ASPIRE
A Study to Prevent Infection with a Ring for Extended Use

Jared Baeten MD, PhD
Thesla Palanee-Phillips, PhD

ASPIRE Protocol Team Meeting
October 2015
Meeting overview

- Welcome back!
- Today, we’ll cover:
  - Updates on ASPIRE & The Ring Study
  - Looking forward to results and to HOPE (hopefully!)
  - Inspection readiness
- But, first, where we’ve been and where we are going in ASPIRE
Outline

Where we have been and where we are going – mostly in pictures
We planned a study

- 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
We learned the meaning of ASPIRE

**aspire** (as·pire)

Pronunciation: /əˈspī(ə)r/

**verb:**

direct one’s hopes or ambitions toward achieving something:

we never thought that we might **aspire to** those heights

**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

**dream:**

Quote from the qualitative component of ASPIRE:

*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.*
We started!

Phase III Trial of Dapivirine Ring Begins in Africa: ASPIRE testing new HIV prevention approach for women

WASHINGTON, D.C., July 24, 2012 – A large clinical trial testing the long-term safety and effectiveness of a new approach for preventing HIV in women – a vaginal ring used once a month – is now underway in Africa, researchers announced today at the XIX International AIDS Conference (AIDS 2012).
We worked in 15 Sites across 4 countries

Blantyre
Lilongwe
Malawi
Cape Town
Durban (7 sites)
Johannesburg
South Africa

Kampala
Uganda

Harare/Chitungwiza (3 sites)
Zimbabwe
We learned how to explain the ring
We went to the community
We provided exceptional prevention services

2,629 Women

HIV prevention package

Placebo ring
1,314 women

HIV prevention package

Dapivirine ring
1,314 women
We worked together

<table>
<thead>
<tr>
<th>Objectives</th>
<th>The Ring Study (IPM 027)</th>
<th>ASPIRE (MTN-020)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study design</td>
<td>Long-term safety and efficacy</td>
<td>Safety and effectiveness</td>
</tr>
<tr>
<td></td>
<td>Double-blind, randomized (2:1), placebo-controlled</td>
<td>Double-blind, randomized (1:1), placebo-controlled</td>
</tr>
<tr>
<td>Endpoints</td>
<td>Expected ~96 endpoints, 2 year on investigational product</td>
<td>Endpoint driven: ~120 endpoints</td>
</tr>
<tr>
<td>Enrollment</td>
<td>Total: 1959 women, ages 18-45</td>
<td>Total: 2629 women, ages 18-45</td>
</tr>
<tr>
<td></td>
<td>Active arm: ~1300</td>
<td>Active arm: ~1315</td>
</tr>
<tr>
<td>Regulatory requirement</td>
<td>3000 women on dapivirine ring for at least 1-year follow-up</td>
<td>1500 women on dapivirine ring for 2-year follow-up</td>
</tr>
<tr>
<td>Participant follow-up</td>
<td>2 years + 6 weeks following ring discontinuation</td>
<td>Minimum 1 year + 4 weeks following ring discontinuation</td>
</tr>
<tr>
<td>Research sites</td>
<td>7 IPM research center partners in South Africa and Uganda</td>
<td>15 MTN research centers in Malawi, South Africa, Uganda, Zimbabwe</td>
</tr>
</tbody>
</table>
We defined our Big Five

- Accrual
- Retention
- Adherence
- Data Quality and Timeliness
- Clinical and Laboratory Safety
We thought about adherence

Efficacy + Adherence → Effectiveness

No adherence = no HIV protection
And then we thought a lot about adherence

VOICE Primary Efficacy Results
Adherence is Everything

Jared Baeten MD PhD
Thesla Palanee PhD

ASPIRE Adherence Meeting
Durban, South Africa
14 March 2013
We did amazing participant engagement
We did amazing participant engagement

The engagement ring, the wedding ring, the vaginal ring - the ultimate partnership!
We did amazing participant engagement
We looked at returned rings

- Unused Ring
- Used Ring: Cream coloured & slimy, reported perfect use
We made our Big Five a reality
We became a team
We continuously worked in communities
We completed accrual June 2014

<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>
We had amazing retention

OVERALL >91% of all expected visits

>97% of visits excluding early terminations
We reminded the world that PrEP is not one size fits all

- Tenofovir-based PrEP is a first proof-of-concept.
- Ultimate goals: multiple options, long acting, safe, effective, low cost and user-friendly
- Maximize choice & optimize effectiveness
We diversified contraception
We shipped a lot of samples
We did a lot of phone calls
We learned

- Women are interested in a ring for prevention.
- Real-time adherence monitoring can be done in a trial, and women are adherent to a ring.
- Women want prevention options.
- Contraceptive options matter.
- Male involvement, in many different ways, is part of prevention in women.
We have amazing data

- >600,000 CRF pages.
- >150,000 samples, including >20,000 plasma samples tested.
- >40,000 rings dispensed, returned, and tested.
- 248 IDIs, 12 FGDs.
We planned

- 2012: IPM 027 (The Ring Study)
- 2013: MTN-020 (ASPIRE)
- 2014: Supporting Safety and PK Studies
- 2015: Dapivirine Ring Regulatory Consultations
- 2016: Results?
### We planned for results

<table>
<thead>
<tr>
<th>EFFICACY IS CLEAR</th>
<th>EFFICACY WITH QUESTIONS</th>
<th>RESULTS UNCLEAR</th>
<th>INSUFFICIENT EFFICACY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Great news!</td>
<td>Good news (?)</td>
<td>Results don’t provide clear answers - additional analysis needed?</td>
<td>Results answer the questions - dapivirine ring is safe but not effective</td>
</tr>
<tr>
<td>Results clearly show dapivirine ring is safe and effective</td>
<td>Results show dapivirine ring is safe and effective</td>
<td>Decision about HOPE not straightforward</td>
<td></td>
</tr>
<tr>
<td>Move to implement HOPE</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**HOPE**

Out of ASPIRE, there is HOPE

**ASPIRE**

A Study to Prevent Infection with a Ring for Extended Use
We planned for success

- **ASPIRE**
  - results
  - Participants informed
  - IRB/EC informed
  - HOPE
    - HOPE approval
    - Former Participants contacted
  - HOPE approval
  - enrollment
  - Approximately 1-year open-label use of dapivirine ring

- **National and community Stakeholders** informed
We are a team

Participants and communities
Acknowledgements

MTN is funded by NIAID (UM1AI068633, UM1AI068615, UM1AI06707), NICHD and NIMH, all of the U.S. National Institutes of Health