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Media Contact On-Site:
Elizabeth-Ann Chandler, +1.404.918.3532
echandler@cdc.gov

Additional Contact (Atlanta):
National Center for HIV/AIDS, Viral Hepatitis, STD,
and TB Prevention - News Media Line
+1.404.639.8895
NCHHSTPMediaTeam@cdc.gov

Preliminary Results from First Safety Study of Daily Tenofovir for HIV Prevention Among MSM Find No Significant Concerns

Preliminary analyses from the first study to examine the clinical and behavioral safety of tenofovir taken daily for HIV prevention among gay and bisexual men suggest no significant safety concerns. A prior study in Ghana, Nigeria and Cameroon found that the drug was safe among heterosexual women at high risk. The MSM study findings were presented today by CDC's Dr. Lisa Grohskopf at the *XVIII International AIDS Conference* in Vienna, Austria.

The approach of taking a daily antiretroviral drug to try to prevent HIV infection is known as pre-exposure prophylaxis, or PrEP, and studies around the world are currently underway to determine if it is effective at reducing HIV infection among individuals at high risk, including MSM. While the results of those studies will be needed to determine if PrEP can prevent HIV, this safety study lends additional assurance that the strategy may be well-tolerated among MSM, should it prove effective.

The Phase II safety study was conducted by the U.S. Centers for Disease Control and Prevention in collaboration with the San Francisco Department of Public Health, the AIDS Research Consortium of Atlanta, and Fenway Community Health in Boston. The trial examined whether a 300 mg tablet of tenofovir disoproxil fumarate taken daily was safe among 400 HIV-negative men who have sex with men (MSM) in San Francisco, Atlanta, and Boston. The study would not have been possible without the commitment and dedication of the trial participants.

Participants were randomly assigned to one of four study arms, and neither researchers nor participants knew an individual's group assignment. Participants in two arms of the study received either tenofovir or placebo (a tablet without active medication) immediately upon enrollment, while participants in the remaining two arms received either tenofovir or placebo after nine months of enrollment. This design allowed researchers to compare risk behaviors among those taking a daily pill and those not taking pills.

Encouraging First Results on Clinical Safety

While additional analyses of trial data are underway, CDC presented preliminary clinical findings during a late-breaker session at the conference today.

Although tenofovir has an excellent safety profile when used as treatment in HIV-positive individuals, all drugs have potential medical risks, and the drug's safety among HIV-negative MSM had not previously been evaluated. The most common side effects of tenofovir among

HIV-positive individuals have been nausea and loss of appetite. However, there have been reports of uncommon, but more serious health problems related to kidney function and reductions in bone mineral density.

To assess clinical safety in this trial, researchers conducted regular laboratory testing among all participants to monitor for any biological abnormalities, such as elevated creatinine or decreased phosphorous, that might indicate the development of such problems. As with all clinical trials, any serious adverse events (SAEs) among trial participants were immediately reported and investigated, regardless of whether they were likely to be related to the drug (e.g. car accidents, serious injuries).

While additional analyses are planned, researchers were encouraged that no serious safety concerns emerged in these preliminary analyses. There were no SAEs among those taking tenofovir that were considered to be potentially drug related, and no significant differences in effect on kidney function between those taking tenofovir and those taking a placebo.

In addition to clinical safety, another key objective of this study was to begin to assess the potential impact of a daily preventative drug regimen on HIV risk behaviors. One of the greatest risks, should PrEP prove to be partially effective at reducing HIV transmission, is that those using PrEP might increase their risk behaviors—a phenomenon called “behavioral disinhibition,” or “risk compensation.” Public health officials have long been concerned that if risk compensation does occur with the use of PrEP, it could potentially offset any prevention benefit of PrEP.

While analysis of behavioral safety data are not yet complete, preliminary analyses suggest there was no increased risk in men taking a study pill compared to those not taking a study pill during their first nine months of study participation.

However, in this study extensive steps were taken throughout the trial to ensure that participants understood they might not be protected from HIV—either because they could be receiving a placebo or because even if they did receive the study drug, it might not ultimately prove to reduce HIV risk. All participants also received regular HIV education, extensive risk-reduction counseling, condoms, and STD testing and treatment throughout the trial.

Study authors stress that while these first results are reassuring, they must be interpreted with caution when planning for potential PrEP implementation. In this trial, participants were counseled that they had only a 50 percent chance of getting PrEP and that the effectiveness of the drug is unknown. If PrEP proves effective, careful planning and additional behavioral studies will be needed to determine the best ways to prevent increases in risk behavior in real world settings when efficacy is known. Additionally, as with any drug, clinical safety would have to be closely monitored over time if PrEP is licensed and approved for use. These findings, in conjunction with other PrEP trials underway, can guide planning for future research and guidance for the counseling, prevention services, and safety monitoring that would need to be implemented in conjunction with PrEP, if it proves effective.

No conclusions about the potential efficacy of PrEP in preventing HIV infection can be drawn from this study, as it was not designed to assess effectiveness. Only three HIV infections occurred among trial participants while taking study pills. All three occurred in the placebo arm, but that could be entirely by chance.

Additional analyses will be conducted in the coming months to more closely examine trends in

risk behavior in each study arm, as well as the relationship between adherence, perception of treatment arm (i.e., do I believe I got tenofovir or the placebo?), perception of PrEP efficacy (i.e., how well do I believe tenofovir works?) and individual risk behavior. Adherence will also be examined in order to better assess acceptability and feasibility of daily PrEP for this population.

Next Steps in Evaluating and Planning for the Potential Use of PrEP

This trial is one of many studies evaluating the safety and acceptability of PrEP among populations at high risk for HIV around the world. Multiple studies are underway to examine whether tenofovir, alone or in combination with emtricitabine (FTC), can reduce the risk of HIV infection among MSM, injection drug users, and heterosexual men and women at high risk for HIV infection. PrEP is one of the most promising new prevention approaches being explored, and if effective, could help address an urgent need for additional solutions to help slow the HIV epidemic in the U.S. and around the world.

More than 2.7 million people continue to become infected with HIV across the globe each year, including more than 56,000 Americans. In the U.S., gay and bisexual men are the risk group most severely impacted; they are the only risk group in which new infections are rising, and account for over half of new HIV infections each year. If PrEP proves effective, it could provide an additional safety net for MSM and other individuals at high risk, when used in combination with other proven prevention strategies, like HIV testing, correct and consistent condom use, and reduction of partners. PrEP could also provide a much needed option for women who are unable to negotiate condom use and could provide some protection for discordant couples (i.e., in which one partner is infected and the other is not).

While it is not possible to predict if—and in which populations—PrEP will prove effective, careful implementation planning would be critical to the success of this and other new prevention strategies. Because no strategy is likely to be 100 percent effective, their future impact on the HIV epidemic will ultimately be determined by how effectively strategies are used in combination to provide the greatest protection for individuals at risk. In planning for potential PrEP implementation, CDC's top priority has been preparing for the rapid development of clinical guidelines to ensure its proper use in the U.S., should it prove effective in clinical trials. The agency has also begun examining how and under what circumstances PrEP could effectively be delivered to populations at highest risk for HIV infection in the United States.

For more complete information on implementation planning in the U.S., see separate CDC fact sheet "[Pre-Exposure Prophylaxis \(PrEP\) for HIV Prevention: Planning for Potential Implementation in the U.S.](http://www.cdc.gov/hiv/prep/resources/factsheets/implementation.htm)"

(<http://www.cdc.gov/hiv/prep/resources/factsheets/implementation.htm>). For more information on CDC's PrEP trials, see CDC fact sheet "[CDC Trials of Pre-Exposure Prophylaxis for HIV Prevention](http://www.cdc.gov/hiv/prep/resources/factsheets/index.htm)" (<http://www.cdc.gov/hiv/prep/resources/factsheets/index.htm>).

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