Safety, Adherence and HIV-1 Seroconversion in DREAM – An Open-label Dapivirine Vaginal Ring Trial

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International Partnership for Microbicides (IPM)
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Disclaimer

The following slides provide educational information and background on an investigational product. Although these slides contain some forward-looking statements, IPM’s Dapivirine Vaginal Ring has not been reviewed or approved by global or national regulatory authorities. All timelines and plans are subject to change pending regulatory reviews.
Dapivirine Vaginal Ring (DVR)

- DVR is a flexible silicone matrix ring containing 25 mg of dapivirine, an HIV-1 non-nucleoside reverse transcriptase inhibitor.

- Dapivirine is slowly released from the ring when placed in the vagina, and the ring is replaced monthly with continuous use.

- Two Phase III trials showed that the DVR was well-tolerated and reduced the risk of HIV-1 infection in women (ages 18-45 years) by approximately 30% compared to placebo.

- Participants who remained HIV seronegative were offered participation in an open-label extension trial, DREAM/IPM 032.

- DREAM/IPM 032 evaluated safety and adherence to DVR use, and HIV-1 incidence over approximately one year of follow-up.
Timeline and Trial Design

- **Feb 2016**: The Ring Study reported primary results
- **Jul 2016**: DREAM initiated
- **Feb 2018**: DREAM completed enrollment
- **Jan 2019**: DREAM last participant out

- All participants received active DVR
- Trial visits occurred monthly up to 3 months after enrollment, and quarterly thereafter
- At each trial visit:
  - All received a comprehensive HIV-prevention package and safety evaluations
  - Used rings were returned for analysis of dapivirine residual levels
Enrollment

In total, at 5 research centers in South Africa and 1 in Uganda:

- 1034 women were screened
- 941/1034, 91.0% women were enrolled
- 150 women rolled over directly from The Ring Study
- 850/941, 90.3% completed at least 1-year follow-up
- 93/941, 9.9% discontinued early:
  - withdrew consent (57/93, 61.3%)
  - *HIV seroconverted (18/93, 19.3%)
  - Lost to follow-up (13/93, 14.0%)
  - Other (5/93, 5.4%)

*In total 26 participants HIV seroconverted; for participants who HIV seroconverted at a scheduled Last Product Use Visit or Exit Visit, the CRF was completed as “Participant completed the entire trial”, and not as “HIV seroconversion”
Demographics

• Mean age was 30 years (range: 20 – 50 years)
  – Majority was 21 – 30 years (57%)
• Most women:
  – had secondary or a higher level of education
  – were single (81%)
  – had a main partner (97%); 12% reported 2 or more partners
  – had children (95%)
  – used long-acting injectable progestins (77%)
• 18% reported STI symptoms at baseline
• 76% reported partner knowledge of ring use
## Results: Safety

<table>
<thead>
<tr>
<th>Safety Parameters</th>
<th>Dapivirine Vaginal Ring (N = 941)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adverse Events (AEs)</strong></td>
<td></td>
</tr>
<tr>
<td>TEAEs</td>
<td>623 (66%)</td>
</tr>
<tr>
<td>Urogenital TEAEs</td>
<td>440 (47%)</td>
</tr>
<tr>
<td>Serious AEs</td>
<td>23 (2%)</td>
</tr>
<tr>
<td>Grade 3 or 4 TEAEs</td>
<td>42 (4%)</td>
</tr>
<tr>
<td>Product-related TEAEs</td>
<td>6 (&lt;1%)</td>
</tr>
<tr>
<td><strong>Pregnancy</strong></td>
<td></td>
</tr>
<tr>
<td>Pregnancies</td>
<td>27 (3%)</td>
</tr>
<tr>
<td><strong>Most frequent Genitourinary AEs</strong></td>
<td></td>
</tr>
<tr>
<td>Chlamydia infection</td>
<td>110 (12%)</td>
</tr>
<tr>
<td>Gynaecological infection</td>
<td>79 (8%)</td>
</tr>
<tr>
<td>Vulvovaginitis</td>
<td>61 (7%)</td>
</tr>
<tr>
<td><strong>Social Harms</strong></td>
<td></td>
</tr>
<tr>
<td>Emotional/Physical/Financial</td>
<td>25 (3%)</td>
</tr>
<tr>
<td>- Reported due to trial involvement</td>
<td>9 (34%)</td>
</tr>
<tr>
<td><strong>HIV-1 Seroconversions</strong></td>
<td></td>
</tr>
<tr>
<td>Participants who HIV-1 seroconverted</td>
<td>26 (2.8%)</td>
</tr>
<tr>
<td>Participants who HIV-1 seroconverted on IP</td>
<td>18 (1.9%)</td>
</tr>
<tr>
<td>- NNRTI resistance mutations</td>
<td>5/18 (28%)</td>
</tr>
</tbody>
</table>

N = number of participants; TEAEs = Treatment-Emergent Adverse Events; NNRTI = Non-nucleoside reverse transcriptase inhibitors; IP = Investigational Product
Results: Adherence

Mean Dapivirine Residual Levels (mg) in Used Rings by the Month Ring was Used

IPM 032 Summary Report Version 2.0; Data cut-off 8 November 2018
Simulating a DREAM Placebo Arm: Bootstrap Method

**Simulation Result:**
HIV-1 incidence: 4.3 per 100 PY (95% CI: 3.4-5.4)
Results: HIV-1 Incidence

• 26/941 (2.8%) HIV-1 seroconversions occurred.
• 18/938* (1.9%) participants were confirmed HIV-1 infected while using DVR, with 1131.23 person-years of follow-up.
• The observed HIV-1 incidence rate (1.59 per 100 PY (95% CI: 0.86-2.33) in DREAM is 63% lower than the placebo rate estimated by bootstrap analysis.

* m-ITT = Modified intent-to-treat population includes all enrolled participants who were confirmed HIV-negative at Enrollment
DREAM: Conclusions

- The Dapivirine Vaginal Ring was well tolerated; and a similar safety profile is observed as in Phase III trials.
- Adherence to ring use appears to be higher in DREAM based on dapivirine ring residual levels.
- The observed HIV-1 incidence rate in DREAM is 63% lower than the placebo rate estimated by bootstrap analysis.
- Although based on simulation, these data support the hypothesis that increased HIV risk reduction may occur when participants know the safety and efficacy results from Phase III trials.
Co-Authors and Acknowledgement

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Women who participated in DREAM

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- \textsuperscript{6}Ndlovu Care Group (NCG)

ประเทศไทย

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