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TRIAL FINDS MICROBICIDE PROMISING AS HIV PREVENTION METHOD FOR WOMEN

MONTREAL, Feb. 9, 2009 -- A clinical trial involving more than 3,000 women in southern Africa and the United States has demonstrated for the first time the promise of a vaginal microbicide gel for preventing HIV infection in women. According to findings presented today at the Conference on Retroviruses and Opportunistic Infections (CROI), PRO 2000 gel (0.5 percent dose) was 30 percent effective. While encouraged by the results, the researchers who conducted the study, known as HPTN 035, say that additional evidence is needed to determine more definitively the effectiveness of PRO 2000.

“These findings provide the first signal that a microbicide gel may be able to prevent women from HIV infection. Indeed, for the millions women at risk for HIV, especially young women in Africa, there is now a glimmer of hope. But these findings also indicate that more research is needed; we can’t yet say that we have an effective microbicide,” said Salim S. Abdool Karim, MBChB, Ph.D., pro vice-chancellor (research) at the University of KwaZulu-Natal in Durban, South Africa, and director the Center for the AIDS Program of Research in South Africa, who led the multi-center study for the U.S. -based Microbicide Trials Network (MTN).

Microbicides are substances intended to reduce or prevent the sexual transmission of HIV and other sexually transmitted infections when applied topically inside of the vagina or rectum. A microbicide can be formulated in many ways, such as a gel or cream or in a vaginal ring. Several candidate microbicides are being tested in clinical trials, although none is yet approved or available for use. Earlier trials have yielded disappointing results or were stopped prematurely.

Currently, women comprise half of all people worldwide living with HIV. In sub-Saharan Africa, women represent nearly 60 percent of adults living with HIV, and in several southern African countries young women are at least three times more likely to be HIV-positive than young men. In most cases, women become infected with HIV through sexual intercourse with an infected male partner. Although correct and consistent use of male condoms has been shown to prevent HIV infection, women often cannot negotiate condom use with their male partners. An effective microbicide could provide women with an HIV prevention method they initiate.

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HPTN 035 evaluated the safety and effectiveness of two candidate microbicides for preventing male-to-female sexual transmission of HIV: BufferGel[®], developed by ReProtect Inc., in Baltimore, Maryland, U.S.A.; and PRO 2000 (0.5 percent dose), developed by Indevus Pharmaceuticals, Inc., in Lexington, Massachusetts, U.S.A. The study was conducted between February 2005 and September 2008 and involved 3,099 women at six sites in Africa and one in the United States. In Africa, the sites were located in Durban and Hlabisa, KwaZulu-Natal, South Africa; Harare, Zimbabwe; Lusaka, Zambia; Blantyre, Malawi; and Lilongwe, Malawi. The U.S. site was in Philadelphia.

Women in the study were randomly assigned in approximately equal numbers to one of four groups: those who used BufferGel prior to engaging in sexual intercourse; those who used PRO 2000 before each sex act; those who used placebo gel (with no active ingredient) prior to sexual activity; and those who used no gel. Women took part in the study for an average of 20 months and were evaluated monthly. All participants received detailed information about the possible risks and benefits of trial participation prior to enrollment and were monitored closely throughout the study. In addition, all participants were counseled on safe sex practices, provided with condoms, and tested and treated for sexually transmitted infections throughout the study.

During the course of the study, 194 women acquired HIV. Of this total, 36 HIV infections occurred among participants who used PRO 2000, while 54 infections occurred among participants who used BufferGel, 51 infections occurred among participants who used placebo gel, and 53 infections occurred among participants who used no gel. Using these data as a basis for determining the effectiveness of the two candidate microbicides, the researchers found that BufferGel had no effect on HIV infection and that PRO 2000 had a 30 percent level of effectiveness in preventing HIV infection. Both gels were found to be safe.

Past microbicides trials raised the possibility that the placebo gel may also have some effect on HIV. The finding in the HPTN 035 trial that the number of HIV infections in the two control arms – placebo gel and no gel – was similar provides useful evidence that the placebo gel has no impact on HIV infection, reported Dr. Abdool Karim.

Relatively few participants dropped out of the study. In fact, 94 percent completed study visits through the follow-up period until study exit. According to the study's results, participants in the three gel groups reported use of the gels in 81 percent of sex acts, and nearly all (99 percent) said they would use the products if approved for HIV prevention. Importantly, women in all three gel groups reported using condoms 72 percent of the time during sex, and women in the no-gel group reported using condoms 81 percent of the time.

Study participants are being informed of the findings and counseled on the continued need to follow safe sex practices in order to avoid possible HIV exposure.

"I am humbled by the dedication and commitment of the women who participate in microbicide studies, but I am particularly impressed by and grateful to the women who took part in HPTN 035. We have reached an important milestone in HIV prevention research, and these women deserve credit for the success of

the study,” commented Sharon Hillier, Ph.D., vice chairman and professor, department of obstetrics and gynecology and reproductive sciences at the University of Pittsburgh School of Medicine, and MTN principal investigator.

HPTN 035 was conducted by African and U.S. researchers affiliated with the MTN, an HIV/AIDS clinical trials network established and funded in 2006 by the National Institute of Allergy and Infectious Diseases (NIAID) with co-funding by 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. Prior to the establishment of the MTN in 2006, the study was led by the NIAID-funded HIV Prevention Trials Network (HPTN), from which the study gets its name.

The study was the first trial to evaluate two gels, each with different mechanisms of action. BufferGel was thought to work by boosting the natural acidity of the vagina in the presence of seminal fluid, which can help to inactivate HIV and other pathogens. PRO 2000 was designed to prevent HIV from attaching to the cells in the genital tract.

PRO 2000 is being tested in another clinical study sponsored by the Medical Research Council and the Department for International Development of the United Kingdom. The trial, known as MDP 301, has completed enrollment of 9,395 women at clinics in South Africa, Tanzania, Uganda, and Zambia and is expected to report results by the end of 2009.

HPTN 035 was funded by NIAID. Indevus Pharmaceuticals, Inc. provided PRO 2000 and ReProtect, Inc. provided BufferGel. The U.S. Agency for International Development (USAID) provided funding to manufacture BufferGel for the study.

In addition to Dr. Abdool Karim, other authors of the study presented at CROI are: Anne S. Coletti, M.S., Family Health International, Research Triangle Park, N.C.; Barbra Richardson, Ph.D., and Benoit Mâsse, Ph.D., University of Washington, Seattle, Wa.; Gita Ramjee, Ph.D., South African Medical research Council, Durban, South Africa; Irving Hoffman, PA, M.P.H., University of North Carolina School of Medicine; Mike Chirenje, MBChB, University of Zimbabwe; Taha Taha, M.D., Johns Hopkins University Bloomberg School of Public Health; Muzala Kapina, MBChB, Centre for Infectious Disease Research in Zambia; Lisa Maslankowski, M.D., University of Pennsylvania; Estelle Piwowar-Manning, Johns Hopkins University; and Lydia Soto-Torres, M.D., M.P.H., NIAID, Division of AIDS.

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For more information about the HPTN 035 clinical study, see <http://www3.niaid.nih.gov/> or <http://www.mtnstopshiv.org/news/studies/17>.

About the MTN

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 reducing the sexual transmission of HIV through the development and evaluation of products applied topically to mucosal surfaces or administered orally.