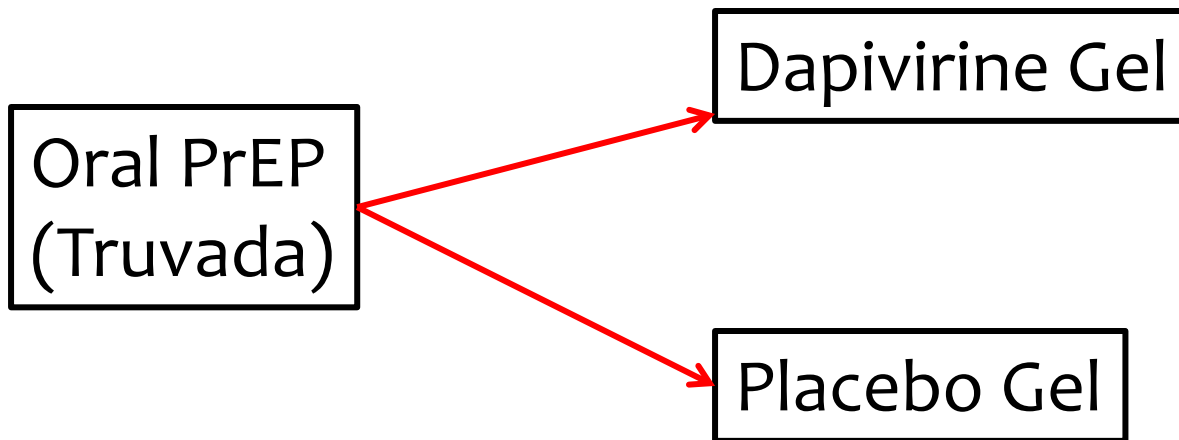
How Would We Design A Phase 3 Rectal Microbicide Trial?

Phase 3 RM Design

- Challenges
 - Oral PrEP would need to be provided as part of prevention package
 - Classical placebo controlled trial no longer possible
- Solutions
 - Non-inferiority trial design (HPTN 083)
 - Active versus placebo gel + oral PrEP

MTN-035

- Phase 2A evaluation of oral PrEP and dapivirine gel
- International
- MSM / TGW
- N = TBD but 400-600



Summary

- Phase 1/2 studies completed for TFV gel
- Need to move away from applicator use
- Dapivirine gel being evaluated prior to initiation of Phase 3 studies
- Need to conduct a Phase 2A study (MTN-035) to characterize patterns of gel / oral PrEP use
- Optimal formulation may be a fast dissolving insert or suppository

Acknowledgements

- Our study participants
- NIH / NIAID / DAIDS
 - Microbicide Trials Network
 - Integrated Preclinical Clinical Program for HIV Topical Microbicides
- ViiV (CHARM-03)
- Craig Hendrix

Thank You

