What do you think about…?

Beyond Phase III: Seeking stakeholder perspectives on next steps with the dapivirine ring for HIV prevention in women

6 August 2014, Lilongwe
Question #1
HIV testing and safety monitoring
In the “real world,” monthly visits (the norm in clinical trials like ASPIRE) are likely to be too burdensome for healthcare systems.

Less frequent visits might be optimal, but only if safety is not being compromised for convenience. One concern is that prolonged periods between HIV testing could increase the chances of drug resistance if a woman gets infected and continues using the dapivirine ring.

- Women in ASPIRE are tested every month for HIV and if a woman tests positive, product is stopped immediately to reduce risk for resistance
- In HOPE (MTN-025) some women would have monthly checks while others would come to the clinic every 3 months
HIV testing and safety monitoring

- Resistance has been rare in prevention trials involving tenofovir-based products
  - Across 5 large trials, there were 143 participants who acquired HIV while using an active product and not one had resistance.

CAPRISA 004 tested tenofovir vaginal gel while iPrEx, Partners PrEP, TDF2 and the Bangkok Tenofovir Study tested daily use of an ARV tablet (tenofovir or Truvada)
HIV testing and safety monitoring

- An open-label trial is an opportunity to collect important information about the implementation of an effective product.

- HOPE (MTN-025) is designed to determine if a 3-month monitoring schedule is safe (compared to 1-month).
  - Do you agree with this schedule?
  - Should we look at even less frequent visits?
  - How often should women be HIV tested?
  - What kind of schedule is most likely to be put in place once the ring is available?
Question

What kind of schedule of visits for safety monitoring and HIV testing should MTN-025 and IPM 032 evaluate?

Discussion
What kind of visit schedule for safety monitoring and HIV testing should MTN-025 evaluate?

1. I am worried about resistance - women should be HIV-tested monthly even if they are in the group making quarterly clinic visits.

2. This is a new product – that’s why all women should have monthly safety checks.

3. Stick to the current design – 1 vs 3 month – because that makes the most scientific sense. We shouldn’t go too far too fast. We can look at other schedules in demonstration projects.

4. You should look at 6-month intervals because that is more likely to be what happens when rings are made available.
Question #2
Concerns about ARV drug resistance
Concerns about drug resistance

- Resistance is only possible in someone who has HIV, and women who enroll in ASPIRE and who will be eligible for HOPE/MTN-025 are HIV negative.

- In ASPIRE, women are tested monthly for HIV and if a woman tests positive, product is stopped immediately to reduce risk for resistance.

  - If a woman gets infected and continues using the dapivirine ring, she could acquire resistance to the same class of ARVs as dapivirine.

  - Women who acquire HIV are linked to HIV care and closely monitored to understand possible resistance to dapivirine that could possibly affect response to treatment with other NNRTIs, including nevirapine and efavirenz.
Concerns about drug resistance

- Resistance is much more likely to occur in the setting of treatment of HIV.
- Resistance has been rare in prevention trials involving tenofovir-based products.
  - Across 5 trials involving ### participants, there were 143 participants who acquired HIV while using an active product and not one had resistance.
- Studies of the dapivirine ring indicate that very little of the drug gets absorbed into the blood, so resistance is less likely to be a concern than with oral ARVs used for either treatment or prevention.

CAPRISA 004 tested tenofovir vaginal gel while iPrEx, Partners PrEP, TDF2 and the Bangkok Tenofovir Study tested daily use of an ARV tablet (tenofovir or Truvada)
Question

- To what extent do you believe community concerns about resistance will be a challenge in the uptake of the dapivirine ring if it is found to be effective in ASPIRE? How can we address potential concerns and/or fears about resistance?

Discussion
The potential for drug resistance with the dapivirine ring will be a major concern within the community.

1. Strongly agree
2. Agree
3. Don’t know
4. Disagree
5. Strongly disagree
Question #3
Reimbursement of participants
Reimbursement of participants

- Participants in clinical trials are reimbursed, and for each study visit. We’ve heard from some participants that this is an incentive to join the study, and moreover, that they have no intention of using the product.
- Should participants in an open-label trial be compensated in the same way as they would in any other clinical trial, including the “parent” trial?
- Should reimbursement be provided in less monetary terms? (e.g., with food vouchers)

Discussion
How should former participants in ASPIRE be reimbursed for their participation in HOPE (MTN-025)?
How should former ASPIRE participants be reimbursed for participation in HOPE (MTN-025)?

1. As an open-label extension trial HOPE (MTN-025) is still a research study – women should be reimbursed in the same way and with the same amount of money.

2. Participants should receive some money, but the amount should be reduced – everyone is getting access to a product that is known to be effective.

3. They shouldn’t be given anything beyond basic transportation or food vouchers. They already get a lot of free services from the study, not to mention an effective product.
Question #4
Male involvement
Question

- How important is male involvement to the success of the dapivirine ring? What approaches should research teams consider when implementing MTN-025 and/or talking about the open-label trial in the community?

Discussion
Question #5
Demand for the ring
Question

- What value will women place on the ring if they know it’s effective? Will they perceive themselves as needing to use it to be protected? Will this translate into actual use of the ring? Is the ring something that women will want and want to use?

Discussion
Question #6
Studies of ring use during pregnancy
Studies of ring use during pregnancy

- We don’t know about the safety of dapivirine during pregnancy and breastfeeding so women in ASPIRE and must use effective methods of contraception, and if they get pregnant, they must stop using the ring.

- The same will be true in the open-label trials: women who are pregnant or breastfeeding or intend to get pregnant cannot participate; those enrolling must use contraception.

- We will not be able to conduct studies (beginning with Phase I safety) involving pregnant and breastfeeding women until after the ring is known to be effective.
Question

- How high a priority is it to move forward with studies in pregnant and breastfeeding women?

Discussion
Safety studies in pregnant and breastfeeding women should be conducted as soon as possible if the dapivirine ring is found safe and effective in ASPIRE.

1. Strongly agree
2. Agree
3. Don’t know
4. Disagree
5. Strongly disagree
A long-acting vaginal ring that provides both contraception and protection against HIV would appeal to women in Africa.

1. Strongly agree
2. Agree
3. Don’t know
4. Disagree
5. Strongly disagree
Question #7
Where do we go from here?
Where do we go from here?

- FACTS 001 is an ongoing Phase III study testing tenofovir vaginal gel used before and after sex that could result in the gel’s regulatory approval
  - Involves 2,059 women at nine trial sites in South Africa
  - Seeks to replicate results of CAPRISA 004, which found tenofovir gel reduced risk of HIV by 39% compared to placebo gel
  - Results, which are expected early 2015, could lead to regulatory approval of tenofovir gel in South Africa and other African countries
Where do we go from here?

- Results of ASPIRE and The Ring Study could lead to regulatory approval of the dapivirine ring
  - IPM plans to seek approval and licensure for the ring based on the results of The Ring Study and ASPIRE as well as several smaller safety studies
  - Is collaborating with key partners to help ensure the ring is made available to women in developing countries at a low cost and as soon as possible.

- Women here could potentially have two female-controlled HIV prevention methods
  - A gel used before and after sex containing the ARV tenofovir
  - A vaginal ring used monthly containing the ARV dapivirine
Question

- If current trials yield two effective HIV prevention products for women – what then? Do we stop here? Or is this just the beginning? What should be the priorities moving forward?

Discussion
Where do we go from here?

1. We should work only on optimizing rollout and uptake of the two available products – tenofovir gel and the dapivirine ring – and not develop new products.

2. We should not roll out even effective microbicides and should instead focus on developing a vaccine and the rollout and uptake of other effective methods (PrEP, treatment as prevention and circumcision).

3. We know from contraception that choice matters. We should roll out the ring and the gel, but not all women will want a gel or a ring. So, we also need to develop additional delivery options.
What about your questions?
Outstanding Issues?