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NIH discontinues tenofovir vaginal gel in 'VOICE' HIV prevention study

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A large-scale clinical trial evaluating whether daily use of an antiretroviral-containing oral tablet or vaginal gel can prevent HIV infection in women is being modified because an interim review found that the gel, an investigational microbicide, was not effective among study participants.

On Nov. 17, an independent data and safety monitoring board (DSMB) recommended that the Vaginal and Oral Interventions to Control the Epidemic (VOICE) study evaluating daily use 1 percent tenofovir vaginal gel be discontinued because there was no difference in effect demonstrated between the drug-containing gel and a placebo gel. The DSMB found a 6 percent HIV incidence rate among participants in the tenofovir gel group and the placebo gel group.

The study is being conducted by the National Institutes of Health (NIH)-funded Microbicide Trials Network (MTN). As the trial's primary sponsor, the National Institute of Allergy and Infectious Diseases (NIAID), part of NIH, concurred with the DSMB's recommendation and has requested that the MTN discontinue use of tenofovir gel (and placebo gel) in the VOICE study. Because the trial is continuing, all other study data remain confidential, so NIAID cannot speculate about why tenofovir gel showed no benefit among VOICE study participants. Factors that may have contributed to this outcome are being further investigated.

Importantly, the DSMB found no major safety concerns with either the

tenofovir gel or oral tablets containing tenofovir and emtricitabine given to women in a different arm of the study. Oral tenofovir and emtricitabine, a combination drug called Truvada that currently is used to treat HIV infection, will continue to be investigated in the VOICE study to determine whether it can prevent HIV infection in women in this trial.

The VOICE study, or MTN-003, began in September 2009 and originally enrolled more than 5,000 HIV-uninfected women in South Africa, Uganda and Zimbabwe. The trial was designed to test the safety, effectiveness and acceptability of two different, daily HIV prevention strategies. One was an investigational microbicide gel containing tenofovir. The other involved oral tablets containing tenofovir either alone (Viread) or co-formulated with the drug emtricitabine (Truvada). The tablets were designed to be taken by HIV-negative women in an approach known as pre-exposure prophylaxis, or PrEP.

The study was first modified in September 2011, following the DSMB recommendation to discontinue evaluating oral tenofovir tablets based on interim data demonstrating that the study would be unable to show a difference in effect between tenofovir tablets and placebo tablets in preventing HIV infection. No safety concerns with oral tenofovir were found. Since that time, the study participants who were taking oral tenofovir have been informed of the discontinuation of this arm of the trial, and currently they are undergoing their final study-associated tests and procedures.

Based on its Nov. 17 scheduled review, the DSMB recommended that the roughly 2,000 women in the tenofovir gel and placebo gel groups stop applying the study product.

The study team will immediately begin informing all VOICE participants of this new development and will soon start the orderly

discontinuation of the two gel arms of the trial. Participants who were using the tenofovir gel or the placebo gel will stop using the product at their next scheduled clinical site visit. They will then return eight weeks later for a final evaluation before exiting the study. At that visit, they will be given information about where they can continue to receive HIV testing and counseling, contraception and other medical and support services. Follow up for all of the VOICE study participants is expected to be completed in June 2012, with final study results anticipated in early 2013.

Although it is disappointing that the study first found oral tenofovir and now daily 1 percent tenofovir gel to be ineffective among the VOICE participants, NIAID recognizes the scientific importance of having clear outcomes and is pleased that the trial will continue to examine the question of whether oral Truvada is a safe and effective HIV prevention measure for women in this study. NIAID thanks all VOICE study participants and site staff for their significant contribution to furthering HIV prevention research. This study is an important component of NIH's comprehensive HIV prevention research program articulated in the HHS National HIV/AIDS Strategy Operational Plan.

NIAID remains committed to supporting research to develop HIV prevention tools that women can implement. Slightly more than half of all new HIV infections globally occur in women, mostly through unprotected sex with HIV-infected men. Safe and effective female-controlled HIV prevention methods would be particularly helpful to women who find it difficult or impossible to refuse sex or to negotiate condom use with their male partners.

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