



Rationale for Trials of Pre-Exposure Prophylaxis for HIV Prevention

Researchers believe that an antiretroviral drug taken as a daily oral preventative is one of the most important new prevention approaches being investigated today. An effective daily preventative could help address the urgent need for female-controlled prevention methods and, when combined with existing prevention measures, could help reduce new HIV infections among men and women at high risk.

The concept of providing a preventative treatment before exposure to an infectious agent is not new. For example, when individuals travel to an area where malaria is common, they are advised to take medication to fight malaria before and during travel to that region. The medicine to prevent illness is then already in their bloodstream if they are exposed to the infectious agent that causes malaria.

Several sources of data suggest that the use of antiretroviral drugs in this manner may be effective in reducing the risk of HIV infection. Theoretically, if HIV replication can be inhibited from the very first moment the virus enters the body, it may not be able to establish a permanent infection. Providing antiretrovirals (ARVs) to HIV-infected women during labor and delivery and to their newborns immediately following birth has been shown to reduce the risk of mother-to-child transmission by about 50%. Additionally, in observational studies, ARV regimens have been associated with an 80% reduction in the risk of HIV infection among health care workers following needle sticks and other accidental exposures, when treatment is initiated promptly and continued for several weeks. Finally, animal studies have shown that tenofovir can reduce the transmission of a virus similar to HIV in monkeys when given before and immediately after a single retroviral exposure. Animal studies have also demonstrated that pre-exposure administration of tenofovir plus emtricitabine provided significant protection to monkeys exposed repeatedly to an HIV-like virus. These data, combined with the drugs' favorable resistance and safety profiles as HIV treatments, make tenofovir and tenofovir plus emtricitabine ideal candidates for HIV prevention trials.

Characteristics of Current PrEP Candidates

Established safety as HIV treatments

Potent antiretrovirals

Long duration of action

Once-daily dosing

Low levels of resistance

Tenofovir was approved by the U.S. Food and Drug Administration in 2001 as a treatment for HIV infection, and the tenofovir plus emtricitabine combination pill was approved for use as an HIV treatment in 2004. More than 150,000 HIV-infected people around the world have now used these drugs. As treatments for HIV-infected individuals, tenofovir and tenofovir plus emtricitabine have been shown to be both safe and effective. They have relatively low levels of side effects and slow development of associated drug resistance, compared with other available HIV treatments. Because the therapies are taken orally only once a day, with or without food, they are also among the most convenient-to-use HIV drugs available today. These trials are designed to evaluate the drugs' safety and efficacy among uninfected individuals. Side effects may differ in HIV-negative populations, and it is not yet known if tenofovir or tenofovir plus emtricitabine can prevent HIV infection in humans.