Pre-Exposure Prophylaxis – Not Just Oral PrEP

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Controlling the HIV Epidemic with Antiretrovirals
London
11th-12th June, 2012
PrEP Mechanism of Action

- Viral disruption
- Prevention of STDs
- Maintenance of normal microflora

Gel/cream:
- Physical barrier
- Lubrication

Inhibition of reverse transcriptase

Inhibition of HIV uptake by dendritic cells (e.g. anti-DC-SIGN)

Fusion/absorption inhibition (e.g. polyanions, co-receptor antagonists)

McGowan I, Biologicals, 2006
Non-Oral PrEP

- Microbicide gels
  - Vaginal
  - Rectal
- Intravaginal rings
  - Antiretroviral
  - Multipurpose
- Films
  - Tenofovir
  - Dapivirine
- Depot injections
  - TMC278 LA
  - S/GSK1265744
Vaginal Microbicides

- Tenofovir 1% Gel
- Evidence of efficacy
  - CAPRISA 004
- Evidence of futility
  - MTN-003 (VOICE Trial)
- Tie breaker
  - FACTS-001 study
Rectal Microbicides

- Lead candidate tenofovir 1% gel
- Phase 1 safety, acceptability, PK/PD studies completed
  - RMP-02/MTN-006
  - MTN-007
- Phase 2 study to start in Q3 2012
  - MTN-017
- Rectal specific combination products in development
## MTN-017

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<td>TNF Gel Daily</td>
<td>TNF Gel With sex</td>
<td>Oral Truvada</td>
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Intravaginal Rings

- Phase 1/2 development ongoing
- Dapivrine ± maraviroc
  - MTN-013
- Phase 3 starting Q3 2012
  - MTN-020
  - IPM-027
- Multipurpose technology
  - Antiretroviral + contraceptive
TMC278LA

- Rilpivirine NNRTI
- IM nanosuspension
- Potential for 1-3 month delivery
- Single dose Phase 1 PK/PD studies ongoing at SSAT, London

- Multiple dose PK/PD to start Q3 2012 in Pittsburgh (MWRI-01*)
  - Colorectal explants
  - Cervicovaginal explants

*Funded by the Bill and Melinda Gates Foundation
## MWRI-01

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<th>Time</th>
<th>Arm 1</th>
<th>Arm 2</th>
<th>Possible Arm 5</th>
<th>Arm 3</th>
<th>Arm 4</th>
<th>Possible Arm 5/6</th>
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<tr>
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<tr>
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**Initial Enrollment**
- Initial

**Secondary Enrollment**
- Secondary
Combination Prevention

Conventional HIV Prevention Package + PrEP

SC ± Oral ± Rectal ± Vaginal

± HIV Vaccine
Vaccine PrEP Interactions

- MTN-022 / HVTN-095
- Exploration of potential interactions between oral/topical PrEP and HIV vaccine
  - DNA NYVAC prime boost
  - Truvada
  - Vaginal tenofovir gel
- Primary objectives
  - Safety
  - Acceptability
  - Systemic immunogenicity
Development of safe and effective PrEP agents including microbicides remains a critical focus for HIV prevention research.

Increased interest in sustained delivery products.

Rectal microbicide development important for both domestic and international MSM and others at risk of infection through RAI.

Innovative trial design will be needed to sustain prevention research agenda.