

# Bangkok Tenofovir Study: PrEP for HIV prevention among people who inject drugs

## Summary

- Daily oral PrEP (pre-exposure prophylaxis) with a tablet containing tenofovir disoproxil fumarate (tenofovir, marketed in the United States under the brand name Viread®) was found to reduce the risk of acquiring HIV by approximately 49 percent in a study of 2,413 men and women who inject drugs in Bangkok, Thailand.
- Those who took the medication consistently had higher levels of protection, similar to findings previously reported from other PrEP trials. In a separate analysis of participants known to be adherent, because they were observed taking their medication and had tenofovir detected in their blood, the risk of HIV acquisition was reduced by approximately 74 percent.
- This is the first study to report results of PrEP efficacy among people who inject drugs. Previous studies have found that PrEP with tenofovir – alone or in combination with emtricitabine (brand name Truvada®) – can reduce the risk of sexual transmission of HIV among heterosexuals and men who have sex with men.

## Trial Design and Study Population

- **Overview:** The Bangkok Tenofovir Study (BTS) examined use of a once-daily antiretroviral pill containing tenofovir disoproxil fumarate as PrEP for preventing HIV infection among adult men and women who inject drugs in Bangkok, Thailand. The CDC- sponsored study was conducted in collaboration with the Bangkok Metropolitan Administration (BMA) and the Thailand Ministry of Public Health. Study medication was donated by the manufacturer, Gilead Sciences.

The primary goal of the study was to determine if PrEP with daily oral tenofovir would reduce the risk of HIV infection among people who inject drugs. Safety, adherence, and participants' risk behavior were also assessed.

- **Study Population:** 2,413 HIV-uninfected men and women who reported injecting drugs during the previous year were recruited to participate in the study at 17 BMA drug treatment clinics in Bangkok. Approximately 80 percent of the population were male (1,924) and 20 percent were female (489). The age of participants ranged from 20 – 60, with a median age of 31 years. People with HIV, people with hepatitis B infection, and women who were pregnant or breast feeding were excluded from the study.

Participants were randomly assigned to one of two arms: 1,204 participants were assigned to receive one 300 mg tablet of tenofovir daily, and 1,209 were assigned to take one placebo tablet daily. Tenofovir and placebo tablets were similar in shape, color, and taste. Neither researchers nor participants knew a participant's group assignment.

Two participants in the placebo arm tested positive for HIV at baseline and were excluded from the analysis, which included the remaining 2,411 HIV-negative participants.

- **Informed Consent:** To ensure that participants fully understood all aspects of their participation in the trial, all volunteers were required to pass a comprehension test prior to providing written informed consent. Participants were free to withdraw from the trial at any time and for any reason.
- **Prevention Services:** To assist participants in eliminating or reducing HIV risk, participants were offered extensive HIV education and risk-reduction counseling, methadone, HIV counseling and testing, condoms, and bleach with instructions on how to clean needles at monthly study visits. Consistent with Thai government policy, sterile syringes were not provided at the clinics, but are available in Thailand at pharmacies, at low cost and without a prescription.



The health of participants was closely monitored throughout the trial, and participants were linked to any necessary medical care. Participants were tested regularly for HIV, and those who became infected during the trial were referred for HIV care and treatment through Thailand's national health system.

- **Scientific and Ethical Review:** All procedures and plans were reviewed by scientific and ethical review committees at CDC and the Ethical Review Committees of the BMA and the Thailand Ministry of Public Health. Additionally, trial data were reviewed regularly by an independent data and safety monitoring board to ensure that continuing the trial was safe and scientifically appropriate. A community relations committee, including people who inject drugs from each of the 17 participating clinics, met with the research team every two months to provide community input throughout the design, implementation, and conduct of the trial.

## Study Results

### Efficacy

- In the primary analysis of all 2,411 participants who began the trial, there were 17 HIV infections among the 1,204 participants taking tenofovir, compared with 33 infections among the 1,207 participants taking placebo, resulting in a 49 percent reduction in risk of HIV acquisition among those receiving tenofovir (95% CI, 9.6 to 72.2;  $p=0.01$ ).
- In a separate analysis conducted among participants known to be taking tenofovir consistently, the level of protection increased to 74 percent (95% CI, 16.6 to 94.0;  $p=0.03$ ). This analysis was limited to the participants who chose to be on directly observed therapy, met pre-established criteria for high adherence (taking a pill at least 71 percent of days and missing no more than two consecutive doses), and had detectable levels of tenofovir in their blood.

### Adherence

- The BTS study is the only PrEP efficacy trial to have offered directly observed therapy (DOT) as an option for participants. At the beginning of the trial and at each monthly visit, participants could select to either take their daily tablets independently at home and record whether they took their pill on daily diary cards, or to come into the clinic daily and have the pill administered by study staff. For those on DOT, the daily diaries were filled out by study staff.
- Adherence in the trial was high overall:
  - Participants were on DOT 87 percent of the time.
  - Based on study drug diaries (which combine diaries from DOT and non-DOT time), participants took study drug an average of 84 percent of days.
  - Adherence did not differ between the group taking tenofovir versus the placebo group ( $p=0.16$ ).
  - More detailed analyses of adherence and trends in adherence over time are underway and will be published in the coming months.

### Risk Behavior

- There were no significant differences in reported risk behaviors between the two study arms.
- Both injection and sexual risk behaviors declined substantially during the trial. The proportion of participants who reported injecting drugs during the prior 12 weeks decreased from 63 percent at baseline to 23 percent at one year; the proportion who shared needles decreased from 18 percent at baseline to 2 percent at one year; and the proportion reporting sex with more than one partner in the past 12 weeks decreased from 22 percent at baseline to 11 percent at one year. All reported risk behaviors remained below baseline throughout follow-up (all  $p<0.0001$ ).
- Additional analyses of risk behavior are underway and will be published in the coming months, including examination of risk behaviors most strongly associated with HIV infection in the study. Preliminary analyses are very consistent with past studies in this population, which indicate that HIV infections during the trial were associated with injection rather than sexual risks.

## Safety & Resistance

- Consistent with other PrEP studies, the trial did not identify any significant safety concerns associated with daily oral use of tenofovir.
- Participants assigned to receive tenofovir were more likely to experience nausea and/or vomiting than those assigned to the placebo group. These symptoms were not reported by many participants after the first two months of treatment. The amount and severity of other adverse events reported were similar among participants in both the treatment and control groups.
- There was no indication of elevated creatinine or renal failure among participants in the tenofovir group.
- No tenofovir resistance was found among participants who became infected during the trial.

## Retention

- Participants were followed for an average of approximately 5 years, with some participating for almost 7 years. Given the length of the study, retention was high, with only 15 percent of participants being lost to follow-up. There was no significant difference in follow-up time, withdrawal, or loss to follow-up between the tenofovir and the placebo groups.

## Reference

Choopanya K. et al. Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): a randomized, double-blind, placebo-controlled phase 3 trial. *Lancet* 2013;381:2083-90