



Mitchell H. Katz, MD
Director of Health

November 23, 2010
For Immediate Release

Eileen Shields, PIO
(415) 554-2507

A Pill a Day Reduces Risk for HIV Infection

Major Study Published in the New England Journal of Medicine Demonstrates the Effectiveness of a New HIV Prevention Tool, Pre-Exposure Prophylaxis (PrEP)

San Francisco, CA – A new HIV prevention strategy that has the potential to slow the global HIV epidemic has been proven effective in a new research trial. The iPrEx Study showed that HIV negative people who were given a daily HIV treatment drug had 44% fewer HIV infections than those who received a placebo. The study, reported in the *New England Journal of Medicine*, is the first evidence that this new HIV prevention method, called pre-exposure prophylaxis or PrEP, reduces HIV infection risk in men who have sex with men and transgender women who are at high risk for HIV infection. The drug used in the trial is known as Truvada[®], a commonly used HIV treatment pill that is a combination of emtricitabine and tenofovir.

The HIV Research Section of the San Francisco Department of Public Health (SFDPH) enrolled 140 participants into this groundbreaking study, which was known locally as Prepare.

Worldwide, a total of 2,499 individuals participated in the six-country study. All study participants received a comprehensive package of prevention services designed to reduce their risk of HIV infection throughout the trial, including HIV testing, intensive safer sex counseling, condoms, and testing and treatment for sexually transmitted infections. Half of the study participants also received the PrEP pill, while the other half received a placebo.

In all, 64 HIV infections occurred among the 1,248 study participants who received the placebo pill, while 36 HIV infections occurred among the 1,251 participants who received Truvada[®]. The average reduction in HIV infection risk of 44% includes all study participants – even those who did not take the daily pill consistently. All studies have some uncertainty -- based on evidence from this study, the likely range for the overall protective effect of Truvada[®] is between 15% and 63%.

The iPrEx study found that PrEP offered more protection to those who reported taking the pill more consistently. Pill use in the study was measured through pill counts, bottle counts, and participants' self-reports. Among those who took the drug on 50% or more of days, risk of HIV infection fell by 50% (95% CI 18-70%); among those who used the pill on 90% or more of days, the PrEP pill reduced infection risk by 73% (95% CI 41-88%).

In addition to pill-taking measures that rely on self-reports, iPrEx also measured levels of Truvada[®] in the blood of study participants. These tests corroborated that participants who were protected against HIV infection were likely taking the study drug more regularly. Among a subset of 77 study participants who were given Truvada[®], detectable levels of the drug were

found in the blood of 51% (22 of 43) of those who remained HIV uninfected, but in only 9% (3 of 34) of participants who became HIV infected. Low or absent drug levels underlie all of the infections that occurred among those who received active PrEP.

“iPrEx proves that PrEP provides important additional protection against HIV when offered with other prevention methods such as HIV testing, counseling, condom use and management of sexually transmitted infections,” said iPrEx Protocol Chair Robert Grant, MD, MPH of the Gladstone Institutes and the University of California at San Francisco. “As with other prevention methods, the greatest protection comes with consistent use. I hope this finding inspires a renewed commitment from communities, industry, and government to stop the spread of HIV.”

“These study results are an historic step forward in developing effective prevention strategies for men who have sex with men and transgender women, populations that are heavily impacted by the HIV/AIDS epidemic worldwide,” said Susan Buchbinder, MD, Director of the HIV Research Section. “The study could not have been completed successfully without the collaboration of our community partners, and the commitment of study participants here in San Francisco, and on 4 continents. We look forward to continuing to work with them all as we move forward to better understand how and for whom PrEP might be implemented.”

Grant Colfax, MD, Director of HIV Prevention for the San Francisco Department of Public Health said, “San Francisco has been at the forefront of HIV prevention and treatment since the beginning of this global epidemic. iPrEx results demonstrate that PrEP has promise as an important addition to the City’s current prevention efforts. We will be consulting with clinicians and community partners to discuss how to optimize delivery of all of our prevention strategies here in San Francisco, including the potential for PrEP among high-risk populations outside of controlled research trials. We need to figure out if the ground-breaking findings of this study can be adapted effectively to reduce new HIV infections at the community level.”

About iPrEx and PrEP

The iPrEx study (Pre-exposure Prophylaxis Initiative) (<http://www.globaliprex.com>), is a double-blind, placebo controlled Phase III clinical trial that began in 2007, following three years of community consultation. iPrEx is the first human efficacy study of oral PrEP to report data. The iPrEx study was sponsored by the U.S. National Institutes of Health (NIH) through a grant to the Gladstone Institutes, a non-profit independent research organization affiliated with the University of California at San Francisco. Additional support for iPrEx was provided by the Bill & Melinda Gates Foundation.

In all, 2,499 men and transgender women who have sex with men (MSM) at high risk for HIV infection participated in the iPrEx study at 11 sites in Brazil, Ecuador, Peru, South Africa, Thailand and the United States. Other studies of PrEP are currently underway among heterosexual men and women, serodiscordant couples and injection drug users. iPrEx researchers believe that those trials should continue, as results from the iPrEx study cannot be extrapolated to predict the impact of PrEP on other populations. Approximately 20,000 participants are currently or expected to be enrolled in PrEP trials worldwide. PrEP was previously demonstrated to be highly effective in animal studies.

In July, 2010, a study known as CAPRISA 004 found evidence that a topical gel containing 1% tenofovir helped reduce HIV negative women's risk of HIV infection via vaginal sex. The topical gel is another form of HIV prevention using antiretroviral drugs currently being explored, in addition to oral PrEP.

The drug used in the iPrEx study, a single-tablet combination of emtricitabine (FTC 200 mg) and tenofovir (TDF 300 mg), is marketed by Gilead Sciences, Inc. under the brand name Truvada[®], and is available generically at prices as low as approximately 40 cents (U.S.) per tablet in the poorest countries of the world. In the U.S. the average price for Truvada[®] could be as high as \$800 - \$1000 per month, excluding the cost of clinical visits and laboratory monitoring. Gilead Sciences provided study drug but did not fund, monitor, or affect study conduct at the iPrEx study sites.

National and international health authorities and regulatory bodies must now meet to review the iPrEx study data and to determine whether and how to recommend use of PrEP for people at increased risk of HIV infection. Much remains to be learned about how to maximize the impact of PrEP and use this new tool most effectively. An 18-month "open label" study of FTC/TDF PrEP, which will provide the drug to HIV uninfected participants in the original study who wish to join, will begin next year and should provide additional information on efficacy, safety, behavior and pill taking. HIV-positive iPrEx participants will also be invited to enroll in this phase of the study for ongoing monitoring.

The impact of HIV on MSM

iPrEx studied the impact of PrEP on one of the populations hardest hit by the global HIV epidemic, men and transgender women who have sex with men (MSM). Globally, even in regions with generalized HIV epidemics such as Africa and Asia, MSM often have much higher rates of HIV infection than the population at large. HIV prevention tools that reduce infection in MSM not only have the potential to save thousands or millions of lives directly, but could also greatly reduce the impact of HIV on all communities at risk by reducing overall prevalence of the disease and thus the global risk of HIV infection.

iPrEx is one of the largest HIV prevention clinical trials to focus on men who have sex with men, the first HIV prevention study to focus on MSM to be conducted in either Africa or Asia, and the first demonstration of a biomedical intervention to prevent HIV infection in MSM.

"These results are a significant milestone for MSM here in the United States and around the world," said Albert Liu, MD, MPH, the study's director at the San Francisco Department of Public Health and medical officer for iPrEx. "Future research will help answer remaining questions about PrEP use, including how to best support people in taking PrEP consistently, who should use PrEP and in what situations, and how to deliver PrEP safely and effectively in different settings."

Side effects, resistance and behavioral issues in iPrEx

Side effects from use of the PrEP pill were mild and infrequent in the iPrEx study. These included a small number of reports of low-grade nausea, which dissipated after several weeks. Such symptoms are relatively common after initiation of antiretroviral therapy, and reassurance from peers and providers in the first few weeks is important to promote long term adherence. In addition, isolated mild elevations of creatinine, indicating a change in kidney function, occurred in a small number of individuals receiving the active drug and resolved spontaneously or with discontinuation of the pill. Slight increases were also detected in headache and unintentional weight loss among participants in the study arm that received FTC/TDF.

The iPrEx study carefully monitored for any indications of HIV drug resistance among individuals who became HIV infected during the study. No iPrEx study participant developed detectable resistance to tenofovir (TDF), one of the component drugs of the PrEP pill used in this study. Two participants who received the active PrEP drug developed resistance to the other PrEP component drug, emtricitabine (FTC), and one participant who received placebo appears to have been infected with a strain of HIV that was already resistant to FTC. All three participants with FTC resistance were HIV-infected at the time of enrollment in iPrEx, but their infection was too new to be detected by standard HIV antibody testing. Drug resistance was not seen among participants taking Truvada[®] who became infected during the study. Investigators emphasize the need for additional testing and clinical screening to ensure that anyone starting PrEP is not already HIV infected.

The concern that the use of the PrEP pill could cause study participants to relax their use of safer sex practices was not demonstrated in the iPrEx study. In fact, self-reported HIV risk behavior decreased among participants in both arms of the study, and condom use increased, likely because of the HIV risk reduction services participants received, as well as education that the efficacy of PrEP was unknown, and that participants may receive a placebo, which would offer no protection. More research is needed to see how risk behavior may change now that information is available about PrEP safety and efficacy.

Additional data from the iPrEx study will be collected, analyzed and released in the coming year. This will include analyses designed to detect any low level side effects related to bone mineral density or kidney function, which have been associated with some HIV therapies in people with HIV. Other analyses will search for any additional evidence of drug resistance, look for evidence of use of the PrEP tablet through measures of drug exposure, and will examine HIV risk behavior through the occurrence of sexually transmitted infections.

“Every year 2.7 million people are infected with HIV, and PrEP has the potential to help bring those numbers down. We have a moral obligation and a public health imperative to quickly act on these results. The HIV prevention field and national HIV policymaking bodies, along with WHO and UNAIDS, must promptly review the iPrEx data, consult with both experts and affected communities, and develop clear plans and recommendations for next steps in research and possible access to PrEP,” said Mitchell Warren, executive director of AVAC, a global HIV prevention advocacy organization.

Additional information about the iPrEx study and PrEP:

Manuscript: <http://www.nejm.org/doi/full/10.1056/NEJMoa1011205>

SFDPH Q&A: www.preparesf.org

iPrEx Study FAQ and fact sheets: www.iprexnews.com

iPrEx study materials from the National Institutes of Health (NIH):

Release: <http://www.niaid.nih.gov/news/newsreleases/2010/Pages/iPrEx.aspx>

Q&A: <http://www.niaid.nih.gov/news/QA/Pages/iPrExQA.aspx>

Background information on pre-exposure prophylaxis for HIV (PrEP) from Global Advocacy for AIDS Prevention (AVAC):

http://www.avac.org/ht/d/sp/i/262/pid/262/cat_id/458/cids/453,458

Information on the iPrEx study drug, FTC/TDF: <http://www.truvada.com/>

About the HIV Research Section

The HIV Research Section is a leader in HIV prevention research working with Bay Area communities to discover effective HIV prevention strategies. Operating under the umbrella of the San Francisco Department of Public Health, HIV Research Section conducts innovative research that is guiding global approaches in HIV prevention, such as HIV vaccines. By collaborating with other researchers and communities throughout the world, HIV Research Section's scientific breakthroughs will be used to help people most affected by the epidemic. Volunteering with HIV Research Section gives participants the opportunity to join a global network of volunteers who are influencing the development of HIV prevention strategies that strive to eliminate HIV/AIDS worldwide. For more information, visit our website at www.HelpFightHIV.org.

###