

## HPTN 052

# Initiation of Antiretroviral Therapy (ART) Prevents the Sexual Transmission of HIV in Serodiscordant Couples

Early initiation of ART led to a 96% reduction in HIV transmission to the uninfected partner.

### Summary

HPTN 052 is the first randomized clinical trial to show that treating HIV-infected individuals with ART can reduce the risk of sexual transmission of HIV to their uninfected partners.

### Study Overview

HPTN 052 is a Phase III clinical trial designed to evaluate the effectiveness of ART to prevent the sexual transmission of HIV in serodiscordant couples—in other words, couples in which only one partner is HIV infected at the time of screening. The study enrolled couples in which the HIV-infected partner had not previously received ART and whose CD4 count fell in the range of 350 to 550 cells/mm<sup>3</sup> at screening. These individuals do not require ART for their own health, according to World Health Organization (WHO) guidelines. The study is also evaluating the optimal time to start ART in order to reduce morbidity and mortality in people with HIV/AIDS.

Couples were randomly assigned to one of two study arms: 1) immediate initiation of ART in the HIV-infected partner upon enrollment, or 2) delayed initiation of ART in the HIV-infected partner until two consecutive CD4 cell counts were at or below 250 cells/mm<sup>3</sup> or an AIDS-defining illness developed (according to the WHO definition).

A total of 1763 HIV serodiscordant couples were enrolled between April 2005 and May 2010 (886 couples were randomly assigned to the immediate ART arm and 877 were randomly assigned to the delayed ART arm). The study is being conducted at 13 sites in Africa, Asia, and North and South America. Ninety-seven percent (97%) of the partnerships are heterosexual.

Each couple agreed to be followed in the study for at least five years. Information is collected on both partners throughout the study, including regular HIV testing in the HIV-uninfected partner and collection of data related to morbidity and mortality of HIV/AIDS in the HIV-infected partner. All participants receive couples counseling, risk-reduction counseling, free condoms, and testing and treatment for sexually transmitted infections (STIs). Primary HIV care is also provided to the HIV-infected partner.

On April 28, 2011, an independent Data and Safety Monitoring Board (DSMB) concluded that the trial had demonstrated a benefit of immediate ART with respect to transmission and a trend suggesting clinical benefit to the HIV-infected partner. The DSMB recommended that the primary study results be announced as soon as possible, given that the findings definitively show that immediate initiation of ART reduces transmission of HIV. The results were released before presentation at a scientific conference or publication in a peer-reviewed journal because of their importance to public health and public health policy.

## Results: HIV Prevention

During the course of the study, 39 participants who had been HIV uninfected at enrollment became infected with HIV. Of those, 28 were identified as genetically linked at the time of the DSMB meeting, meaning the HIV-infected partner was the likely source of the infection. The other 11 transmissions were unlinked or are still being analyzed. Three different methods were used to confirm these critical results.

Only one linked infection occurred in the immediate ART arm; the other 27 linked transmissions occurred in the delayed ART arm, before ART was initiated. This demonstrates that early initiation of ART led to a 96% reduction in HIV transmission to the HIV-uninfected partner. The single transmission event in the face of therapy appears to have occurred before ART could lead to viral suppression. Further analyses among cases have demonstrated at least one more linked transmission in the delayed ART arm, further increasing the power of ART to prevent HIV transmission.

## Results: Therapeutic Benefit of Early Initiation of ART

One hundred and five (105) morbidity and mortality events were noted, with 40 in the immediate ART arm, and 65 in the delayed ART arm, showing a trend toward benefit in favor of the immediate ART arm. Morbidity and mortality endpoints include WHO Stage 4 events, severe bacterial infections, tuberculosis, and death. Among these endpoints, there were 3 and 17 extra-pulmonary tuberculosis events in the immediate and delayed arms, respectively. Twenty three (23) deaths occurred among HIV-infected participants, with 10 in the immediate ART arm and 13 in the delayed ART arm.

## HPTN 052: The Way Forward

All of the Institutional Review Boards/Ethics Committees overseeing the study and the study participants have been notified of these results. Initiation of ART has been offered to all participants in the delayed ART arm. All participants in the study will continue to be followed for at least one more year. The results of HPTN 052 are being used to generate new WHO policies related to the management of HIV discordant couples. The results support ongoing studies in the HPTN network that include the use of treatment of HIV infection as part of a cohesive, combination HIV-prevention strategy.

## Additional Background

HPTN 052 is being conducted by the HIV Prevention Trials Network (HPTN). The HPTN is funded by the Division of AIDS (DAIDS)/US National Institute of Allergy and Infectious Diseases (NIAID)/US National Institutes of Health (NIH). Myron S. Cohen, MD, HPTN investigator at the University of North Carolina at Chapel Hill, North Carolina, is the Protocol Chair.

Study drugs are provided free of charge by Abbott Laboratories; Boehringer Ingelheim Pharmaceuticals, Inc.; Bristol-Myers Squibb; Gilead Sciences, Inc.; GlaxoSmithKline; and Merck & Co., Inc.

To learn more about the HIV Prevention Trials Network, visit [www.hptn.org](http://www.hptn.org).