Tenofovir Vaginal Gel Delivers HIV Prevention

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FROM THE 18TH INTERNATIONAL AIDS CONFERENCE

VIENNA — The unqualified success of tenofovir vaginal gel in cutting the spread of HIV infection in a randomized, 3-year study of more than 800 women produced heady excitement at the conference, as well as sober recognition that the gel needs more testing and is likely at least 3 years away from a marketed product.

After 30 months, the 422 women who completed the study in the tenofovir gel

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group had a 39% relative cut in their rate of new HIV infections, compared with the 421 completers in the placebo arm. The infection rate curves began to diverge within the first 6 months of the study and then continued to separate. Among the 38% of women who used the gel during more than 80% of their events, the active gel cut the HIV infection rate by a relative 54%. Concurrently with the meeting report, the results appeared in an article online (Science 2010;doi:10.1126/science.1193748).

Starting with the researchers who ran the Center for the AIDS Program of Research in South Africa (CAPRISA) 004 trial, a series of experts acknowledged tenofovir gel's performance as a major advance, but just one step in a process.

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DR. Q.A. KARIM

"The CAPRISA 004 study is the first step. Additional studies are urgently needed to confirm and extend the findings," said Dr. Salim S. Abdool Karim, director of CAPRISA in Congella, South Africa, and a professor of clinical epidemiology at Columbia University, New York, who presented the results.

"This is the first step, but it was not a licensing trial," said Quarraisha Abdool Karim, Ph.D., associate director of CAPRISA and an epidemiologist at Columbia, who ran the study with her husband and reported the results along with him.

"It is exciting, and we all felt that in the room today," said Sheena McCormack, a clinical epidemiologist with the Medical Research Council in London. noting that the report triggered eruptions of applause and a final standing ovation from a packed, lunchtime hall of several thousand people. "It's proof of concept of microbicides" as a viable way to interrupt HIV transmission, and proof of concept of an antiretroviral drug for prophylaxis. "But it is not ready to roll out globally. Five other prophylaxis effectiveness trials are in process. This is a step in the right direction, but just one step in the path." Ms. McCormack said.

"The CAPRISA 004 study is an exciting scientific achievement that moves us one step forward to gaining another effective tool to prevent HIV infection," said Dr. Anthony S. Fauci, director of the National Institute of Allergy and Infectious Diseases in Bethesda, Md.

It was actually a highly successful first step along two different paths. Not only did the results show a significant cut in the HIV incidence rate from 9 cases per 100 women-years with placebo to 6 cases per 100 women-years with use of tenofovir gel before and after sex, but the regimen also cut the transmission rate of herpes simplex virus type-2 (HSV2) in half.

The apparently completely independent ability of tenofovir gel to block HSV2 transmission "is a major bonus," commented Tim Farley, Ph.D., a statistician in the department of reproductive

health and research for the World Health Organization in Geneva. "It will be relatively easy to confirm in a non-HIV infected population. I wouldn't be surprised if getting the HSV2 indication goes faster because it's easier to do; HSV2 is not life threatening."

CAPRISA 004, a proof-of-concept trial, ran at two South African clinic locations: a rural site in the KwaZulu-Natal Midlands, and an urban site in Durban. The researchers randomized 889 eligible women, all HIV negative and sexually active. Participants applied either a 1% tenofovir vaginal gel or placebo gel once up to 12 hours before sex, and then a second time within 12 hours following sex. People in the region where the study took place have a low rate (less than 1%) of anal sex.

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The prespecified HSV2 analysis focused on women in the study who were HSV2 negative at baseline, 202 who completed the tenofovir arm and 224 who completed the placebo arm. Other marketed drugs similar in class to tenofovir, such as cidofovir and adefovir, have activity against HSV, so it was worth checking if tenofovir gel did too, said Dr. Salim S. Abdool Karim. The active gel cut new HSV2 infections by a relative 51% over 30 months, compared with placebo. The analysis showed that the tenofovir gel blocked the HIV and HSV2 infections "by two independent mechanisms. We see protection against HSV2 in women who were HIV negative and in HIV positives," he said.

The study also showed no sign of tenofovir resistance in women who became infected despite use of the drug, a benign adverse effect profile, no safety issues in pregnancy, and no increase in HIV risk behavior. During the study, all women received regular counseling that reinforced the need for condom use whenever possible. The purpose of the gel was to give women protection when a condom wasn't used. ■