Welcome and State of the Network

Cape Town,
South Africa
27th September 2016
The HIV/AIDS Epidemic in 2016

- 17 million people were accessing antiretroviral therapy
- 36.7 million people globally were living with HIV
- 2.1 million people became newly infected with HIV
- 1.1 million people died from AIDS-related illnesses

UNAIDS 2015 Data
The Cost of the Epidemic

• US$ 19 billion was invested in the AIDS response in low- and middle-income countries

• Domestic resources constituted 57% of the total resources for HIV in low- and middle-income countries in 2015.

• Recent updated UNAIDS estimates indicate that US$ 26.2 billion will be required for the AIDS response in 2020

UNAIDS 2015 Data
Emerging Problems

• Ongoing challenges with adherence
• Emergence of antiretroviral resistance to first line tenofovir containing regimens
• In the US only 30% of people living with HIV have achieved viral suppression
  — CDC 2014
• The majority of new infections in the US are transmitted by people not in medical care
• HIV prevention remains a priority
HIV Prevention in 2016

• Clear evidence for PrEP effectiveness
  – Proud (UK) & IperGay (France) studies

• WHO recommends PrEP for all population groups at substantial risk of HIV infection
  – Populations with an HIV incidence of about 3 per 100 person-years or higher

• The dapivirine antiretroviral intravaginal ring demonstrated to be safe and effective for HIV prevention
PrEP Access Problems
The HIV Prevention Research Agenda

• Ongoing PrEP demonstration projects
• Open-label evaluation of the DPV intravaginal ring (DREAM and HOPE)
• Phase 1 evaluation of novel microbicide candidates and formulations
• Phase 2/3 evaluation of LA PrEP and bnAb
• Phase 3 evaluation of the ALVAC/gp120 with MF59 adjuvant HIV vaccine regimen
# The HIV Prevention Score Card

<table>
<thead>
<tr>
<th>Method</th>
<th>Clinical Trials</th>
<th>Implementation</th>
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<tbody>
<tr>
<td></td>
<td>Safety &amp; Effectiveness</td>
<td>Cost</td>
</tr>
<tr>
<td>Oral PrEP</td>
<td>+++ / +++</td>
<td>$$$$$$</td>
</tr>
<tr>
<td>LA PrEP</td>
<td>++ / ?</td>
<td>$$$$$$$$</td>
</tr>
<tr>
<td>Antibodies</td>
<td>++ / ?</td>
<td>$$$$$$$$</td>
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<tr>
<td>Vaccines</td>
<td>++ / +</td>
<td>$$$$$$$$</td>
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<tr>
<td>Microbicide gels</td>
<td>+++ / +</td>
<td>$$$$$$$$</td>
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<tr>
<td>Intravaginal rings</td>
<td>+++ / ++</td>
<td>$$$$$$$$</td>
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<tr>
<td>Circumcision</td>
<td>+++ / +++</td>
<td>$$$$$$$$</td>
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MTN Activities in 2015/2016
Completed MTN Trials (1)

- MTN-017
  - Phase 2 rectal safety and acceptability study
- MTN-011 study
  - PK/PD coital study of TFV gel
- MTN-014 study
  - Rectal/vaginal safety and PK study of RGTFV gel
- MTN-020 (ASPIRE) study
  - Phase 3 evaluation of the DPV IVR
Completed MTN Trials (2)

- MTN-023
  - Phase 2a safety study of a DPV IVR in adolescent females in the US
- MTN-024
  - Phase 2a safety study of the DPV IVR in post menopausal women in the US
- MTN-027
  - Phase 1 safety and PK study of MK-2048/Vicriviroc (MK-4176)/MK 2048A IVR
- MTN-028
  - Phase 1 PK study of IVR containing Vicriviroc (MK-4176) and MK-2048
The ASPIRE Study

Incidence

Risk reduction 75% (95% CI 18-92)
Risk reduction 66% (95% CI 6-88)
Risk reduction 38% (95% CI -39-72)
Risk reduction 11% (95% CI -78-55)

E Brown, IAS 2016
Ongoing MTN Trials

• MTN-015 & MTN-016
• MTN-025 (HOPE Study)
  – A Phase 3B open-label follow-on trial to assess the continued safety of and adherence to a vaginal ring containing dapivirine in women
• MTN-029
  – Phase 1 PK study of the DPV IVR in lactating women
• MTN-032
  – Assessment of ASPIRE and HOPE adherence
Pending MTN Trials (1)

- **MTN-026**
  - Phase 1 rectal safety and PK study of DPV Gel

- **MTN-031**
  - A Phase 1, randomized, double-blind pharmacokinetic and safety study of dapivirine/levonorgestrel vaginal rings

- **MTN-033**
  - An open label randomized Phase 1 pharmacokinetic study of dapivirine gel administered rectally to HIV-1 seronegative adults

- **MTN-034 (REACH)**
  - A Phase 2a crossover trial evaluating the safety of and adherence to a vaginal matrix ring containing dapivirine and oral FTC/TDF in an adolescent female population
Pending MTN Trials (2)

- MTN-037
  - A Phase 1 rectal safety and pharmacokinetic study of PC-1005 (MIV-150/Zinc Acetate/Carrageenan Gel)

- MTN-038
  - A Phase 1 study of the 90 day tenofovir vaginal ring

- MTN-039
  - Safety and PK study of TDF and EVG administered rectally
Opportunities & Challenges
Opportunities for the MTN

- Building on the foundation of the ASPIRE trial
  - The HOPE study
  - DPV IVR safety studies in new populations
- Moving towards a three month DPV and tenofovir IVR
- Development of a combination contraceptive / antiretroviral IVR
- Moving rectal microbicides towards Phase 3
  - Evaluate new products
  - Take the best into a global Phase 2A study
Challenges for the MTN

• Building upon the ASPIRE and Ring data to demonstrate the value of the DPV IVR for HIV prevention

• We all need to be ambassadors for topical microbicides
  – Safety, acceptability, affordability, and scalability
  – Oral PrEP may not be the first choice for everyone

• Generating compelling data and rigorous trial designs to advance rectal microbicides into an effectiveness study

• Donor fatigue
  – Several large prevention studies are ongoing or planned and may limit funds for microbicide research
Farewells in 2016
Willard Cates Jr, MD, MPH

1942-2016
Ian McGowan MD PhD FRCP
Acknowledgements

• Our wonderful participants
• Our incredible site staff
• Our generous funders
  – The Microbicide Trials Network is funded by the National Institute of Allergy and Infectious Diseases (UM1AI068633, UM1AI068615, UM1AI106707), with co-funding from the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the National Institute of Mental Health, all components of the U.S. National Institutes of Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.