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Reduced Glycerin Formulation of Tenofovir Vaginal Gel Safe for Rectal Use

Reformulated gel could serve as an anti-HIV product for both vagina and rectum

PITTSBURGH, May 17, 2012 – A change in the formulation of tenofovir gel, an anti-HIV gel developed for vaginal use, may make it safer to use in the rectum, suggests a study published online this week in the Journal of Antimicrobial Chemotherapy. In laboratory tests of rectal tissue, researchers from the Microbicide Trials Network (MTN) found that the reformulated gel was less harmful to the lining of the rectum than the original vaginal formulation, and just as effective in protecting cells against HIV.

"The lining of the rectum is much more fragile than the vaginal epithelium, so we can't be certain a product like tenofovir gel that is safe for vaginal use will be completely safe to use in the rectum," said lead study author Charlene Dezzutti, Ph.D., associate professor of obstetrics, gynecology and reproductive sciences at the University of Pittsburgh School of Medicine and principal investigator of the MTN Network Laboratory. "We are very encouraged by our laboratory data that suggest the reformulated gel could be safer for rectal use, and serve as a dual compartment gel for use in both the vagina and rectum."

Tenofovir gel has shown some promise in reducing HIV risk in women through vaginal sex. But because the rectal epithelium – the lining of the rectum that serves as the first line of defense against HIV – is much thinner than the vaginal lining, the gel may not be safe or effective to use rectally. By its nature, tenofovir gel is hyperosmolar – contains a higher concentration of sugars and salts relative to cells. This quality could have a harmful effect on the rectal lining by causing epithelial cells to shrink as they purge water to achieve balance. Weakened in this manner, the rectal epithelium may be less able to protect against HIV.

To make tenofovir gel safe and more amenable to rectal use, researchers from CONRAD, a research organization which holds the rights to develop the gel, reformulated it with a reduced amount of glycerin, a common additive found in many gel-like products. In laboratory tests conducted by MTN researchers, the reformulated gel was three times less likely to cause cells in rectal tissue to release water, and equally effective against HIV as the vaginal formulation.

Data from an early phase clinical trial of the reduced glycerin gel presented in March 2012 at the 19th Conference on Retroviruses and Opportunistic Infections (CROI), suggested it was safe and acceptable in 65 HIV-negative men and women who used it rectally once a day for one week. Results from this study, called MTN-007, and future studies will have important implications for the development of a rectal microbicide that could help protect against HIV or other sexually transmitted infections during anal sex.

As follow-up to MTN-007, researchers are now planning a Phase II, multi-site trial called MTN-017 that will involve 186 men who have sex with men, and transgender women at clinical sites in Peru, South

Africa, Thailand, and the U.S. Participants will cycle through three study regimens: reduced glycerin tenofovir gel used daily, reduced glycerin tenofovir gel used before and after anal sex, and daily use of the antiretroviral tablet Truvada®. MTN-017 will allow researchers to collect additional information about the gel's safety and acceptability in the rectum, and compare it to the use of Truvada.

In addition to Dr. Dezzutti, other authors of the study are Lisa Rohan, Ph.D., University of Pittsburgh; Lin Wang, M.D., Ph.D., Magee-Womens Research Institute ; Kevin Uranker, Magee-Womens Research Institute; Cory Shetler, Magee-Womens Research Institute; Marilyn Cost, Magee-Womens Research Institute; J.D. Lynam, Magee-Womens Research Institute; and David Friend, Ph.D., CONRAD, Arlington, Va.

Tenofovir gel contains the antiretroviral tenofovir, which is commonly used in the treatment of HIV. The vaginal formulation of tenofovir gel was found safe and effective in reducing the risk of HIV in women who used it before and after vaginal sex in a study called CAPRISA 004. More recently, however, MTN researchers conducting the VOICE Study closed the tenofovir gel arm of the trial after a routine review of study data determined that the gel, while safe, was not effective in preventing HIV among the women in that study group, who were asked to apply it vaginally every day. In the meantime, a Phase III trial called FACTS 001 is currently evaluating the vaginal formulation of tenofovir gel using the same regimen as CAPRISA 004, with results expected in 2014.

Both the oral and vaginal formulations of tenofovir were developed by Gilead Sciences, Inc., of Foster City, Calif. In 2006, Gilead Sciences assigned the rights for tenofovir gel to CONRAD, of Arlington, Va. and the International Partnership for Microbicides of Silver Spring, Md.

The study was conducted through the MTN, which is funded by the National Institute of Allergy and Infectious Diseases Division of AIDS with co-funding from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development and the National Institute of Mental Health.

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About the Microbicide Trials Network

The Microbicide Trials Network (MTN) 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 U.S. 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 who are devoted to preventing or reducing the sexual transmission of HIV through the development and evaluation of products applied topically to mucosal surfaces or administered orally.

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