ASPIRE activation: Where we are and where we are headed

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ASPIRE Protocol Team Meeting
1 October 2012
Where we are
MTN-020 / ASPIRE

- A Multi-Center, Randomized, Double-Blind, Placebo-Controlled Phase III Safety and Effectiveness Trial of a Vaginal Matrix Ring Containing Dapivirine for the Prevention of HIV-1 Infection in Women
ASPIRE Overview

3,476 Women

- HIV prevention package
  - Placebo ring
    - 1,738 women
  - Dapivirine ring
    - 1,738 women
ASPIRE to date

- January - March 2011
  - Concept approved by MTN Executive Committee
  - Protocol Consultation Meeting with Site Investigators
- May – July 2011
  - NIAID SWG, PSRC
- September 2011
  - v1.0 to sites for IRB submission
- October 2011
  - Community Consultation, Operational Walk-Through
- January 2012
  - DSMB protocol review
- June, July 2012
  - First site training (Cape Town), first activation (Kampala)
- August 21, 2012
  - First enrollment (Kampala)
## Site activations

<table>
<thead>
<tr>
<th>Site</th>
<th>Date of activation</th>
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</thead>
<tbody>
<tr>
<td>MA – Blantyre</td>
<td>APPROVALS PENDING</td>
<td>SA – MRC/Verulam</td>
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<td>4 SEP 2012</td>
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<td>ZI – Zengeza</td>
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</table>
Communications

- Weekly Protocol Management calls (W, 6 AM Pacific)
- Biweekly CRM calls with sites
- Weekly priority emails from FHI360 to sites – collating protocol team priorities
- Monthly team calls = site-driven exercises – sharing experiences
- Listservs : cross-site communications/sharing
Numbers that matter

- 3476 = total number of women enrolled
- >95% = retention, product distribution
- 100% = attention to data quality, safety

Everything else flows from these
Where we are going
Timeline

2011
• Initiate site IRB and regulatory approval process

2012
• IRB/regulatory approvals, trainings, first enrollment, next DSMB 9 November 2012

2013
• Enrollments and follow-up continue

2014
• End of participant follow-up

2015
• Results
The Big Five

Accrual

Adherence

Retention

Data Quality and Timeliness

Clinical and Laboratory Participant Safety
Accrual
# Enrollments (27 SEP 2012)

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<tr>
<th>Site</th>
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<th># enr</th>
<th>scr:enr ratio</th>
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<tbody>
<tr>
<td>SA – Cape Town</td>
<td>19 SEP 2012</td>
<td>5</td>
<td>3</td>
<td>1.7</td>
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<tr>
<td>SA – CAPRISA eThekwini</td>
<td></td>
<td>1</td>
<td>0</td>
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<tr>
<td>SA – MRC/Botha’s Hill</td>
<td>10 SEP 2012</td>
<td>39</td>
<td>14</td>
<td>2.8</td>
</tr>
<tr>
<td>SA – MRC/Chatsworth</td>
<td>11 SEP 2012</td>
<td>27</td>
<td>11</td>
<td>2.5</td>
</tr>
<tr>
<td>SA – MRC/Isipingo</td>
<td>19 SEP 2012</td>
<td>13</td>
<td>4</td>
<td>3.3</td>
</tr>
<tr>
<td>SA – MRC/Tongaat</td>
<td>17 SEP 2012</td>
<td>25</td>
<td>5</td>
<td>5.0</td>
</tr>
<tr>
<td>SA – MRC/Verulam</td>
<td>13 SEP 2012</td>
<td>33</td>
<td>8</td>
<td>4.1</td>
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<tr>
<td>SA – MRC/Umkomaas</td>
<td>14 SEP 2012</td>
<td>26</td>
<td>13</td>
<td>2.0</td>
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<tr>
<td>UG – Kampala</td>
<td>21 AUG 2012</td>
<td>52</td>
<td>35</td>
<td>1.5</td>
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<tr>
<td><strong>TOTAL</strong></td>
<td><strong>221</strong></td>
<td><strong>93</strong></td>
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<td><strong>2.4</strong></td>
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Enrollment timelines

- N=3476
- Estimated that accrual will require *approximately* 12 months, with total study duration approximately 24 months
  - Regulatory preference that all participants will achieve 12 months on study product
  - Balance efficient / rapid recruitment with quality
  - Continuous involvement of community (and not just for enrollments)
## Site targets

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<tr>
<td><strong>ASSIGNED TOTAL</strong></td>
<td></td>
<td><strong>2896</strong></td>
<td></td>
</tr>
<tr>
<td><strong>UNASSIGNED</strong></td>
<td></td>
<td><strong>580</strong></td>
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Getting to 3476

- To date, defined site targets for start-up
  - Additional assignments pending site capacity, performance, etc.
  - Discussions between now and early 2013 for remaining numbers
  - *We are all in this as a team*
Adherence
## Learning from PrEP trials

<table>
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<tr>
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<th>HIV protection efficacy for FTC/TDF versus placebo in randomized comparison</th>
<th>% of blood samples with tenofovir detected</th>
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<tbody>
<tr>
<td>Partners PrEP</td>
<td>75%</td>
<td>81%</td>
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<tr>
<td>TDF2</td>
<td>62%</td>
<td>79%</td>
</tr>
<tr>
<td>iPrEx</td>
<td>44%</td>
<td>51%</td>
</tr>
<tr>
<td>FEM-PrEP</td>
<td>6%</td>
<td>26%</td>
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Clear dose-response between evidence of use & HIV protection
Adherence is key…

- Products don’t work if they aren’t used

- How can we set up a culture in ASPIRE so that women can openly report non-use?
Retention
Retention is adherence

- Every missed visit is a month of **zero** adherence
Retention starts before day 1

- Every enrolment should be considered
  - ASPIRE is a monthly, multi-hour commitment until sometime in 2014…
  - Trust your instincts, trust team instincts

- How can we continue to create cultures that make sites places where participants want to spend several hours each week?
  - How do we remind ourselves and participants about their important volunteerism?
Safety
Safety

- Safety is the co-primary endpoint of the study
  - Evaluating whether the product is safe is just as important as whether the product is effective for HIV prevention
  - Regulatory authorities will scrutinize safety data and careful attention to safety documentation is critical
Laboratory

- Laboratory results and archived samples are central to this study
  - Careful attention to performance of every lab test, every sample for storage is critical
Quality
We are all in this together

- We all work together – all parts of the study are all our business

  Recruitment  QC/QA
  Retention    Regulatory
  Adherence    Safety Monitoring
  Sample collection  Space/facilities
  Staff morale    Study drug/pharmacy
  Community/outreach  Contraception
  Communications  Lab-clinic interface
  Lab quality     Monitoring follow-up
Mistakes happen

- We all make errors
  - But recognizing and acknowledging errors and then developing corrective and preventative action plans is key

- No one knows how to do this perfectly
  - Cross-site, cross-team sharing is important

- Do not let protocol deviation policies become paralyzing
Pay attention to the data

- Follow the metrics –
  - Enrollments
  - Retention
  - Contraceptive use
  - QCs
  - Etc.
Pay attention to the participants

- Participants give much to be in this study
  - Time
  - Blood
  - Privacy
  - Effort

*We have much to learn from them.*
MTN-020 / ASPIRE
IT TAKES A TEAM

Malawi College of Medicine – JHU Research Project

UNC Project - Malawi