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Researchers launch first-ever phase II safety study of rectal microbicide to prevent HIV

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Taking an important step toward the development of a product to prevent HIV infections associated with unprotected anal sex, researchers today announced the launch of a global Phase II clinical trial of a potential rectal microbicide. The trial, led by the U.S. National Institutes of Health (NIH)-funded Microbicide Trials Network (MTN), is testing the rectal use of a reduced glycerin gel formulation of the antiretroviral drug tenofovir.

"As the HIV epidemic continues to impact people worldwide, we urgently need new ways to prevent sexual transmission of the virus, especially from unprotected anal sex – the highest risk sexual behavior for HIV acquisition," said Ross D. Cranston, M.D., of the University of Pittsburgh School of Medicine, who is leading the study with Javier R. Lama, M.D., M.P.H., of IMPACTA in Lima, Peru. "Rectal microbicides, gel-based antiretroviral products applied into the rectum, are being developed for use by both men and women to help reduce this risk."

Known as MTN-017, the Phase II study will enroll 186 HIV-negative men who have sex with men (MSM) and transgender women in Peru, South Africa, Thailand and the United States, including Puerto Rico, to assess the safety of a reduced glycerin gel formulation of tenofovir, its acceptability to participants, and how much of the drug is absorbed into the body. It is a follow-up trial to an earlier study, MTN-007, which found that the reduced glycerin gel was safe and acceptable to both men and women who used it in the rectum daily for a one-week period.

During MTN-017, study participants will cycle through three study regimens, each lasting eight weeks: reduced glycerin tenofovir gel used daily, reduced glycerin tenofovir gel used before and after anal sex, and daily use of the antiretroviral tablet Truvada® (emtricitabine/tenofovir disoproxil fumarate), developed by Gilead Sciences, Inc. This design will allow researchers to collect information about the gel's safety and acceptability in the rectum, and compare it to the use of oral Truvada, which was approved for use as HIV prevention by the U.S. Food and Drug Administration in 2012. Truvada was approved for the treatment of HIV infection in combination with other antiretrovirals in 2004.

"The results of MTN-017 will be vitally important to the biomedical HIV prevention field," explained Dr. Lama. "They will determine whether we can move ahead with further testing of the gel's effectiveness in preventing the transmission of HIV from unprotected anal sex. We know that rectal microbicides will never replace condoms, but if found safe and effective, they could provide an additional tool to help reduce HIV risk."

Throughout the study, researchers will regularly test participants' blood to assess the presence of drug – a determinant of whether they are using their assigned study products. Testing will be conducted every four weeks and results will then be shared with participants as part of their counseling sessions on product use.

"By monitoring product use as the study is underway, we will have a much better sense of whether participants are adhering to the assigned study regimens," said Ian McGowan, M.D., Ph.D., co-principal investigator of the MTN and professor of medicine, University of Pittsburgh School of Medicine. "The unique design of our study, which does not include a placebo, allows us to address any concerns or issues with adherence in a more real-time fashion, rather than waiting until after the study has concluded."

MTN-017 will be conducted at the following trial sites, pending necessary approvals: In Peru – the IMPACTA Clinical Research Site in Lima; in South Africa – the Desmond Tutu HIV Foundation in Cape Town; in Thailand – the Research Institute for Health Sciences in Chiang Mai and the Thailand MOPH-US CDC Collaboration in Bangkok; and, in the United States – The Fenway Institute in Boston; the University of Pittsburgh; the San Francisco Department of Public Health, and the University of Puerto Rico Maternal-Infant Studies Center in San Juan.

The study is being conducted through the MTN, which is funded by the National Institute of Allergy and Infectious Diseases (NIAID), the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the National Institute of Mental Health, all part of the NIH. The study products are being provided by Gilead Sciences, Inc., of Foster City, Calif., and by CONRAD, of Arlington, Va. Truvada is a registered trademark of Gilead Sciences. In 2006, Gilead assigned a royalty-free license for tenofovir gel to CONRAD and the International Partnership for Microbicides of Silver Spring, Md.

CONRAD developed the reduced glycerin formulation of tenofovir gel being evaluated in MTN-017, which differs from the formulation originally developed for vaginal use. It did so in response to an earlier study called RMP-02/MTN-006, which found that the vaginal gel caused gastrointestinal side effects in some study participants.

The vaginal formulation of tenofovir gel continues to be evaluated for preventing the transmission of HIV through vaginal sex in women. Ongoing is a Phase III trial called FACTS 001 that is testing its use before and after sex among women in South Africa, with results expected in 2015. FACTS 001 hopes to replicate the results of CAPRISA 004, which found this regimen reduced the risk of HIV by 39 percent compared to placebo gel. The VOICE Study (Vaginal and Oral Interventions to Control the Epidemic), however, found daily use of the

gel not effective among its study participants; most of the women did not use the product daily as recommended.

Provided by Microbicide Trials Network