Strategies to Improve Adherence to Vaginal Rings

ADHERENCE TO HIV PREVENTION AND TREATMENT:
KEY POPULATIONS IN SUB-SAHARAN AFRICA
Cresta Lodge, Harare, Zimbabwe
26 April 2018
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Potential Conflicts and Financial Disclosures

• I have no conflicts to declare in relation to this programme and presentation.

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Overview

• Dapivirine Vaginal Ring
• Oral PrEP vs. Dapivirine Vaginal Ring
• Phase III to Phase IIIb
• Phase IIIb Open-Label Interim Results
• Adherence Strategies
• “Inside my Purse”
• Conclusion
**Dapivirine Vaginal Ring**

**Dapivirine:**
- Highly potent NNRTI ARV
- IPM holds exclusive worldwide rights for Dapivirine through Janssen Sciences Ireland UC

**Dapivirine Vaginal Ring:**
- Flexible silicone vaginal ring developed by IPM
- Sustained-release of dapivirine locally to site of potential HIV infection during vaginal sex
  - Minimal systemic absorption
- Women insert the ring themselves and replace it monthly
- Two Phase III trials showed the ring was well-tolerated and reduced the risk of HIV-1 infection in women (ages 18-45) by approximately 30% relative to placebo
- Dapivirine Vaginal Ring ring is currently under regulatory review by the European Medicines Agency under Article 58
# Oral PrEP vs Dapivirine Vaginal Ring

<table>
<thead>
<tr>
<th>Oral Pre-Exposure Prophylaxis (PrEP)</th>
<th>Dapivirine Vaginal Ring (DVR)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>What is...</strong></td>
<td></td>
</tr>
<tr>
<td>• Antiretroviral oral medication</td>
<td>• Reduce risk of acquiring HIV-1 infection</td>
</tr>
<tr>
<td>• HIV infection prevention</td>
<td>• Not used for treatment</td>
</tr>
<tr>
<td><strong>How does it work...</strong></td>
<td></td>
</tr>
<tr>
<td>• Truvada blocks an enzyme called HIV nucleoside reverse transcriptase</td>
<td>• Dapivirine blocks an enzyme called HIV non nucleoside reverse transcriptase</td>
</tr>
<tr>
<td><strong>When should you take...</strong></td>
<td></td>
</tr>
<tr>
<td>• Estimated that it takes at least 7 days for PrEP to reach high levels of protection</td>
<td>• Continuous use important</td>
</tr>
<tr>
<td>• When used pills daily and correctly, Truvada provides 92%–99% reduction in HIV risk</td>
<td>• At least 30% HIV-1 risk reduction</td>
</tr>
<tr>
<td>• Highest level of HIV risk reduction is still unknown</td>
<td></td>
</tr>
<tr>
<td><strong>What happens if you miss a dose...</strong></td>
<td></td>
</tr>
<tr>
<td>• Very important to take PrEP (Truvada®) every day</td>
<td>• Dapivirine ring should be kept in the vagina at all times and replaced every month</td>
</tr>
</tbody>
</table>
Phase III to Phase IIIb (OLE)

- IPM 027: The Ring Study
- IPM 027 Amendment 5
- IPM 032: DREAM
- MTN-020: ASPIRE
- MTN-025: HOPE
Phase IIIb

<table>
<thead>
<tr>
<th>Enrolment by October 2017</th>
<th>IPM 032</th>
<th>MTN-025</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of research centres</td>
<td>6</td>
<td>14</td>
</tr>
<tr>
<td>Countries</td>
<td>South Africa, Uganda</td>
<td>Malawi, South Africa, Uganda, Zimbabwe</td>
</tr>
<tr>
<td>Enrolled</td>
<td>941</td>
<td>1407</td>
</tr>
</tbody>
</table>

- Majority of participants from South Africa
- Main reasons for screening failures are
  - HIV-positive
  - Currently pregnant/planning to become pregnant or breastfeeding
  - Not available for all visits
  - Not using contraception
## Interim Results: Participant Characteristics

<table>
<thead>
<tr>
<th>ENROLMENT DEMOGRAPHICS</th>
<th>IPM 032 n (%)</th>
<th>MTN-025 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>29 (25,34)</td>
<td>31 (27,37)</td>
</tr>
<tr>
<td><strong>Age range (years)</strong></td>
<td>18-21</td>
<td>13%</td>
</tr>
<tr>
<td><strong>Marital status</strong></td>
<td>Married</td>
<td>53%</td>
</tr>
<tr>
<td><strong>Partners</strong></td>
<td>Main partner</td>
<td>Not recorded</td>
</tr>
<tr>
<td><strong>Sexually Transmitted Infections</strong></td>
<td>18%</td>
<td>16%</td>
</tr>
</tbody>
</table>

**Data cut off:**
- IPM 032 - 29 Sep 2017
- MTN-025 - 6 Oct 2017
**Interim Results: Adherence to Ring Use**

Ring residual levels of ≤ 23.5 mg dapivirine indicate at least some ring use

– Proportion of returned rings containing ≤ 23.5 mg dapivirine increased as compared to Phase III clinical placebo-controlled trials

<table>
<thead>
<tr>
<th>Phase IIIb</th>
<th>IPM 032</th>
<th>MTN-025</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DREAM</td>
<td>HOPE</td>
</tr>
<tr>
<td>≤ 23.5 mg residual levels</td>
<td>~96%</td>
<td>~89%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Phase III</th>
<th>IPM 027</th>
<th>MTN-020</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>The Ring Study</td>
<td>ASPIRE</td>
</tr>
<tr>
<td>≤ 23.5 mg residual levels</td>
<td>~83%</td>
<td>~77%</td>
</tr>
</tbody>
</table>
Interim Results: Adherence to Ring use

Data cut off:
- IPM 032 - 29 Sep 2017
OLE Preliminary Results

- A similar safety profile is observed as in Phase III
- Adherence to ring use appears higher, based on dapivirine ring residual levels
- Observed HIV-1 incidence rate has been half of the expected placebo rate estimated by modelling
- Although based on modelling, these interim data support the hypothesis that increased ring use and HIV risk reduction occurs when participants know the safety and efficacy results from Phase III trials
Comparison to other Open-Label Data

The HIV-1 incidence observed as of Q3 2017 in the two DVR OLE trials compare favorably to that seen in prior open-label extension studies, for example iPrEx OLE:

- **HIV incidence in iPrEx OLE among the subset with high PrEP adherence was zero**
- **Similar adherent subset analyses are not yet available for Dapivirine Vaginal Ring (DVR)***
## Adherence Strategies

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Research Team Capacity Strengthening</strong></td>
<td>• Profile analysis, skill set training, team dynamics, knowledge sharing and best practices implementation</td>
</tr>
<tr>
<td><strong>Protocol Compliance</strong></td>
<td>• Missed/late visits, ring expulsion/removal trends and male and female condom use</td>
</tr>
<tr>
<td><strong>Adherence Support Tools</strong></td>
<td>• Counseling tools, messaging boards and audio visuals in waiting areas</td>
</tr>
<tr>
<td><strong>Person-centred Counseling Approach</strong></td>
<td>• Visual inspection of rings and dapivirine residual result sharing</td>
</tr>
<tr>
<td><strong>Adherence Meetings</strong></td>
<td>• Informal small or large group discussions</td>
</tr>
<tr>
<td><strong>Ad hoc</strong></td>
<td>• Telephonic support and home visits</td>
</tr>
<tr>
<td><strong>Community Engagement</strong></td>
<td>• Formal stakeholder and broader community involvement</td>
</tr>
<tr>
<td><strong>Women and male engagement</strong></td>
<td></td>
</tr>
</tbody>
</table>
Adherence Messaging Tools

The Ring Study Participant Result Tool
Addresses some of the questions which participants may have regarding Phase III results released early 2016.

DREAM Adherence Tool
Promote adherence by addressing some of the questions which participants might have regarding removals and expulsions of the ring.

Participant Feedback Tool
Assist to explain the concept of amount of dapivirine released from the ring into the vagina in relation to the level of HIV risk reduction.
Women in Research Communities

- Engage older women who have influence in young women’s daily lives and decisions
- Hosting of participant events outside research settings
- Collaborate with higher education institution targeting young women as potential end users
- Identify new partners to collaborate with regarding women issues in the broader health context - holistic

Approximately 3050 non study participants attended IPM and research centre educational events and activities in 2017
Male Engagement to Enhance Ring use

Purpose:
- Encourage dialogue on men’s sexual health and HIV prevention
- Educate on female sexual and reproductive health
- Garner support for biomedical HIV prevention research
- Introduce the dapivirine vaginal ring as a possible option in future

Engagement Mechanisms:
- Set dialogue platforms through informal men focused activities (e.g. sports, taverns and car wash spots)
- Create questions and feedback opportunities in groups and 1-to-1
- Customize educational materials on a variety of topics

Outcomes:
- Support for trial and clinical research in the community
- Enhance participants’ partner support
- Understand and encourage retention and adherence to product use
INSIDE MY PURSE - an Interactive Blog

IPM Facebook

• for adolescent girls, young women in the African context
• particular attention to sexual and reproductive health
• 17k engagements on the post launching blog

Inside My Purse

INTERNATIONAL PARTNERSHIP FOR MICROBICES
FEBRUARY 2018 | Combination Prevention, Condoms, Male and Female, General, Hormonal Contraceptives, and HIV, HPV Vaccines, Microbicides, Multipurpose Prevention Technologies, PHP, Treatment, Voluntary Medical Male Circumcision
Website

The International Partnership for Microbicides (IPM) has launched an interactive blog, insidemypurse.co.za, by and for adolescent girls and young women across Africa. With sexual and reproductive health as its primary focus, the platform encourages visits and contributions from everyone who cares about promoting health, wellness and empowerment among young women.

http://insidemypurse.co.za
Conclusion

Women continue to become infected with HIV at alarmingly high rates, especially in sub-Saharan Africa.

A range of prevention products are needed - including condoms, daily PrEP, long-acting rings and other methods in development.

No single approach will meet all women’s needs or get the epidemic under control.

If approved, the ring could expand women’s options with the first long-acting HIV prevention method.
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