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## QUESTIONS AND ANSWERS

### MTN-026

#### Phase I Safety and Pharmacokinetic Study of Dapivirine Gel for Rectal Use

##### 1. What is the aim of MTN-026/IPM 038?

MTN-026 is a Phase I study testing whether dapivirine, an antiretroviral (ARV) drug that prevents HIV from replicating, is safe when used as a gel in the rectum. The study will also evaluate the drug concentration in blood, rectal fluid and tissue, and explore the gel's general acceptability. Results of MTN-026 will help determine whether further testing can be conducted on the safety and acceptability of dapivirine gel, and eventually, its effectiveness as a potential [rectal microbicide](#) to prevent HIV through anal sex.

##### 2. Who is conducting and funding the study?

MTN-026 is being led by the [Microbicide Trials Network](#) (MTN), an HIV/AIDS clinical trials network established in 2006 by the National Institute of Allergy and Infectious Diseases (NIAID) with co-funding from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development and the National Institute of Mental Health, all components of the U.S. National Institutes of Health (NIH). The developer of dapivirine gel is the [International Partnership for Microbicides](#) (IPM), a non-profit product development partnership based in Silver Spring, Maryland. The protocol chair for the study is Ross D. Cranston, M.D., F.R.C.P., of the Fight AIDS Foundation in Barcelona, Spain.

##### 3. Why is this study important?

Anal sex is a common behavior that is practiced by people around the world. According to some estimates, the risk of becoming infected with HIV through anal sex is 20 times greater than vaginal sex because the rectal lining, the mucosa, is thinner and much more fragile than the lining of the vagina. In addition, there are far more cells vulnerable to HIV infection just under the lining in the rectum compared to the cervix and vagina.

Condoms are an effective method to prevent HIV infection through anal sex, but many people can't or don't want to use them every time they have sex. Similarly, pre-exposure prophylaxis (PrEP) – an HIV prevention strategy in which people take a pill called Truvada® daily to prevent infection – has been shown to be highly effective, however, not all at risk individuals may be willing or able to access it. Just as there are multiple contraception options for women who choose to prevent pregnancy, a rectal microbicide could give people who practice anal sex an additional choice for HIV prevention.

##### 4. When will the trial begin and how long will it last?

The study will begin in September 2017, with results anticipated in mid-2018.

##### 5. Where will MTN-026 be conducted?

MTN-026 will be conducted at two clinical sites in the United States (Birmingham, Alabama and Pittsburgh, Pennsylvania) and one in Bangkok, Thailand. All are NIAID-funded clinical research sites affiliated with the MTN.

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## **6. What are microbicides?**

Microbicides are products applied inside the vagina or rectum that are intended to protect against HIV acquired through sex. A microbicide can be formulated in many ways, such as a gel, douche or suppository, or as a vaginal ring that releases the active ingredient over time.

## **7. Why are rectal microbicides needed?**

Worldwide, nearly 37 million people are currently living with HIV. Since the epidemic began in the early 1980s, about 78 million people have been infected and 39 million people have died of HIV-related causes. Although the rate of new infections has stabilized in many countries around the world, HIV continues to disproportionately affect racial minorities, gay men and other men who have sex with men, and transgender women.

Just as there are multiple contraception options for women who choose to prevent pregnancy, a rectal microbicide could give people who practice anal sex an additional option for HIV prevention.

## **8. What product is being studied in MTN-026?**

The product being tested in MTN-026 is a gel containing dapivirine (also known as TMC-120), a type of ARV called a non-nucleoside transcriptase inhibitor (NNRTI) that binds to and disables HIV's reverse transcriptase enzyme, a protein that HIV needs to multiply. IPM began developing dapivirine as a microbicide in 2004 through a royalty-free licensing agreement with Janssen Sciences Ireland UC. This license has since been expanded to a worldwide rights agreement.

## **9. What do we know about dapivirine?**

Initially developed as an oral agent to be used in the treatment of HIV, research indicated that dapivirine was well-suited as a microbicide for HIV prevention given its favorable safety profile and physical and chemical properties. Numerous clinical safety studies of dapivirine, formulated as either a vaginal gel or a vaginal ring, have been conducted by IPM and its partners, with results from two Phase III safety and efficacy studies of dapivirine as a vaginal ring – MTN's [ASPIRE](#) study and IPM's [The Ring Study](#) – finding it was safe and helped reduce women's HIV risk. MTN-026 is the first study to assess the safety of dapivirine gel used rectally, and as such, is advancing efforts to develop products to curb the high rate of HIV infections attributed to condomless anal sex.

## **10. How is MTN-026 designed?**

MTN-026 is a Phase I trial designed to evaluate the safety of dapivirine gel used rectally, as well as determine the degree that dapivirine concentrates in the blood, rectal fluid and tissue. The study will enroll HIV-uninfected men and women who will be randomized to receive either dapivirine gel or a placebo (inactive) gel. While in the clinic, participants will use an applicator to insert their assigned gel first as a single dose, and then for 7 consecutive days following a two week break.

Tests and procedures performed as part of the study will determine the clinical safety of the products, and how much drug is absorbed in blood, rectal fluid and tissue. To explore the acceptability of the gel, study participants will be asked about any side effects they may have experienced and their likes and dislikes about the product, gel applicator and administration method.

As part of the study, all participants will receive HIV risk reduction counseling and condoms, and be tested for HIV and sexually transmitted infections.

## **11. How many people will be enrolled into MTN-026?**

Approximately 27 men and women will be enrolled into the study.

## **12. What is being done to ensure the safety of the participants?**

MTN-026 was designed according to stringent ethical and scientific guidelines with numerous measures to

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protect the safety and well-being of participants. As with all NIH-funded studies, the study incorporates a multi-tiered safety review process and is conducted with oversight from regulatory and research authorities. The protocol has undergone rigorous review by NIAID, the U.S. Food and Drug Administration, institutional review boards (IRBs) and in-country regulatory and ethics bodies.

### **13. Will participants in the study provide informed consent?**

Written informed consent will be obtained from each participant prior to screening and enrollment in MTN-026. The process will ensure individuals understand the procedures, as well as possible risks and benefits of the study. Participants will be under no obligation to participate and can leave the study at any time, without consequence.

### **14. What other products are being tested as rectal microbicides?**

In early 2016, MTN researchers reported results from a study called [MTN-017](#), which was the first Phase II study of a rectal microbicide gel containing tenofovir, an ARV commonly used to treat people with HIV in combination with other ARVs. Developed originally as a vaginal microbicide, the gel used in MTN-017 was formulated to contain less glycerin, a common additive found in many gel-like products, to make it more suitable for use in the rectum. Results of MTN-017, which enrolled 195 gay men and other men who have sex with men and transgender women at trial sites in Peru, South Africa, Thailand and the United States, indicated that the gel was safe, with most participants highly adherent to its use. Study participants found the gel most acceptable when used around the time of sex, compared to daily use.

Researchers are also working on the development of products designed specifically for use in the rectum. Two Phase I studies, CHARM-01 and CHARM-02, comparing the safety, acceptability and distribution of three formulations of tenofovir gel – the vaginal formulation, the reduced glycerin formulation and a rectal-specific formulation of tenofovir have been completed. Another recently completed study, CHARM-03, comparing the safety, acceptability and distribution of maraviroc gel to oral maraviroc, is expecting to report results in early 2018. These studies, funded by the NIH, are being led by the Combination HIV Antiretroviral Rectal Microbicide (CHARM) Program based at the University of Pittsburgh.

Other research-based programs, such as DREAM (Delivery of Rectal Enema as Microbicide), which is exploring the delivery of tenofovir as a single dose enema, and PREVENT (Griffithsin-based Rectal Microbicides for PREvention of Viral ENTry), which is addressing the need for a non-ARV based rectal microbicide, are also underway. Both DREAM and PREVENT are funded by the NIH.

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For more information about MTN-026, visit <http://www.mtnstopshiv.org/news/studies/mtn026>. Information about other MTN studies can be found at <http://www.mtnstopshiv.org/news>

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