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Bottoms Are Up at the HIV Research for Prevention Virtual Conference

Rectal microbicide gels well-tolerated, with dosing changes necessary for HIV protection

PITTSBURGH, 2 February, 2021 – Researchers seeking to develop on-demand and behaviorally congruent HIV prevention options for people who practice anal sex are reporting the results of three early phase clinical trials of rectal microbicides at this week's HIV Research for Prevention (HIV R4P) Virtual Conference. The Phase I studies, led by the U.S. National Institutes of Health (NIH)-funded Microbicide Trials Network (MTN), found both of the gel-based products well-tolerated, with higher doses of the active drugs likely required to provide protection from HIV and other sexually transmitted infections (STIs). The results are being presented at the oral abstract session, *Bottoms Up: New insights about rectal infections and HIV/STI prevention*, on Wednesday, Feb. 3.

Rectal microbicides are topical products being developed and tested to reduce a person's risk of HIV and other STIs from anal sex. On-demand products refer to those that could be used around the time of sex, while behaviorally congruent rectal microbicides deliver anti-HIV drugs via products people may be already using as part of their sex routine. Researchers are interested in exploring these products as possible alternatives to systemic pre-exposure prophylaxis, or PrEP.

"It's naïve to believe that oral products and other systemic delivery methods for PrEP will work for everyone," said Craig Hendrix, M.D., professor, Johns Hopkins University School of Medicine, who heads rectal microbicide research at the MTN. "There are some people who only want HIV prevention on-demand. They don't want drug in their body when they don't need it there. There are others who would like to have something that's behaviorally congruent, like a lube or a douche they're already using, but with a protective anti-HIV medication added. It's a matter of finding something that meets individual needs so that we can cover more people with products that work best for them."

The MTN-026 study, being presented by Craig Hoesley, M.D., professor, University of Alabama at Birmingham, evaluated the rectal safety of a gel containing 0.05 percent of the antiretroviral (ARV) drug dapivirine, as well as the levels of drug detected in blood, rectal fluid and rectal tissue after use. The gel formulation of dapivirine was originally developed for vaginal administration by the non-profit International Partnership for Microbicides (IPM), who also developed the monthly dapivirine vaginal ring that is advancing toward potential regulatory approvals for use by cisgender women to prevent HIV transmission. The MTN-026 study enrolled 27 HIV-negative cisgender and transgender men and women at sites in Thailand and the United States who were randomized to receive either dapivirine gel or a placebo (inactive) gel. While in the clinic, participants used an applicator to insert their assigned gel, first as a single dose, and then for seven consecutive

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days following a two-week break. Study results showed that the gel was well-tolerated and acceptable to participants, with tissue concentrations suggesting a longer-acting formulation or a higher-dose gel would be required to provide effective protection from HIV transmission through anal sex.

A second study of dapivirine gel used as a rectal microbicide, MTN-033, being presented by Ken Ho, M.D., M.P.H., assistant professor, University of Pittsburgh School of Medicine, explored the safety and drug levels of the 0.05 percent dapivirine gel administered rectally with an applicator versus a lubricant (without an applicator) through anal sex with a simulated phallus. Given that using lube is a common practice during anal sex, researchers were interested in whether enough dapivirine could be delivered in this behaviorally congruent way to protect against HIV. The study, conducted at one clinical site in the United States with 16 HIV-negative cisgender men who have sex with men, found that after delivery of dapivirine gel as a rectal lube, drug levels in blood were a third of the levels observed after delivery with an applicator, which was more than expected based on prior studies of lube-based rectal gels. However, dapivirine did not remain in tissue long enough to provide sustained protection. Even so, researchers are encouraged by these results because they support the possibility of a medicated lube as a promising behaviorally congruent strategy for prevention of HIV transmission from anal sex.

The final rectal microbicide study, MTN-037, also being presented by Dr. Ho, evaluated the safety of a microbicide gel called PC-1005 for use in the rectum. Developed by the Population Council, PC-1005 is a multipurpose prevention technology gel that contains 0.002 percent MIV-150 (a potent ARV), 0.3 percent zinc acetate dihydrate (an anti-herpes simplex virus type 2, or HSV-2, agent) and 3 percent carrageenan (a potent anti-HIV agent and gellant). In laboratory and animal studies, PC-1005 was shown to be active against several STIs, including HIV, human papillomavirus (HPV) and HSV-2. MTN-037, which included 12 HIV-negative cisgender men and women at two sites in the United States, found that the gel was safe and well-tolerated with low systemic MIV-150 exposure. Through tissue sampling, researchers also concluded that a longer-acting formulation or higher dose of MIV-150 would be required to deliver an adequate amount of the drug for it to be effective at preventing the rectal transmission of HIV.

“Taken together, these studies show us that these drugs can be dosed rectally, including as an anal lube, get into the rectal tissue, and also provide evidence of virus suppression,” concluded Dr. Hendrix. “As first in human trials, they represent a good starting point for optimizing the product formulations. We’ll need some changes to make products like these viable, but they provide proof of principle that we can deliver an on-demand drug rectally.”

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These studies will be presented on Wednesday, Feb. 3, starting at 17:30 UTC (12:30 pm ET) during Oral Abstract Session 16 – “Bottoms Up: New insights about rectal infections and HIV/STI prevention.”

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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 whose work is focused on the 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 http://www.mtnstopshiv.org.