
Backgrounder

CAPRISA 004 Trial to Assess the Effectiveness and Safety of 1% Tenofovir Gel in Preventing HIV Infection

The CAPRISA 004 trial to assess the effectiveness and safety of a vaginal gel containing the antiretroviral drug tenofovir for the prevention of HIV infection in women in South Africa has been completed. Scientists are analyzing the data, and results will be presented at the XVIIIth International AIDS Conference in Vienna, Austria, on Tuesday, July 20, 2010.

The trial is being conducted by a consortium that includes the Centre for the AIDS Programme of Research in South Africa (CAPRISA) at the University of KwaZulu-Natal (UKZN) in Durban, FHI, North Carolina, USA, and CONRAD, Virginia, USA. It is funded by the United States Agency for International Development (USAID) and TIA, a biotechnology agency of the South African government's Department of Science and Technology. In addition, Gilead Sciences provided tenofovir for the manufacture of the gel used in the study. Tenofovir gel is a candidate microbicide—a substance that could be applied topically to reduce the risk of acquiring HIV and potentially other sexually transmitted infections (STIs).

About half of all the people living with HIV are women. In Africa, about 60 percent of new HIV infections are acquired by women and girls. Correct and consistent use of male condoms has been shown to prevent HIV infection, but women are often unable to negotiate condom use with their male partners. The CAPRISA 004 study is part of a global effort to develop an HIV prevention method that women can initiate themselves. If proven effective, such a method could be an important addition to current methods of HIV prevention.

Tenofovir is an antiretroviral drug that prevents HIV from growing (replicating) inside cells. It has been tested in thousands of HIV-infected individuals and is approved as an HIV treatment by a number of regulatory agencies. As a result, the drug is now used in a tablet form, in combination with other antiretrovirals, to treat HIV in many countries. Studies in animals have shown that the topical use of tenofovir gel can prevent transmission of a virus that is similar to HIV, but this effect has yet to be shown in humans.

The CAPRISA 004 study was designed according to the most rigorous international ethical standards. It was reviewed and approved by the UKZN's Biomedical Research Ethics Committee and by an independent ethics committee convened by FHI. In addition, data on safety, enrollment, and efficacy were reviewed at pre-defined intervals by an independent Data Safety and Monitoring Board (DSMB). The study has been conducted under the oversight of the South African Medicines Control Council.

The CAPRISA 004 study involved 889 South African women (ages 18 to 40 years) who were HIV-negative, sexually active, and at high risk of becoming infected with HIV. About half of the women were given vaginal applicators containing a 1% concentration of tenofovir gel, and half were given applicators filled with a placebo gel that looks identical to the study gel but does not contain tenofovir. Neither researchers nor participants knew an individual's gel assignment.

Each participant was asked to insert a first dose of the assigned study gel within 12 hours before sexual intercourse and to insert a second dose as soon as possible within 12 hours after intercourse, using only two doses over 24 hours regardless of the frequency of intercourse.

At monthly visits, participants reported their use of the gel and whether they had experienced any side effects. Because the safety of tenofovir gel use during pregnancy is unknown, the women were tested monthly for pregnancy and were taken off the product if they became pregnant. Participants received free condoms, treatment for STIs, and regular counseling on how to prevent HIV and STIs—measures that constitute the widely accepted standard for HIV prevention services.

In addition to determining the effectiveness of tenofovir gel against HIV, CAPRISA 004 will also assess the gel's safety when it is used for substantially longer periods of time (up to 2.5 years) than it has been used in previous clinical safety studies. Tenofovir resistance and its potential effects on an individual's viral levels will be assessed among women who acquired HIV during the trial.

Women found to be HIV positive during the screening process in the study, or who acquired an HIV infection during the study, were counseled and referred to the best care and support services available in their communities, including CAPRISA treatment and research programs.

If tenofovir gel is proven to be safe and effective in preventing HIV infections in this trial, confirmatory studies involving more women will likely be required before the product could undergo an approval process by the relevant drug regulatory authorities, such as the South African Medicines Control Council.

CAPRISA (www.caprisa.org) is a multi-institutional AIDS research organization, with its headquarters at the University of KwaZulu-Natal in Durban, South Africa. CAPRISA is a designated UNAIDS Collaborating Centre for HIV Prevention Research. The main goal of CAPRISA is to undertake globally relevant and locally responsive research that contributes to understanding HIV pathogenesis, prevention and epidemiology, as well as the links between tuberculosis and AIDS care. CAPRISA comprises four research programmes: HIV pathogenesis & vaccines, HIV and TB treatment, Microbicides, and HIV prevention and epidemiology. For more information, go to www.caprisa.org.

FHI (www.fhi.org) is a global health and development organization whose rigorous, science-based approach builds programs that create lasting change. Founded in 1971, FHI maintains offices and staff worldwide, helping to forge strong local relationships that enable us to make measurable progress against disease, poverty, and inequity—improving lives for millions. For more information, please contact: Beth Robinson, Deputy Director, Knowledge Management, FHI, PO Box 13950, Research Triangle Park, NC 27709 USA email: brobinson@fhi.org.

CONRAD (www.conrad.org) was established in 1986 and is a Division of the Department of Obstetrics and Gynecology at Eastern Virginia Medical School (EVMS) in Norfolk, VA, where it has laboratories and a clinical research center. The main office is located in Arlington, VA with additional offices in West Chester, PA and collaborators around the world. CONRAD is committed to improving reproductive health by expanding the contraceptive choices of women and men and by helping to prevent the transmission of HIV/AIDS and other sexually transmitted diseases.

Technology Innovation Agency, formerly known as **LIFElab** (www.tia.org.za) is the trade name of the (South African) East Coast Biotechnology (ECoBio) Regional Innovation Centre. TIA provides funding to

biotechnology projects which focus on human health and bioprocessing. The specific focus of the human health portfolio is infectious diseases such as HIV/AIDS, TB and malaria.

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