UNIVERSITY OF WASHINGTON
INTERNATIONAL CLINICAL RESEARCH CENTER
PARTNERS PrEP STUDY

PARTNERS PrEP STUDY DEMONSTRATES THAT PrEP SIGNIFICANTLY REDUCES HIV RISK: KEY MESSAGES

SUMMARY

On 13 July 2011, the Partners PrEP Study Team announced that its independent Data and Safety Monitoring Board (DSMB) had recommended, after review of the study data, that the study results be publicly reported and the use of placebo discontinued, because of clear demonstration of HIV protection due to pre-exposure prophylaxis (PrEP) in the study population.

WHAT IS THE PARTNERS PrEP STUDY?

- The Partners PrEP Study is a double-blind, placebo-controlled, phase III clinical trial to assess the safety and efficacy of oral PrEP for the prevention of HIV infection, using the antiretroviral medication tenofovir (TDF), either alone or in combination with emtricitabine (FTC/TDF).

- The study population for the Partners PrEP Study was heterosexual African HIV serodiscordant couples, that is, in which one partner had HIV and the other did not. The study is funded by the Bill & Melinda Gates Foundation. Study drug was donated by Gilead Sciences, Inc. The University of Washington International Clinical Research Center is the study sponsor and coordinated the trial, in collaboration with investigators at the study sites.

- The Partners PrEP Study enrolled 4758 HIV serodiscordant couples from 9 clinical trial sites in Kenya and Uganda. HIV uninfected partners were randomly assigned in equal numbers to one of three study groups: one group received TDF, one FTC/TDF, and one placebo. The study was double-blinded. The study began in July 2008 and enrollment was completed in November 2010.

- All study participants received a comprehensive package of HIV prevention services, which included intensive safer sex counseling (both individually and as a couple), HIV testing, free condoms, testing and treatment for sexually transmitted infections, and monitoring and care for HIV infection.

- Previous studies had found that TDF and FTC/TDF are well-tolerated and safe when used daily by HIV uninfected for men and women, but the HIV prevention effects of these medications for HIV prevention in heterosexual populations was unknown.

WHAT DID THE PARTNERS PrEP STUDY FIND?

- The analysis reviewed by the Partners PrEP Study DSMB at its 10 July 2011 meeting included data through 31 May 2011.

- Through 31 May 2011, a total of 78 HIV infections occurred in the study: 18 among those assigned TDF, 13 among those assigned FTC/TDF, and 47 among those assigned placebo.

Thus, those who received TDF had an average of 62% fewer HIV infections (95% CI 34 to 78, p=0.0003) and those who received FTC/TDF had 73% fewer HIV infections (95% CI 49 to 85, p<0.0001) than those who received placebo. PrEP reduced HIV risk in both women and men.

- Importantly, PrEP was found to be safe: the rate of serious medical events was similar for those assigned to TDF, FTC/TDF, and placebo. Ten percent of women annually became pregnant during the study and they were discontinued from the study medication during pregnancy; pregnancy rates were similar across the three arms and there was no evidence that TDF or FTC/TDF was associated with pregnancy complications.

- Adherence to the daily PrEP medication was very high – more than 97% of dispensed doses of the study medications were taken. More than 95% of participants were retained in study follow-up.

- The Partners PrEP Study is continuing: those receiving TDF and FTC/TDF PrEP will continue on those medications and those receiving placebo will start TDF or FTC/TDF PrEP.

WHAT DOES THE PARTNERS PrEP STUDY TELL US?

- **Pre-exposure prophylaxis (PrEP) is an important strategy to prevent HIV infection**. In the Partners PrEP Study, persons without HIV took anti-HIV medications daily to prevent becoming infected. The results of the study demonstrate that PrEP should become an integral part of global efforts for HIV prevention and be part of evidence-based combination HIV prevention.

- **The Partners PrEP study found high safety and significant efficacy of both TDF and FTC/TDF in reducing HIV acquisition risk in heterosexual African men and women.** The Data Safety Monitoring Board recommended stopping the placebo arm and making the study results public.

- **Both TDF and FTC/TDF PrEP significantly reduced HIV risk.** There was not a significant difference in efficacy between the TDF and FTC/TDF arms. Additional data, from the Partners PrEP Study and other studies, may help to determine if safety or HIV prevention effects are sufficiently different for TDF versus FTC/TDF to warrant one or the other being widely implemented for HIV prevention.

- **The Partners PrEP Study is an international clinical study which tested whether PrEP prevents acquisition of HIV in HIV serodiscordant couples**. The study sites are overseen by researchers affiliated with Kenyan and Ugandan universities and hospitals, and is coordinated by the University of Washington in the United States. The study conduct was excellent, including high retention (more than 95% of participants throughout follow-up) and adherence to the study medication (with 97% of dispensed doses taken), testifying to the high motivation of the study participants and the site research teams.

- **PrEP offers an urgently needed and highly effective tool for HIV prevention.** Other placebo-controlled trials of tenofovir-containing PrEP are ongoing or completed [see table below]. The Partners PrEP data add to the efficacy of topical tenofovir gel among HIV-uninfected women in the CAPRISA 004 trial and daily oral FTC/TDF PrEP among HIV-uninfected men who have sex with men in the iPrEx trial. There may be different levels of PrEP efficacy for HIV prevention depending on the populations and ability to use a gel or

take a pill daily. The ongoing VOICE trial will provide important data on adherence and efficacy of both oral and topical tenofovir-based PrEP among African HIV-uninfected women at risk of HIV. Together, these results will provide a comprehensive evaluation of efficacy, safety, adherence, and HIV resistance of PrEP in different populations.

LARGE SAFETY AND EFFICACY STUDIES OF ORAL AND TOPICAL TENOFOVIR FOR HIV PREVENTION, JULY 2011

Location	Sponsor/ Funder	Population	Agent	Status
Ghana, Nigeria, Cameroon *FHI safety study* *(phase II study)*	FHI	936 high-risk women	Oral TDF	**Results published 2007. Safety demonstrated**
US *CDC Extended Safety Study* *(phase II study)*	CDC	400 MSM	Oral TDF	**Results reported July 2010. Safety demonstrated**
Thailand *Bangkok Tenofovir Study*	CDC	2400 IDU	Oral TDF	Fully enrolled Results 2011-2012
Botswana *TDF2 Study*	CDC	1200 women and men	Oral FTC/TDF	**Results anticipated July 2011**
South Africa *CAPRISA 004* *(phase II study)*	CAPRISA / USAID	889 women	Vaginal tenofovir gel (coital use)	**Vaginal tenofovir gel reduced HIV risk by 39% (95% CI 6-60%, p=0.02)**
Brazil, Ecuador, Peru, S. Africa, Thailand, US *iPrEX*	UCSF/ NIH&BMGF	2499 MSM	Oral FTC/TDF	**Oral FTC/TDF PrEP reduced HIV risk by 42% (95% CI 15-63%, p=0.005)**
Kenya, South Africa, Zimbabwe *FEM-PrEP*	FHI / USAID& BMGF	1951 high-risk women	Oral FTC/TDF	**Early closure 2011** **No evidence of protection against HIV**
Kenya, Uganda *Partners PrEP Study*	UW / BMGF	4758 HIV discordant couples	Oral TDF Oral FTC/TDF	**Oral TDF PrEP reduced HIV risk by 62% (95% CI 34-78%, p=0.0003)** **Oral FTC/TDF PrEP reduced HIV risk by 73% (95% CI 49-85%, p<0.0001)**
South Africa, Uganda, Zimbabwe *VOICE / MTN 003*	MTN / NIH	5000 women	Oral TDF, Oral FTC/TDF Vaginal tenofovir gel (daily use)	Fully enrolled Results late 2012

- **Now, more than ever, research on PrEP in populations is important, as well as research on how to deliver PrEP effectively to populations at greatest risk for HIV.** Evaluation of any new intervention almost always requires more than one study – often several – to gain as much information as possible about its safety and effectiveness in different populations who could potentially benefit. Each of the ongoing studies evaluating PrEP is critical for advancing understanding about the safety and effectiveness of this strategy among different populations. Results from one study will not necessarily predict the results for other studies, because of the important differences in population, frequency and route of HIV exposure, and potential for different adherence.

- **Antiretrovirals also reduce risk of HIV transmission from HIV infected partners.** The HPTN 052 trial recently demonstrated significant efficacy of antiretrovirals for treatment of HIV-infected persons in reducing their risk of transmitting HIV to their uninfected partners. Thus, evidence is growing that antiretrovirals can reduce both infectiousness and susceptibility. Given that all effective strategies to date have partial efficacy to date, it will be

essential to assess the coverage and efficacy of a combination of partially effective HIV prevention strategies in different populations.

- **New prevention tools are needed to combat HIV, including among HIV serodiscordant couples.** Stable heterosexual couples in which one person has HIV and the other HIV does not are a large and important risk group for HIV infection in Africa. HIV serodiscordant couples have built lives together, want to remain as couples and often want to have children together and want to do so safely. Prevention methods are needed, research into optimal delivery of prevention is essential, and couples need choices of effective HIV prevention strategies.

- **Active and meaningful engagement in research includes timely communication.** The teams at each Partners PrEP Study research site understand the importance of maintaining relationships of trust with study participants, their partners and members of the community. As part of this commitment, the study team is already informing their Institutional Review Boards (IRBs), international and in-country stakeholders, and study participants about the results of the Partners PrEP Study.

Partners PrEP Study Team

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Data management provided by DF/Net Research, Inc. (Seattle, USA) and site laboratory oversight by Contract Laboratory Services (CLS) of the Wits Health Consortium (University of the Witwatersrand, Johannesburg, South Africa). Study medication donated by Gilead Sciences (Foster City, CA).