Fact Sheet

Safety

Background

A primary goal of the FEM-PrEP clinical trial, in addition to assessing the effectiveness of Truvada in preventing HIV infection in women, is to evaluate its safety when used daily by women who are not infected with HIV.

What is the safety profile of Truvada?
Truvada is a combination of the antiretroviral (ARV) drugs tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC). It is licensed as an HIV treatment by the drug-regulatory agencies in a number of countries, including Kenya, Tanzania, South Africa, Zimbabwe and the United States. It has been shown to be safe when taken by HIV-positive people for the treatment of HIV.

Because Truvada had not been assessed as a drug to prevent HIV, a primary goal of PrEP clinical trials is to evaluate its safety among HIV-negative people. The iPrEx clinical trial, which released its results in November 2010, found no substantial safety concerns when Truvada was taken by men who have sex with men to prevent HIV.

What safety concerns did FEM-PrEP monitor and assess?
In HIV-positive women, use of Truvada is associated with relatively mild side effects, such as diarrhea, nausea, fatigue, headache, dizziness and rash. Truvada has also been associated with some uncommon, but serious, side effects, including liver problems and kidney impairment.

Because the health and well-being of the women in the study are our highest priorities, the FEM-PrEP team carefully monitored and addressed any adverse events among the trial's participants. Liver and kidney function were monitored on a regular schedule at weeks 4, 12, 24, 36 and 52 after the participant began taking the study pill—and then one month after the participant stopped taking the study pill (week 56). Other safety concerns that were monitored included the use of Truvada during pregnancy, the development of TDF or FTC resistance in women who became infected with HIV, and the development of liver abnormalities in women with hepatitis B virus infection.

The local research teams also monitored whether participation in the trial led to any social harm, such as stigmatization, relationship difficulties, and physical or verbal abuse.

How were these safety issues monitored?
The health of the participants was monitored during the trial through the aid of questionnaires and laboratory tests. Each participant was tested monthly for HIV and pregnancy before receiving her 30-day supply of the study pill. Potential abnormalities in blood, liver or kidney function were assessed at week four and quarterly after enrollment, and abnormal laboratory results were closely monitored. Physical examinations were done at screening, at the final visit, and when clinically indicated.

Social harms were identified by the study staff members during clinic visits, in-depth interviews, and during routine interactions with the community; all instances of potential harm were reported to the lead investigator at the site. The site investigator reported to FHI and the local ethics board (if required) any occurrence of social harm (following procedures similar to those used to report serious adverse events). A study counselor consulted with any participant who reported experiencing a social harm as a result of her participation in the study.

Who monitored participant safety?
Physicians at each site assessed all laboratory results and adverse events. The study protocol gave clear guidance on when participants needed to be taken off the study pill, temporarily or permanently. Any serious adverse events and liver and kidney side effects were reported to physicians at FHI, who closely monitored the follow-up provided for these conditions and the results. FHI physicians also monitored combined data from all the FEM-PrEP sites.

An Independent Data Monitoring Committee (IDMC) met regularly to review trial data to ensure that participants were not being adversely affected by taking a daily dose of the study pill. If the members of the IDMC had identified any safety concerns, they could have recommended that the study modify its procedures or be discontinued due to harm.

What type of safety concerns would prevent a participant from enrolling in the study or have her taken off the study pill after she had been enrolled?
A potential participant was not enrolled in the study if: 1) she had serious and active illnesses, including active liver disease or active hepatitis B virus infection; 2) she were taking drugs that may have side effects on the kidneys; or 3) tests showed that she had inadequate kidney or liver function. Pregnant women were not enrolled because Truvada's effects on a fetus are unknown. All participants had to be willing to use a non-barrier, study-approved method of contraception at enrollment.

Participants could be taken off of the study pill either permanently or temporarily if they developed any of these conditions, until the problem had been resolved or stabilized. Participants who became pregnant during the study stopped taking the study pill and were asked to continue follow-up evaluations. (A participant could resume taking the study pill at the end of her pregnancy unless she was breastfeeding.) Any participant who tested HIV positive was taken off of the study pill immediately and permanently. She received post-test counseling and referral to HIV care and treatment services.

FEM-PrEP Preliminary Safety Findings

The use of Truvada was associated with some known side effects that were not serious.

Further analyses of the safety data are planned. The database will not be final until all participants complete their final study visits. The cleaning of the database and subsequent analyses will take several months. The results will be shared once they are known.

How can I learn more about the FEM-PrEP clinical trial?
Please contact Beth Robinson, Associate Director, Project Communications. E-mail: brobinson@fhi.org