Vaginal Rings:

Clinical Evaluation of the Dapivirine Vaginal Ring

Sharon L. Hillier, Ph.D.

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

Joint Civil Society and MTN Community Working Group Meeting
8 October, 2011, Cape Town
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.
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:
Acknowledgements

MTN is funded by NIAID (5U01AI068633), NICHD and NIMH, all of the U.S. National Institutes of Health