

## Sample External Questions and Answers (Q&A)



### Questions and Answers

August 10, 2006

#### **Family Health International Study of Daily Oral Tenofovir to Prevent HIV among Women at High Risk of Infection**

##### **What is tenofovir?**

Tenofovir is an anti-HIV drug that works by inhibiting an important enzyme in the HIV life cycle, called nucleotide reverse transcriptase. In HIV-infected individuals, tenofovir stops HIV from invading cells that have not yet been infected with the virus. It is taken in the form of a pill, it is long lasting, it has relatively few side effects, and most strains of HIV are slow to develop resistance to it. Tenofovir is approved by regulatory agencies and already used in many countries as part of a drug combination to treat HIV. Studies in monkeys have also shown that it can prevent transmission of a virus that is similar to HIV, but it is not yet known if it can prevent HIV transmission in humans. Tenofovir is manufactured and was provided free of charge for the study by Gilead Sciences, located in Foster City, California.

##### **What was this study testing?**

This clinical trial was conducted in three African countries to study daily oral tenofovir for the prevention of HIV among heterosexual women at high risk of infection. To do so, participants were randomized to receive either tenofovir or a placebo once a day for the duration of the trial. All participants also received HIV risk-reduction counseling, condoms, and treatment for sexually transmitted infections as medically indicated during monthly clinic visits throughout the trial.

##### **Why was this study important?**

Current HIV prevention programs stress abstinence, being faithful to uninfected partners, and—if neither is possible—using condoms. Despite knowledge of these prevention strategies, an estimated 11,000 people become infected with HIV each day. Moreover, many sexually active individuals, especially women, have difficulty ensuring faithfulness or negotiating condom use in their relationships, and additional prevention strategies are needed. If effective, tenofovir could be a promising addition to condoms because it is taken orally and would provide a constant level of protection against HIV, regardless of the timing of intercourse.

##### **Who conducted the study?**

Family Health International, a non-profit research and service organization based in Research Triangle Park, North Carolina, managed the trial and was responsible for all aspects of the study. Local staff from the study sites in Africa served as the research investigators. The research was supported by a grant awarded to Family Health International in 2002 by the Bill & Melinda Gates Foundation.

##### **Where did the study take place?**

The study was conducted in the three African cities of Douala, Cameroon; Ibadan, Nigeria; and Tema, Ghana. These sites were selected because their populations have high rates of HIV infection, which is an important factor for determining the effectiveness of possible HIV prevention drugs. If tenofovir is shown to be safe and

effective, HIV prevention programs that provide tenofovir can be established at these sites, so that women at risk for HIV can be reached and can benefit from this intervention.

### **Who participated in the study?**

Nine hundred thirty-six heterosexual, HIV-negative women were included in the study. Four hundred were from Ghana, 400 from Cameroon, and 136 from Nigeria. To be eligible, all volunteers had to be sexually active HIV-uninfected women between ages 18 and 35 years.

### **How were participants evaluated throughout the study?**

Participants were tested for HIV at a screening visit, an enrollment visit, and once a month during follow-up. With each HIV test, pre-test and post-test HIV prevention counseling was also provided. Side effects and any reported changes in health, whether considered by the study investigators to be potentially related to the study drug or not, were evaluated, treated if necessary, and recorded each month. In addition, liver function and kidney function were evaluated every three months to identify other possible reactions to the drug.

### **What precautions were taken to help participants prevent HIV?**

Women were counseled monthly on safer sexual practices such as reducing their number of sexual partners and using condoms during every sexual act. Male condoms were also provided to them. In past prevention trials, these services have been proven to reduce the risk of HIV among participants. For example, results of a microbicide trial conducted by Family Health International in Cameroon, which used similar HIV prevention strategies, showed a 50 percent lower incidence of HIV among trial participants than among community members tested before the trial.

### **How long did the study last?**

Enrollment began in June 2004 and ended in March 2005. After enrollment, each woman was to be followed for up to 12 months. Follow-up data available differed by trial site. Because of early withdrawal of the study drug from Cameroon and Nigeria, women there did not complete the trial as planned.

### **When and why was the study drug withdrawn in Cameroon and Nigeria?**

The study drug was prematurely withdrawn in Cameroon in February 2005 and in Nigeria in March 2005. In Cameroon, the study was closed after the Ministry of Public Health suspended provision of the study product to participants to allow review of study procedures in the wake of media controversy over oral tenofovir research there and elsewhere. However, follow-up of women already enrolled in the trial continued until September 2005. In Nigeria, FHI closed the study due to operational issues.

### **What did the safety data from the study show?**

No statistical differences were found in severe liver or kidney abnormalities between women in the tenofovir group and women in the placebo group. The numbers of other side effects and health changes were also similar between the two groups. The most common reported events for both groups were malaria, vaginal yeast infections, stomach pains, and headache.

### **How many women became infected with HIV during the study?**

Eight women on study drug or placebo became infected with HIV. Two of the infections occurred among women receiving tenofovir, and six occurred among women receiving placebo.

### **How do the HIV data break down by country?**

Of the two women in the tenofovir group who became infected with HIV, one was from Ghana and one was from Cameroon. Of the six in the placebo group, two were from Ghana, one was from Nigeria, and three were from Cameroon.

**What can we conclude from the results?**

These results provide no evidence that short-term use of oral tenofovir for HIV prevention causes harm, since the women receiving tenofovir and those receiving placebo did not differ substantially in terms of liver and kidney function or other health changes. However, not enough data are available to determine whether tenofovir protects against HIV infection.

**What happened to participants who became infected with HIV?**

Those who became infected were referred to HIV care and support services. Local investigators identified facilities within the study countries that offered HIV-related psychological, social, and medical services, and participants who become infected were counseled and referred to those sites.

**What procedures are in place to ensure that the women who became infected with HIV are receiving the services they were promised?**

All of the women who became infected with HIV during the study were referred to a health counselor who referred them to local hospitals for HIV care and support services. The health counselor also offered to accompany each woman to her first visit to help her register for services. Family Health International has also been in contact with study staff, local hospitals, and local nongovernmental organizations to ensure that the women will have continuing access to such services. In Cameroon, for example, Family Health International has signed a contract with a local hospital to provide 15 years of care and treatment to the women who became infected there, and a nongovernmental organization has agreed to provide additional psychosocial support. Similar negotiations are under way in Ghana. In addition, the one woman from Nigeria who became infected was enrolled in the President's Emergency Plan for AIDS Relief program there.

**What are the implications of this study?**

Daily oral use of TDF in HIV-uninfected women was acceptable and was not associated with increased clinical or laboratory adverse events. Although the effectiveness data are inconclusive, the trial strongly supports the need for additional studies to test the effectiveness of oral tenofovir in preventing HIV infection in humans. Now that tenofovir has been demonstrated to be safe and acceptable for HIV-negative individuals at risk, it is crucial to determine if this approach can effectively reduce risk for HIV infection.

**What similar studies of oral tenofovir are being conducted?**

The Centers for Disease Control and Prevention is testing tenofovir among diverse populations in two countries: injecting drug users in Bangkok, Thailand, and men who have sex with men in Atlanta and San Francisco, USA. The Centers for Disease Control and Prevention is also studying tenofovir in combination with another drug, emtricitabine, in heterosexual men and women at high risk of HIV infection in Gaborone and Francistown, Botswana. Finally, the National Institutes of Health and The University of California at San Francisco are planning to study the same combination of drugs in men who have sex with men in Lima, Peru.

**Does Family Health International have any plans to continue studying tenofovir for HIV prevention?**

Family Health International is identifying and preparing potential sites for future studies of tenofovir alone or tenofovir plus emtricitabine among both men and women at high risk of HIV infection. A protocol is also being developed in conjunction with the CAPRISA Project of Mandela University in Durban, South Africa, to study whether a topical gel containing tenofovir, used as a microbicide, can also prevent HIV infection.

**What is Truvada? Why study two different drugs?**

Truvada is the name for the fixed-dose combination of tenofovir and emtricitabine, described above. Family Health International and others are interested in studying this drug combination because there are significant data suggesting the promise of both tenofovir and tenofovir plus emtricitabine. Because we don't yet know for certain how the animal data will correlate to human protection, we believe it is essential to move forward as quickly as possible to evaluate both of these promising interventions.