HPTN 069: Update

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Maraviroc for PREP: Advantages

- Entry inhibitor
- MVC safety profile X 5 years Gulick IAS 2012
- MVC achieves high tissue levels
  - 3X higher in vaginal secretions Dumond JAIDS 2009
  - 8-26X higher in rectal tissue Brown JID 2011
- MVC prevented HIV infections in animal model Neff PLoS One 2010
- MVC drug resistance is uncommon
- MVC once-daily dosing possible Rosario Brit J Clin Pharm 2008
- MVC used uncommonly for HIV treatment

MVC for PREP: Disadvantages

- Limited safety data in HIV-uninfected individuals
- Increased pathogenicity of some viral infections (e.g., West Nile virus)
- Other theoretical safety risks
- Not labeled for once-daily dosing
- Some potential for drug-drug interactions
- Not active against X4 virus

HPTN 069/ACTG 5305
NEXT-PREP

Novel Exploration of Therapeutics for PREP

HPTN 069 Design

- **Primary objective: Assess safety and tolerability of PrEP regimens to prevent HIV transmission in at-risk MSM**

- **Study Design**
  - **Phase II, double-blind, randomized**
  - **4 arm/multi-site (12 sites – US only)**
  - **400 participants to be enrolled**

Study Arms

- There are 3 active study drugs
  - maraviroc (MVC)
  - emtricitabine (FTC)
  - tenofovir (TDF)

- Regimens being tested are:
  - maraviroc + FTC placebo + TDF placebo
  - maraviroc + emtricitabine + TDF placebo
  - maraviroc + tenofovir + FTC placebo
  - tenofovir + emtricitabine + MVC placebo

Secondary Objectives

- Changes in lipids
- Changes in bone mineral density (BMD)
- Drug Interaction between the MVC, FTC and TDF – Drug Interaction Subset (n=72)
- Tissue concentrations (MVC, FTC, TFV, FTC-TP, TFV-DP) – Tissue Subset (n=60)
  - Immune activation; HIV infectivity
- Adherence – CASI, EDM, and drug concentrations
- Sexual behavior using CASI, SMS
- QOL assessments

Key Inclusion/Exclusion Criteria

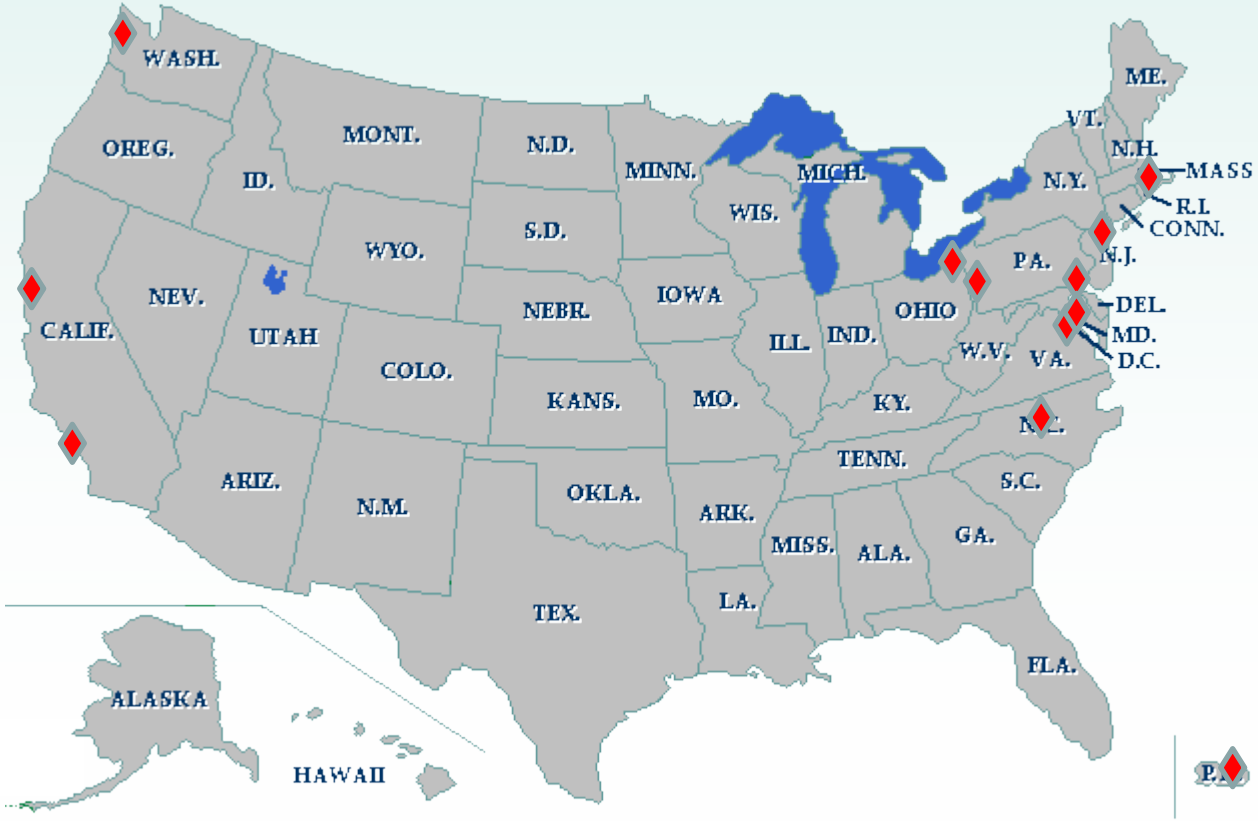
INCLUSION

- Male ≥18 years old
- At-risk: History of receptive or insertive anal intercourse without use of condoms with ≥1 HIV-infected partner or partner of unknown HIV serostatus within 3 months of study entry

EXCLUSION

- Any reactive HIV test results at screening or enrollment, even if HIV infection is not confirmed
- Ongoing intravenous drug use

HPTN 069 Sites



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ACTG
AIDS CLINICAL TRIALS GROUP

HPTN
HIV Prevention Trials Network

HPTN 069: Status

- Fully approved by HPTN and ACTG
- Final Version 2.0 (4/9/12)
- FDA reviewed, IND number assigned
- Site IRB approvals
- CRFs, CASI, CTAs completed
- Study drugs received from Gilead and ViiV
- Anticipated to open in June 2012

- Cohort of 200 women to be added
- Primary analysis: Safety and tolerability in a combined population of at-risk MSM and women

Core Protocol Team

Protocol Chair/Co-Chairs:
Trip Gulick, Ken Mayer, Tim Wilkin

SCHARP: Ying Chen, Leslie Cottle

HPTN Network Lab:
Sue Eshleman, Paul Richardson, Joe Margolick

HPTN CORE: Marybeth McCauley, Philip Andrew, Teresa Nelson, Jonathan Lucas

DAIDS: David Burns, Wairimu Chege, Fulvia Veronese, Ana Martinez

Pharmaceutical Partners:
Gilead - Jim Rooney; ViiV - Alex Rinehart

Other Investigators: Rivet Amico, Adriana Andrade, David Bangsberg, Todd Brown, Sally Hodder, Raphy Landovitz, Kate MacQueen, Bruce Schackman