

Vaginal Rings:

Clinical Evaluation of the Dapivirine Vaginal Ring

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Next Steps for HIV Prevention in Women:
Tenofovir Gel and Beyond

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What is a microbicide?

- A substance designed to prevent or reduce the sexual transmission of HIV or other sexually transmitted infections (STIs) when applied inside the vagina or rectum.
- Vaginal microbicides can be formulated as a:
 - Gel
 - Cream
 - Film
 - Ring
- Be used daily, with sex, or monthly
- Ideally, be safe, effective, low cost and user-friendly



HIV Prevention for Women: Tenofovir Gel and Beyond

- Providing additional evidence about tenofovir gel is clearly a priority (VOICE, FACTS 001)
- Tenofovir gel could be the first microbicide approved for use
 - Would approval mean our work is done?



Our work is not done!

- We need to look at microbicides that contain different ARV compounds, maybe even combinations of ARVs
- We need to look at different formulations besides a gel
- We need to look at different dosing strategies that may make it easier for some women

Why Adherence Matters

- If a product is active against HIV but it's not used, it won't help reduce HIV.
- Women's preferences are not all the same
- A product that best suits a woman's lifestyle and needs is more likely to be used
- Vaginal rings that need to be replaced every 4 weeks may have benefits over dosage forms that need to be used more frequently

What is a vaginal ring?

- In the U.S. and Europe, vaginal ring products are licensed for both contraception delivery and hormone replacement.
- Vaginal rings are designed to allow for the slow, continuous delivery of a drug or multiple drugs over a period of weeks.
- They stay in place during sex and are not usually felt by the partner
- After a month, they are removed and thrown away



The story of dapivirine

- Dapivirine is an antiretroviral drug that was developed by Tibotec Pharmaceuticals to be taken orally for *treating* HIV
- When used to treat people with HIV, it had a favorable safety profile and was effective in reducing the “viral load” so we know it works in the body against HIV
- Tibotec assigned a royalty-free license to the International Partnership for Microbicides (IPM) in 2004



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Clinical Safety

- Multiple trials have evaluated the safety of dapivirine
- Phase 1 and 2 studies conducted with dapivirine
 - Therapy Indication (11 total trials, N = 211):
 - Eight studies in healthy volunteers
 - Three studies in HIV+ patients
 - Microbicide Indication
 - Vaginal Gels: Five studies completed (N = 214)
 - Vaginal Rings: Five studies completed; one study to report results later in 2011
- Across all clinical trials and with multiple formulations and dosing regimens, dapivirine products were shown to be generally safe and well tolerated

About dapivirine ring

- Studies have shown that high levels of drug can be delivered throughout the cervix and vagina for up to one month
- Studies have shown that women find using the ring acceptable
 - Includes a study of women in Africa
- A trial of safety and acceptability is due to have results later this year:
 - 280 women in Kenya, Malawi, South Africa and Tanzania

Now What?

- IPM is committed to developing the dapivirine ring
- Phase I and Phase II studies support moving into Phase III testing
- Originally there were to be two Phase III trials
 - IPM sought alternative ways to coordinate funding and clinical trial capacity
- Given the importance of the dapivirine ring product, NIH and MTN offered resources to conduct the Phase III trial

The Plan: Two studies

- MTN has designed and will conduct a single pivotal Phase III trial – ASPIRE (MTN-020)
 - Safety and effectiveness

- IPM will conduct a long-term Phase II safety trial in at least 1000 women on active product who will be followed for at least 2 years – The Ring Study (IPM 027)
 - Safety data



IPM's Role in MTN-020

- IPM remains regulatory sponsor and license holder for the dapivirine ring
- IPM will lead the overall clinical development program, regulatory process and eventual access, if approved
- Provide the rings for the ASPIRE Phase III trial

Working Together

- Both studies are critical to getting the dapivirine ring approved
- The partnership between IPM and MTN has a common goal and shared vision:



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