



Drug Resistance

HIV drug resistance happens when the virus adapts to an anti-retroviral (ARV) drug, so the drug is less effective as a treatment for an HIV infection. Drug resistance may occur in different ways:

1. Drug resistance may develop in individuals, whether or not the person is taking the drug, if he or she becomes infected with an already resistant virus from the sexual partner who is the source of his or her infection.
2. Drug resistance may be acquired when the virus is exposed to low levels of the drug. Sub-optimal levels of drug, and the inability to suppress the virus, may lead to the virus developing resistance to the drug.
3. Drug-resistant viruses may occur spontaneously, even in people who are not taking the drug. HIV reproduces at a very high rate, often mutating with each replication cycle. This rapid rate of mutation can lead to the formation of a drug-resistant virus. Hence many HIV-infected people carry very low levels of drug resistant viral strains. In these people, the growth of the drug-resistant virus is enhanced when the drug selectively suppresses the drug-sensitive viruses. This allows the drug-resistant strain to become the dominant virus.

Was there a risk of drug resistance in the FEM-PrEP trial?

A woman who remained HIV negative while she was taking Truvada was not at risk for drug resistance. Because she had no HIV in her body, a drug-resistant virus could not have emerged. However, drug resistance is a hypothetical concern for women who become infected with HIV while they are taking Truvada. FEM-PrEP scientists were aware of this possibility and monitored the participants closely throughout the trial.

In general, the risk of drug resistance was low for a participant in the FEM-PrEP trial because Truvada contains two ARVs. Research shows that HIV-positive people who take more than one ARV are less likely to develop a resistant version of HIV. Even so, a strain of HIV could have developed that was resistant to one or both ARVs in Truvada.

For many scientists, doctors, advocates, and others, the importance of conducting trials to find another method of HIV prevention outweighs the relatively low risk of HIV resistance.

What actions were taken by the FEM-PrEP staff to *minimize* the possibility of drug resistance during the trial?

The best way to prevent resistance is to prevent the infection—which is the research team’s goal in this study of pre-exposure prophylaxis (PrEP). Scientists implemented several procedures to reduce the possibility of HIV resistance. All participants received intensive risk-reduction counseling to help them remain uninfected. Each participant was tested every four weeks for HIV, so anyone who became HIV positive was quickly diagnosed and immediately taken off the study drug. Therefore, if the participant had been using the study pill containing Truvada (rather than the placebo), she would have been exposed to the drug for only a short period of time because participants received only a few weeks supply of study pills at a time. This limited exposure would reduce the risk of a drug-resistant virus becoming the dominant virus.

What is FEM-PrEP doing to *assess* resistance?

All participants who became HIV positive during the trial are being followed closely for one year after the diagnosis to see whether a drug-resistant virus will appear in their blood. When possible, resistance testing for tenofovir (TDF) and emtricitabine (FTC) is performed on a specimen from the time when the virus was detected in a woman’s body, even if she had not developed antibodies at that time. If a participant is found to have drug resistance, the testing will be repeated at weeks 12, 24, 36 and 52 after her HIV diagnosis, as necessary. Resistance testing will stop after the first visit in which no resistance is detected.

FEM-PrEP Drug Resistance Findings

Analyses of the drug resistance 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