Implementation Update
ASPIRE Protocol Team Meeting
October 2014
Meeting overview

- A great afternoon:
  - Where we are now: update from ASPIRE, The Ring Study, Laboratory Center, and qualitative component
  - Site presentations: Maximizing adherence and retention, community perspectives, contraceptive counseling as women leave ASPIRE
  - Preparing for closeout: coming soon…!
Outline

ASPIRE

- Looking back
- Looking ahead
ASPIRE

Looking Back
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
Developing dapivirine ring for HIV prevention

- Dapivirine is a non-nucleoside reverse transcriptase inhibitor of HIV
- Formulated into a flexible silicone ring, it could provide a reliable, long-lasting, woman-initiated method to protect against HIV acquisition
- MTN-020 was designed as a pivotal clinical trial to provide the strength of evidence to support licensure of dapivirine ring for HIV prevention, along with complementary studies:
  - IPM 027 (efficacy & safety)
  - >25 completed phase I/II studies
  - ongoing/planned work in adolescents/post-menopausal women, drug-drug interactions
Challenges of the past: adherence and learning from PrEP trials

No adherence = no HIV protection
15 Sites across 4 countries

Blantyre
Lilongwe
Malawi

Cape Town
Durban (7 sites)
Johannesburg
South Africa

Kampala
Uganda

Harare/Chitungwiza (3 sites)
Zimbabwe
Timeline

2011
• Initiate site IRB and regulatory approval process

2012
• IRB/regulatory approvals, trainings, START!

2013
• Enrollments, follow-up

2014
• Completion of enrollment, follow-up

2015
The Big Five

Accrual

Retention

Data Quality and Timeliness

Clinical and Laboratory Safety

Adherence
## Accrual on target & on schedule

<table>
<thead>
<tr>
<th>Site</th>
<th>First enr</th>
<th># enr</th>
</tr>
</thead>
<tbody>
<tr>
<td>MA – Blantyre</td>
<td>13 JUN 13</td>
<td>130</td>
</tr>
<tr>
<td>MA – Lilongwe</td>
<td>17 JUN 13</td>
<td>142</td>
</tr>
<tr>
<td>SA – Cape Town</td>
<td>19 SEP 2012</td>
<td>166</td>
</tr>
<tr>
<td>SA – CAPRISA eThekwini</td>
<td>10 OCT 2012</td>
<td>244</td>
</tr>
<tr>
<td>SA – MRC/Botha’s Hill</td>
<td>10 SEP 2012</td>
<td>180</td>
</tr>
<tr>
<td>SA – MRC/Chatsworth</td>
<td>11 SEP 2012</td>
<td>150</td>
</tr>
<tr>
<td>SA – MRC/Isipingo</td>
<td>19 SEP 2012</td>
<td>117</td>
</tr>
<tr>
<td>SA – MRC/Tongaat</td>
<td>17 SEP 2012</td>
<td>103</td>
</tr>
<tr>
<td>SA – MRC/Verulam</td>
<td>13 SEP 2012</td>
<td>150</td>
</tr>
<tr>
<td>SA – MRC/Umkomaas</td>
<td>14 SEP 2012</td>
<td>103</td>
</tr>
<tr>
<td>SA – WRHI</td>
<td>30 OCT 2012</td>
<td>213</td>
</tr>
<tr>
<td>UG – Kampala</td>
<td>21 AUG 2012</td>
<td>253</td>
</tr>
<tr>
<td>ZI – Seke South</td>
<td>01 NOV 12</td>
<td>224</td>
</tr>
<tr>
<td>ZI – Spilhaus</td>
<td>30 OCT 12</td>
<td>230</td>
</tr>
<tr>
<td>ZI – Zengeza</td>
<td>13 NOV 12</td>
<td>224</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td></td>
<td><strong>2629</strong></td>
</tr>
</tbody>
</table>
Screen outs

- Final numbers:
  - 5446 screened, 2629 enrolled (2.1 ratio)
  - 356 (7%) did not complete screening
  - 50 (1%) declined enrollment
  - 2411 (44%) ineligible
    - 847 (35%) HIV+
    - 198 (8%) pregnant; 31 (1%) breastfeeding
    - 488 (20%) clinical/laboratory exclusion
    - 735 (30%) “other” including investigator decision
Who enrolled?

- Median age: 26 years
  - 39% <25 years, 14% ≥35 years
- Unmarried: 41% overall, 92% in SA
- 100% had a primary partner in past 3 months
  - 17% had ≥1 other partner in past 3 months
- STIs common at screening: 12% CT, 4% GC, 7% TV, 1% syphilis

A population at risk for HIV and in need of new prevention strategies
Retention

Current #s:
- Month 1: 98%
- Month 3: 96% (97% when accounting for early terminations)
- Month 6: 94% (96%)
- Month 12: 90% (97%)
- Month 18: 88% (98%)

RETENTION SUMMARY:

OVERALL = 92.1% of all expected visits
EXCLUDING TERMINATIONS = 97.1%
LAST 3 MONTHS = 97.7%
Adherence Action!

- What we’ve done together:
  
  Recognition of adherence a priority across all ASPIRE sites
  Participant and staff engagement activities
  Careful counselling for challenging cases
  Fun waiting room discussions and social events
  HIV ribbon and ring activities
  Male partner engagement efforts
  Learning from qualitative component of ASPIRE
  Visual inspection of rings and collection of used rings
  Testing of plasma and rings, with real-time action, tailored to each site’s needs
## Data Quality and Timeliness

### DATA MANAGEMENT QUALITY REPORT
Previous Month: August 2014

<table>
<thead>
<tr>
<th>Site</th>
<th>Total Records</th>
<th>Total QCs</th>
<th>QC Rate Per 100 Records (Goal &lt; 5)</th>
<th>%CRF Records Faxed within 7 days (Goal ≥ 95%)</th>
<th>Mean Days to Fax in AE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Blantyre/Malawi</td>
<td>1274</td>
<td>18</td>
<td>1.4</td>
<td>98%</td>
<td>33.5</td>
</tr>
<tr>
<td>2. Lilongwe/Malawi</td>
<td>1229</td>
<td>28</td>
<td>2.3</td>
<td>90%</td>
<td>5.8</td>
</tr>
<tr>
<td>3. Emavundleni/Cape Town</td>
<td>1411</td>
<td>33</td>
<td>2.3</td>
<td>99%</td>
<td>2.9</td>
</tr>
<tr>
<td>4. CAPRISA eThekwini</td>
<td>2482</td>
<td>63</td>
<td>3.8</td>
<td>97%</td>
<td>11.0</td>
</tr>
<tr>
<td>5. MRC - Botha’s Hill</td>
<td>1711</td>
<td>48</td>
<td>2.8</td>
<td>91%</td>
<td>7.4</td>
</tr>
<tr>
<td>6. MRC - Chatsworth</td>
<td>1153</td>
<td>21</td>
<td>1.8</td>
<td>96%</td>
<td>0.7</td>
</tr>
<tr>
<td>7. MRC - Isipingo</td>
<td>996</td>
<td>17</td>
<td>1.7</td>
<td>98%</td>
<td>10.5</td>
</tr>
<tr>
<td>8. MRC - Tongaat</td>
<td>765</td>
<td>23</td>
<td>3.0</td>
<td>100%</td>
<td>2.9</td>
</tr>
<tr>
<td>9. MRC - Verulam</td>
<td>1180</td>
<td>14</td>
<td>1.2</td>
<td>100%</td>
<td>0.2</td>
</tr>
<tr>
<td>10. MRC - Umkomaas</td>
<td>933</td>
<td>16</td>
<td>1.7</td>
<td>99%</td>
<td>1.3</td>
</tr>
<tr>
<td>11. WRHI/Johannesburg</td>
<td>1685</td>
<td>75</td>
<td>4.5</td>
<td>99%</td>
<td>8.9</td>
</tr>
<tr>
<td>12. MY-JHU/Kampala, Uganda</td>
<td>2329</td>
<td>36</td>
<td>1.5</td>
<td>99%</td>
<td>3.3</td>
</tr>
<tr>
<td>13. Seke South/Zimbabwe</td>
<td>1832</td>
<td>16</td>
<td>0.9</td>
<td>97%</td>
<td>2.1</td>
</tr>
<tr>
<td>14. Spilhaus/Zimbabwe</td>
<td>1890</td>
<td>13</td>
<td>0.7</td>
<td>97%</td>
<td>2.9</td>
</tr>
<tr>
<td>15. Zengeza/Zimbabwe</td>
<td>1728</td>
<td>21</td>
<td>1.2</td>
<td>98%</td>
<td>1.3</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>22556</strong></td>
<td><strong>472</strong></td>
<td><strong>2.1</strong></td>
<td><strong>97%</strong></td>
<td><strong>6.7</strong></td>
</tr>
</tbody>
</table>
Safety

- Safety monitoring
  - Evaluating whether the product is safe is just as important as whether the product is effective for HIV prevention
  - Excellent safety monitoring
Laboratory

- Laboratory results and archived samples are central to this study.
- Real-time shipping and testing of plasma and residual drug levels in ASPIRE is revolutionary.

THANK YOU FOR ALL THE HARD WORK.
Team communications

- Monthly Protocol team calls
  - Tremendously valuable, site-driven, sharing experiences
- IoR calls regards the PK data
- Qualitative calls
- Weekly priority emails from FHI360 to sites
- Collating protocol team priorities
- Listservs
  - Cross-site communications/sharing
- FHI360 Site assessment visits
- Patrick Ndase, MTN Regional Physicians site visits
ASPIRE

Looking Ahead
Accural → Retention → Adherence → Safety → Quality

- Smart accrual
- High retention
- Motivated adherence (engagement)
- 100% attention to data quality & participant safety, including reproductive health choices

*Everything else flows from these*
End of follow-up

- ASPIRE protocol planned to continue until at least 120 HIV seroconversions were accrued, to provide the required statistical power to assess HIV protection with confidence.

- We anticipate that the required number of HIV seroconversions will be accrued in the first half of 2015, permitting us to initiate study close-out.

- The plan for close-out (more this afternoon) will focus on an orderly exit of study participants between March and June 2014, followed by rapid data cleaning and database closure.
Retention and adherence have been priorities since Day 1. How can we keep them as priorities until the last day of data collection?

- ASPIRE is a many-month, multi-hour commitment
  - We have amazing retention now
  - Let’s maintain this all the way to the end

- How can we keep up the enthusiasm and commitment all the way until the last participant exit?
MTN-015 and 016

- The **only** controlled data on periconception safety and early HIV disease related to dapivirine exposure will come from these studies.
  - A few more months to get this valuable information
ASPIRE calendar

- January 2011 and ongoing
  - Multilevel consultations on the science and implementation, leading to protocol version 1.0 in September 2011
- August 2012 - present
  - Start and go! Enrollments, follow-up, highest-quality execution of all protocol aspects
- November 2012, May 2013, November 2013, May 2014
  - DSMB reviews
- November 2014
  - DSMB review
- March-June 2015, then Q3 2015
  - Participant exits, final data cleaning
- By the end of 2015
  - Results
What we have learned

- Adherence
- Importance of prevention options
- Involving men
- Contraceptive action
Adherence monitoring in MTN-020

- Monthly shipping, testing, and review of plasma and residual ring dapivirine data, according to a pre-defined plan

- Information is reviewed by-site, rather than by-subject, preserving blinding.

- Results? We are optimistic!
Prevention options

- Quotes from the qualitative component of ASPIRE:

- Self-efficacy: *The ring is different from the condom ‘because’ you can wear it and your man will not feel it ‘but’ you will know that “I am protecting myself”.*
Prevention options

- Quotes from the qualitative component of ASPIRE:

- Study clinics as important spaces: *I am not talking about other people but I am talking about myself, that I know I have used the ring, I insert it in the clinic and I remove it here, in the clinic. Nobody forced me to come here, I came on my own and I like being here.*
Prevention options

- Quotes from the qualitative component of ASPIRE:

  - Looking ahead: *If we find something that helps us it will not just help me alone but it will also help future ‘generations’. This is something which is good.*
Male involvement

- Two-thirds of participants at baseline reported having told their primary partners about their plans to use the ring in the trial.

- However, some participants in the trial face social risks because of participating in an HIV prevention trial / using an HIV prevention option.

- We have learned much (and can teach much) about male involvement in prevention work.
Contraceptive Action Team

- Incredible motivation, amazing change, and true leadership for women’s health
  Jun-14

- In addition, an unbelievably low rate of pregnancies (~3% per year), vs. >10% per year in prior studies
We are all in this together

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

Recruitment
Retention
Adherence
Sample collection
Staff morale
Community/outreach
Communications
Lab quality

QC/QA
Regulatory
Safety Monitoring
Space/facilities
Study drug/pharmacy
Contraception
Lab-clinic interface
Monitoring follow-up
What does ASPIRE mean?

aspire (as·pire)

Pronunciation: /əˈspī(ə)r/

verb

[no object]
direct one’s hopes or ambitions toward achieving something:
we never thought that we might aspire to those heights

[with infinitive]:
other people will aspire to be like you

ASPIRE
\ə-ˈspī(-ə)r\
noun:
1. A Phase III study that seeks to determine whether a woman’s use of a vaginal ring containing dapivirine is a safe and effective method for protecting against HIV infection.
2. A Study to Prevent Infection with a Ring for Extended Use

verb:
1. To seek to end the HIV epidemic < We aspire to prevent HIV>
ASPIRE …

ONE CHANCE

OUR CHANCE
Thank you

Participants and communities
Acknowledgements

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