PrEP Cuts Sexual HIV Transmissions 62% to 78% in Men and Women

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A second African study also reported at the conference—TDF2, conducted in Botswana—found that Truvada reduced new HIV infections by at least 63 percent among mostly single heterosexual men and women, with efficacy approaching 78 percent among study volunteers who were believed to be collecting their medications regularly.

The promising results of Partners PrEP, along with those of the TDF2, follow on the heels of the November 2010 iPrEx clinical trial results, which documented an average 44 percent reduction in new HIV infections among men who have sex with men and transgender women who used daily Truvada as PrEP, compared with those using a daily placebo. Among those who reported using Truvada religiously in iPrEx—meaning at least 90 percent of doses were taken correctly each month—PrEP cut new infections by 73 percent.

Another study reported in April 2011, dubbed FEM-PrEP, yielded more disappointing results. According to a planned interim check of the day, the study monitors found an equal number of new HIV infections among women using Truvada PrEP compared with those using placebo. Thus, all eyes fell on Partners PrEP and TDF2 to determine whether antiretrovirals (ARVs), used by women (and heterosexual men) at risk for HIV infection, could potentially serve as an effective prevention tool.

Partners PrEP
Jared Baeten, MD, PhD, and Connie Celum, MD, MPH, both of the University of Washington at Seattle, presented the results on behalf of the Partners PrEP study team.

The trial enrolled 4,758 HIV-serodiscordant couples, in which one partner was HIV positive and the other partner was HIV negative.

Provided that the HIV-negative partners had normal liver, kidney and blood markers, they were randomized to receive Viread once a day, Truvada once a day or placebo once a day. Couples were to be followed by the researchers for up to 36 months.

Study sites included four centers in Kenya and five centers in Uganda.

Comprehensive care was provided to the study participants. HIV-negative volunteers received

monthly HIV and pregnancy testing, monthly symptom and quarterly laboratory safety monitoring and monthly provisions of study medications along with individualized adherence counseling, which included instructions not to share study drugs. HIV-positive participants were seen quarterly and received semi-annual CD4 count testing. They also received ongoing HIV primary care and, depending on their CD4 counts, referrals to receive ARV treatment.

In addition, all participants received risk reduction counseling, free condoms and condom counseling, contraception counseling and provision, screening and treatment for other sexually transmitted infections (STIs), and counseling and referral for other HIV prevention interventions, including male circumcision where applicable.

The study, as designed, was halted July 10, 2011, after safety monitors noted key efficacy differences between the two groups. They recommended that the data be shared publicly and the placebo group be discontinued.

More than 60 percent of those enrolled in the study were men, and the average age of the volunteers was 33. Ninety-eight percent were married couples who had been together for an average of seven years. CD4 counts among the HIV-positive partners averaged 495 upon entering the study, and viral loads were low, around 8,000 copies.

Nineteen percent of the HIV-positive volunteers started ARV treatment during the study.

The adherence rate, determined through monthly pill counts, was high, with 97 percent of dispensed doses taken. Baeten and Celum's group has not yet evaluated blood levels of medications, which are needed to confirm the more rudimentary pill-count measures of adherence.

There were 90 infections in the study, 12 of which were documented at enrollment and were likely acute infections that weren't detected during the screening process. This left 78 confirmed HIV cases during the study itself. Forty-seven infections occurred in the placebo group, compared with 18 in the Viread group and 13 in the Truvada group.

These findings translated into 62 percent fewer HIV infections among those using Viread and 73 percent fewer infections among those using Truvada. Statistically speaking, however, the effects of Viread and Truvada were similar—there was no significant difference between the two groups, meaning that the difference could have been due to chance.

Viread and Truvada significantly reduced the risk of HIV infection in both men and women, a finding that refutes the conclusion of FEM-PrEP. Viread reduced new HIV infections by 68 percent of women and 55 percent of men. Truvada reduced new infections by 62 percent and 83 percent, respectively.

No statistically significant differences in the number of deaths, serious side effects or laboratory-documented adverse events were reported. Diarrhea was statistically more likely among those

taking Truvada compared with placebo, though this was documented in less than 5 percent of the study participants after one month of PrEP.

As for sexual behavior, 27 percent of couples reported unprotected sex in the month before enrollment. There was a decline in this behavior during the follow-up period in both study groups. Of note, however, one third of the study volunteers—both HIV positive and HIV negative—reported having extramarital sex during the trial.

Baeten and Celum noted that some variables of the study are still being explored, notably HIV drug resistance among those who seroconverted in the trial, along with the drug level testing mentioned above.

The study is continuing, albeit with those assigned to receive placebo now being offered active PrEP.

TDF2
The results of TDF2 were presented by Michael Thigpen, MD, of the U.S. Centers for Disease Control and Prevention (CDC).

The study enrolled 1,219 men and women; 16 never started study medication, and three were found to be HIV positive during the enrollment process. About 50 percent of the final 1,200 participants were assigned to take daily Truvada, whereas the other half received daily placebo.

Between 30 percent and 35 percent of the volunteers did not complete the study.

The vast majority (about 88 percent) were between 21 and 29 years old, and roughly 45 percent were women. Unlike Partners PrEP, roughly 94 percent of those enrolled in TDF2 were single.

As with Partners PrEP, comprehensive HIV counseling and condom distribution were provided in TDF2.

Throughout the study, there were nine HIV infections in the Truvada group, compared with 24 infections in the placebo group. This finding suggested that Truvada PrEP reduced new HIV infections by 62.8 percent.

When the researchers looked only at those who seroconverted within 30 days of their last scheduled study visit—meaning those who had refilled their study drugs and had medication available—there were 77.9 percent fewer infections among those who took Truvada compared with placebo.

Some gender differences were noted, but Thigpen remarked that the study was primarily focused on safety and didn’t have the numbers necessary to allow for detailed efficacy comparisons. Throughout the study, there were seven infection among women in the Truvada group and 14 infections among women in the placebo group, but this difference was not statistically significant,

meaning it could have occurred by chance. Among men, with two and 10 infections respectively, the difference was statistically significant.

Looking only at those who seroconverted within 30 days of their last scheduled study visit, the only statistically significant difference was among the women, with three and 13 infections, respectively. One man in the Truvada group and six in the placebo group seroconverted in this particular group, a difference that was not statistically significant.

One volunteer who was HIV-antibody negative but had acute infection upon starting the trial developed high-level resistance to Truvada as a result of taking the drug.

As for safety, researchers noted that dizziness, nausea and vomiting were statistically more likely in the Truvada group compared with the placebo group. No differences in lab tests of safety were reported.

Adherence, as measured by pill counts, was about 84 percent—slightly lower than the adherence rates documented in Partners PrEP. Evaluations of drug levels in blood samples have not yet been conducted.

Sexual behavior during the study was similar in both groups. Roughly 14 percent reported having sex with more than one partner in the month before their last study visit, whereas condom use during vaginal sex was about 80 percent in both groups.

In conclusion, Thigpen said that daily Truvada was found to be effective and safe for preventing HIV infection among heterosexual men and women, overall, compared with placebo. “Data suggests efficacy for men and women separately,” he added, “but the study was not large enough to draw definitive conclusions by gender.”

In addition to further exploring the data collected in TDF2, Thigpen said that the CDC and its public health partners plan to fully review all heterosexual PrEP trial data and will develop specific guidance for its use among heterosexual men and women.
