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BACKGROUND

MTN-026

Phase 1 Safety and Pharmacokinetic Study of Dapivirine Gel for Rectal Use

Summary

- MTN-026 is a Phase I study evaluating whether a gel containing an antiretroviral (ARV) drug called dapivirine is safe for use in the rectum. The study, which will include approximately 27 HIV-uninfected men and women at sites in the United States and Thailand, and will help determine whether further testing on the safety and acceptability of dapivirine gel as a potential rectal microbicide for the prevention of HIV through anal sex can be conducted in a larger population. Results are anticipated in 2018.
- MTN-026 is a study of the [Microbicide Trials Network](#) (MTN), an HIV/AIDS clinical trials network established in 2006 by the National Institute of Allergy and Infectious Diseases 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. Dapivirine gel was developed by the [International Partnership for Microbicides](#) (IPM), a non-profit product development partnership based in Silver Spring, Maryland. Protocol chair for the study is Ross D. Cranston, M.D., F.R.C.P., of the Fight AIDS Foundation, Barcelona, Spain.
- Numerous studies have been conducted on the safety and acceptability of dapivirine as either a vaginal gel or ring. Two Phase III trials ([ASPIRE](#) and [The Ring Study](#)) that evaluated the efficacy and long-term safety of a monthly dapivirine vaginal ring among more than 4,500 women in Africa, found it was safe and helped reduce women's HIV risk. MTN-026 is the first study to evaluate dapivirine as a potential rectal microbicide.
- MTN-026 is part of a research agenda at the MTN focused on the development of HIV prevention products for men and women who engage in condomless anal sex, a major risk factor for HIV infection.

Why this Study is Important

Microbicides are products applied inside the vagina or rectum that are intended to protect against HIV infection acquired through sex. Products currently being tested in clinical trials contain ARV drugs, many of which are commonly used to treat people with HIV. Although the majority of microbicide research has focused on products to prevent HIV infection associated with vaginal sex,

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important strides are being made in research aimed at addressing the need for rectal microbicides.

Anal sex is a common sexual behavior practiced by both men and women around the world. According to some estimates, the risk of becoming infected with HIV during anal sex is 20 times greater than vaginal sex because the rectal lining is thinner and more fragile than the vaginal lining. While condoms are an effective method to prevent HIV infection through anal sex, many people can't or don't want to use them every time they have sex. Similarly, oral 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.

MTN researchers reported results from the first Phase II study of a rectal microbicide, a gel containing the ARV tenofovir, in early 2016. The study, [MTN-017](#), evaluated whether a reduced-glycerin formulation of tenofovir gel was safe and acceptable as a rectal microbicide. Results indicated that the gel used in MTN-017 was safe, with most study participants highly adherent to its use. The gel was found most acceptable when used around the time of sex, compared to daily use.

In addition to reduced-glycerin tenofovir gel, researchers are exploring other ARV-based products as potential candidates for rectal microbicides. A gel containing dapivirine is one such product. Dapivirine was initially developed as an oral agent to be used in the treatment of HIV, however researchers decided it may be better suited as a microbicide for HIV prevention given its favorable safety profile and physical and chemical properties. 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.

How the Study is 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 approximately 27 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, 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.

The Product Being Studied

Dapivirine, also known as TMC-120, is a type of ARV called a non-nucleoside transcriptase inhibitor (NNRTI). NNRTIs bind to and disable HIV's reverse transcriptase enzyme, a protein that HIV needs to make copies of itself. IPM began developing dapivirine as a microbicide in 2004 through a

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royalty-free licensing agreement with Janssen Sciences Ireland UC. This license has since been expanded to a worldwide rights agreement. Numerous clinical safety studies of dapivirine, formulated as either a vaginal gel or ring, have been conducted by IPM and its partners, with results from two Phase III efficacy studies of a vaginal ring containing dapivirine indicating it was safe and helped reduce women's HIV risk.

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About the Microbicide Trials Network

The [Microbicide Trials Network \(MTN\)](http://www.mtnstopshiv.org) is an HIV/AIDS clinical trials network established in 2006 by the National Institute of Allergy and Infectious Diseases 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 National Institutes of Health. Based at Magee-Womens Research Institute and the University of Pittsburgh, the MTN brings together international investigators and community and industry partners whose work is focused on the development and rigorous evaluation of promising microbicides – products applied inside the vagina or rectum that are intended to prevent the sexual transmission of HIV – from the earliest phases of clinical study to large-scale trials that support potential licensure of these products for widespread use. More information about the MTN is available at www.mtnstopshiv.org.

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