



Pregnancy and Contraceptive Effectiveness in the FEM-PrEP Trial

Background

What were the pregnancy-related eligibility criteria for participation in the FEM-PrEP clinical trial?

Women were eligible to participate in the FEM-PrEP trial if they were not pregnant, not breast-feeding, and did not want to become pregnant during the time they would be in the study. All participants were required to use an effective contraceptive method to enroll in the study.

Why were participants required to use an effective contraceptive method if they wanted to participate in FEM-PrEP?

There are few human data on Truvada's effects on a fetus. The safety of the participants is FEM-PrEP's top priority, and therefore women who became pregnant during the study had to stop taking the study pill. If many participants stopped taking the study pill during the course of the study, it would have been difficult to determine whether Truvada was truly effective for HIV prevention among the women in the study.

Is there any evidence that Truvada can alter a woman's fertility or harm a fetus?

Animal studies have not found evidence that Truvada alters female fertility or harms a fetus. Well-controlled studies of pregnant women who have taken Truvada have not been published. An Antiretroviral Pregnancy Registry is currently monitoring the health of babies born to women who were taking Truvada while they were pregnant. To date, this registry has not identified any risk of harm to these babies.

What family planning services were provided during FEM-PrEP?

- **Contraceptive counseling.** At screening, women were counseled about the importance of avoiding pregnancy during the study, and they were told about the risks and benefits of various contraceptive methods. If the participants were not already using a study-approved contraceptive method, they were offered a choice of study-approved methods. At enrollment, participants were required to be on contraception. Participants were also encouraged to continue using effective contraception throughout the course of their study participation. At each follow-up visit, participants were counseled regarding whether their chosen contraceptive methods continued to meet their needs. They were also counseled on the importance of condom use for the prevention of HIV and other

sexually transmitted infections. Participants were free to switch contraceptive methods during the trial and were not discontinued from the trial if they chose to stop using effective contraception.

- **Free contraception.** Study-approved contraceptive methods included injectable contraceptives, combined oral contraceptive pills, intrauterine devices (IUDs), and hormonal implants (at some sites). These methods were provided, free of charge, at the study sites (or via referral) throughout the course of the study. In addition, women were provided with male condoms and female condoms (where available), which provided added backup pregnancy prevention.
- **Pregnancy testing.** Participants were tested for pregnancy at screening, enrollment, and then on a near-monthly schedule during the course of the trial.

What contraceptive methods did women use in this study?

Approximately a third of the women chose to use oral contraceptives and two-thirds chose to use injectable contraceptives. Very few women chose to use hormonal implants or IUDs.

What happened when a participant became pregnant during the study?

If a participant became pregnant during the study, she was asked to stop taking the study pills. Pregnant women were referred to antenatal clinics as they desired. Pregnant women were also asked to return to the study clinic for follow-up visits (after they had stopped taking the product). If the participants agreed, information was collected about pregnancy outcomes; one goal of the study was to collect data on potential effects of short-term Truvada exposure on the fetus.

How long might a participant have been exposed to Truvada if she was found to be pregnant during the trial?

The FEM-PrEP trial was designed to reduce a pregnant participant's exposure to Truvada by testing the participants for pregnancy every 4 weeks. As stated above, participants who became pregnant were taken immediately off the study pill as soon as the pregnancy was detected.

Are there interactions between antiretroviral medications and hormonal contraceptives?

Both antiretroviral (ARVs) drugs and hormonal contraceptives are metabolized by the liver, and both kinds of drugs can affect liver enzymes. Theoretically, these drugs could affect each other's metabolism. Such interactions could lead to decreases in contraceptive or ARV effectiveness, or increases in toxicity of either drug. These interactions are more likely with protease inhibitors (PIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs). Studies to date have shown no significant interactions between hormonal contraceptives and nucleoside or nucleotide reverse transcriptase inhibitors (NRTIs) such as the ARVs in Truvada, integrase inhibitors, or CCR5 antagonists.

FEM-PrEP Preliminary Pregnancy Findings

Women in FEM-PrEP were required to use an effective method of contraception. At enrollment, 66 percent were using injectables and 30 percent were using oral contraceptives. The overall pregnancy rate was 9 percent; the highest pregnancy rates were among women using oral contraceptives.

Among study participants randomly assigned to the Truvada arm, observed pregnancy rates were higher than among women randomly assigned to the placebo arm. This is unexpected and inconsistent with known drug interactions involving tenofovir (TDF) and contraceptive hormones, and with known metabolic effects of emtricitabine (FTC). Possible explanations include differential pill adherence by

group, previously undefined drug-drug interactions, chance, or a combination of factors (including yet unknown factors).

Further analyses of the pregnancy 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?

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