MTN researchers begin safety study of a 90-day vaginal ring containing tenofovir

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A vaginal ring designed to protect women against both HIV and herpes simplex virus type 2 (HSV-2) is being tested in a new study that aims to determine whether its use for three months is safe. The Phase I study, known as MTN-038, is being conducted by researchers from the National Institutes of Health-funded Microbicide Trials Network (MTN) at three U.S. trial sites.

No biomedical prevention method currently exists for HSV-2, the most common cause of genital herpes. HSV-2 infection also increases the risk of acquiring HIV, especially among women, who account for nearly half of those living with HIV worldwide.

The vaginal ring being evaluated in the study contains an antiretroviral (ARV) drug called tenofovir, a mainstay drug used in the treatment of HIV. Truvada, a tablet containing both tenofovir and a second ARV, emtricitabine, is approved in many parts of the world for HIV prevention as well—a strategy known as PrEP, or pre-exposure prophylaxis. With PrEP, a person takes Truvada, orally, every day. The ring, however, is meant to remain inside the vagina for 90 days at a time.

MTN-038 is one of two studies evaluating full 90-day use of the tenofovir ring and the first to enroll participants. In earlier studies conducted by CONRAD, a not-for-profit research and development organization that developed the tenofovir vaginal ring, women used the ring on average for approximately 15 days. No safety concerns were observed during these initial studies, which also suggested the ring could deliver enough drug to be protective against both HIV and HSV-2.

The tenofovir ring is not the first tenofovir-based HIV prevention product for women to be tested. A vaginal gel, also developed by CONRAD, underwent extensive testing, including in large-scale trials conducted in Africa, that found tenofovir gel to be safe but not necessarily a product that women in that region would use, either daily or before and after sex.

"No product can be effective if it's not used consistently, and that was a challenge for the women in these studies," commented MTN Principal Investigator Sharon Hillier, Ph.D., professor and vice chair of the department of obstetrics, gynecology and reproductive sciences at the University of Pittsburgh School of Medicine and Magee-Womens Research Institute. "Women need a range of options that will work within the context of their lives—products that they can and are willing to use. Many women, we have learned, say that a longer-acting product, like a vaginal ring, would be an attractive option."

Interestingly, it was while testing tenofovir gel for HIV prevention that researchers learned, unexpectedly, that tenofovir also had activity against HSV-2.

"A product that offers protection against both HIV and HSV-2 could have an important public health impact, but first we need to establish that the tenofovir vaginal ring is safe and acceptable when used for 90 days. We hope to answer these and other key questions in the MTN-038 study so that later-phase effectiveness studies might follow," said Albert Liu, M.D., M.P.H., MTN-038 protocol chair and study director of clinical research at the Bridge HIV Clinical Research Site, San Francisco Department of Public Health, one of the three sites conducting the study.

MTN-038 will enroll approximately 48 healthy, HIV-negative participants who will be randomized to use either the tenofovir vaginal ring or a placebo ring containing no active product for 90 consecutive days, including during menstrual periods. Medical and laboratory tests will be conducted to determine its safety. Other laboratory tests will assess how much active drug is present within the vagina, in

blood (systemically) and elsewhere in the body. Participants will be asked questions about their use of the ring, what they liked or disliked about it and whether using it interfered with sex, for example. The study is expected to take approximately one year to be conducted, with results anticipated mid-2020.

The ring is made of a flexible material for easy insertion and removal. A new ring contains 1.4g of tenofovir. Approximately 10 mg of drug is released each day.

CONRAD is providing both the active tenofovir ring and placebo ring products for the MTN-038 study, as well serving in an advisory capacity, with funding support from the U.S. Agency for International Development (USAID)/U.S. President's Emergency Plan for AIDS Relief (PEPFAR).

"We are delighted to be collaborating with the MTN on this critical study and look forward to its important contributions. In order to increase uptake and adherence, women need combination HIV/HSV prevention products that fit into their lifestyles. We believe the 90-day tenofovir vaginal ring formulation will be much easier and more convenient to use than its vaginal gel counterpart, and hope that through continued clinical development, it becomes a new effective and safe option for women," said Gustavo Doncel, M.D., Ph.D., CONRAD's scientific and executive director.

CONRAD developed the 90-day tenofovir ring in collaboration with the University of Utah and Northwestern University, as well as a second ring containing both tenofovir and the hormonal contraceptive levonorgestrel (LNG) designed to protect against unintended pregnancy in addition to HIV and HSV. Both rings are being evaluated by CONRAD and partners, including the U.S. Centers for Disease Control and Prevention, in an expanded safety and acceptability study taking place in Kenya. CONRAD holds a license to develop tenofovir-based prevention products for women from Gilead Sciences, Inc.

Another vaginal ring product—the monthly dapivirine ring developed by the International Partnership for Microbicides (IPM) - is currently under regulatory review. The MTN conducted several key studies that are included in the dossier of data that IPM is submitting to regulatory authorities. If approved, the dapivirine ring would be the first biomedical HIV prevention method developed specifically for cisgender women. Importantly, it would provide women with another user-controlled option in addition to oral PrEP. In the meantime, MTN is evaluating a 90-day dapivirine ring and a dual-purpose ring containing both dapivirine and LNG. Unlike tenofovir, dapivirine is not active against HSV.

Provided by Microbicide Trials Network