POPULATION COUNCIL’S MPT DEVELOPMENT PROGRAM

Tom Zydowsky
IMPT CT Meeting
September 14, 2016
MPT Development Overview

Brady M, Tolley E. Aligning product development and user perspectives: social-behavioural dimensions of multipurpose prevention technologies. BJOG 2014; 121 (Suppl. 5): 70-78
PC’s MPT Strategy

- Focus on Approved + Approved or Approved + Experimental pathway initially
- Develop
  - user-initiated, on demand or sustained release (< 90 days) products
  - broad spectrum products with or without contraception (cMPT and MPT, respectively)
- Collaborate with external organizations to accelerate MPT development
## PC’s cMPT Pipeline

<table>
<thead>
<tr>
<th>MPT</th>
<th>Indications</th>
<th>Development Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>MZC gel + SILCS diaphragm*</td>
<td>HIV, HSV, HPV and unintended pregnancy</td>
<td>Proposed Phase 1</td>
</tr>
<tr>
<td>MZC + HC vaginal ring</td>
<td>HIV, HSV, HPV and unintended pregnancy</td>
<td>Preclinical</td>
</tr>
<tr>
<td>Griffithsin + HC vaginal ring#</td>
<td>HIV and HSV and unintended pregnancy</td>
<td>Early preclinical</td>
</tr>
</tbody>
</table>

MZC = MIV-150 + zinc acetate + carrageenan (experimental)
HC = hormonal contraceptive (approved for vaginal administration)

* Collaboration with PATH  
# Collaboration with Oak Crest
MZC Gel Overview

- **MIV-150**
  - NNRTI with good resistance profile
  - Active against different HIV clades and multi-drug resistant HIV

- **Zinc Acetate (ZA)**
  - RTI with good resistance profile
  - *In vivo* activity against SHIV-RT and HSV-2 (in a carrageenan gel)
  - Inhibits forward progressive human sperm motility and the human sperm acrosome reaction

- **Carrageenan (CG)**
  - Attachment and entry inhibitor; blocks HPV in vitro and *in vivo*
  - Potentiates ZA’s anti-HSV-2 activity *in vivo*

- **MZC attributes**
  - One-two-punch against HIV
  - Broad spectrum antiviral activity *in vivo*: HIV, HSV and HPV
  - Phase 1 vaginal trial finished; vaginal Phase 1B and rectal trials planned
  - Physical compatibility with SILCS diaphragm
SILCS Diaphragm: Designed to Meet User Needs

- Easy to insert
- Comfortable to wear
- Stable, confident fit
- Easy to remove
- Single-size device
  - Fits most women
  - No need for pelvic exam
  - Simplifies supply logistics and delivery

![Diaphragm Image]
SILCS Commercialization Status

- SILCS technology licensed to Kessel medintim GmbH in 2010
- Regulatory approvals achieved in multiple countries, including Europe, Canada, Australia, and U.S.
- Launched first in EU countries in 2013 as Caya® contoured diaphragm; now marketed in 25+ countries
- Developed country introduction used to build experience and raise awareness and interest in developing countries
- CayaGel (a CE mark certified contraceptive gel containing lactic acid) marketed for use with the Caya® contoured diaphragm
- MZC gel proposed to replace Caya Gel
# TPP for MZC Gel + SILCS

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration of protection</strong></td>
<td>8 hours</td>
</tr>
<tr>
<td><strong>Number of pregnancies expected (per 100 women-years)</strong></td>
<td>18 for typical use; 14 for perfect use</td>
</tr>
<tr>
<td><strong>Antiviral efficacy</strong></td>
<td>HIV: 70%  HSV: 60%  HPV: 90%</td>
</tr>
<tr>
<td><strong>API amounts in 4 gram of MZC gel</strong></td>
<td>MIV-150: 0.07 mg  zinc acetate: 3 mg  carrageenan: 30 mg</td>
</tr>
<tr>
<td><strong>Gel storage conditions and shelf-life</strong></td>
<td>Stable for 30 months at 30°C/65% RH, and 18 months at 40°C/75% RH.</td>
</tr>
<tr>
<td><strong>Cost of MZC gel (per 4 gram dose)</strong></td>
<td>&lt;$0.10</td>
</tr>
</tbody>
</table>
Value Proposition: Gel + SILCS

• Alternative delivery system with added value
  – Comparable to vaginal applicators for delivery of gels
  – Reusable for 2 years = reduced cost for packaging and delivery
  – Less environmental impact due to reuse of delivery system
  – Holds gel high in the vagina = less messiness and gel leakage

• Potentially less stigma by associating product with contraception
  – FP methods are generally accepted by couples; less stigma than use of a product for HIV prevention alone

• cMPT: Broad spectrum HIV/STI protection + contraception
  – Women more interested in a product that offers dual protection
SILCS Diaphragm as an MPT

- **Objective:** Assess acceptability and preference for the SILCS for microbicide gel delivery compared to gel delivery from a prefilled applicator
- **Method:** 106 South African women used each method during five separate sex acts
- **Results:**
  - 83% of women felt comfortable with SILCS
  - 68% interested in using SILCS + gel if it could protect from both unintended pregnancy and HIV
  - 18% interested in SILCS for pregnancy protection
  - 14% interested in microbicide gel for HIV prevention

Beksinska, Smit, Maphumulo, et. al. Poster at ESC Congress, April 2016
## Draft Clinical Plan for MZC Gel + SILCS

<table>
<thead>
<tr>
<th>Study</th>
<th>Status</th>
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</thead>
<tbody>
<tr>
<td><strong>MZC Gel Only</strong>: 14 day Phase 1 vaginal safety</td>
<td>Completed</td>
</tr>
<tr>
<td><strong>MZC Gel Only</strong>: 28 day Phase 1 B expanded vaginal safety with male tolerance/penile safety</td>
<td>Proposed (STAR STI CTG)</td>
</tr>
<tr>
<td><strong>MZC Gel + SILCS</strong>: Post-coital Testing (PCT)</td>
<td>Proposed</td>
</tr>
<tr>
<td>Randomized X-over of SILCS + 4ml MZC gel, K-Y or N-9</td>
<td></td>
</tr>
<tr>
<td><strong>MZC Gel + SILCS</strong>: 3-6 month Phase 2B</td>
<td>Proposed</td>
</tr>
<tr>
<td>- 1º Contraception</td>
<td></td>
</tr>
<tr>
<td>- 2º HIV prevention (HSV, HPV)</td>
<td></td>
</tr>
<tr>
<td><strong>MZC Gel + SILCS</strong>: Two Pivotal Phase 3 safety and efficacy trials</td>
<td>Proposed</td>
</tr>
<tr>
<td>- 1º HIV prevention</td>
<td></td>
</tr>
<tr>
<td>- 2º Contraception, HSV, HPV</td>
<td></td>
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</tbody>
</table>
Risks and Gaps

• **Technical feasibility**
  - Contraceptive/HIV/STI efficacy of MZC gel

• **Strategic**
  - Unknown role within overall contraceptive and MPT method mix
    - Market analysis
    - Acceptability, interest and uptake
    - Cost effectiveness/health impact modeling
  - Potentially complex regulatory pathway for a cMPT
Summary

• The SILCS diaphragm is an approved contraceptive, with a demonstrated consumer interest, and growing markets.

• SA women are more interested in a Gel + SILCS cMPT compared to a diaphragm or gel alone.

• MZC is active against HIV, HSV and HPV, (and sperm?) and completed Phase 1 vaginal trial.

• MZC + SILCS could help meet the SRH needs of women in developing countries.
Acknowledgments
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