

STATUS OF THE BOTSWANA TDF2 STUDY OF PRE-EXPOSURE PROPHYLAXIS FOR HIV PREVENTION



About the TDF2 Study

TDF2 is one of several clinical trials around the world working to identify a new strategy to reduce the impact of HIV in Botswana and globally. The study was designed to determine the safety and efficacy of a daily tenofovir-emtricitabine pill (brand name Truvada®) in reducing HIV infection among heterosexual men and women in Botswana — a strategy called pre-exposure prophylaxis, or PrEP. Approximately 1,200 people are enrolled in the trial. The study is being conducted by BOTUSA, a partnership between the Botswana Ministry of Health and the U.S. Centers for Disease Control and Prevention.

Planned Changes to the Study

The TDF2 study will be adapted due to unanticipated challenges that make it very unlikely that the trial will be able to determine if tenofovir-emtricitabine is effective in reducing the risk of HIV infection. The trial protocol and timeline will be revised to focus instead on the other remaining study questions — primarily behavioral and clinical safety and adherence. The study's independent data safety and monitoring board has conducted ongoing evaluations of safety data, and has identified no safety concerns to date.

While the trial met its original enrollment goals, this study will not be able to determine efficacy given much lower than anticipated HIV incidence in the study population (likely due to declining HIV rates in Botswana generally, and to extensive HIV prevention services provided to all participants), and challenges in retaining participants in this highly mobile population of young adults.

While trial expansion was considered as a potential solution, after a thorough analysis, CDC determined that even with a doubling of participants to 2,400, it would be unlikely that a valid efficacy result could be obtained due to the lack of required retention to date.

Low retention rates have been due to many factors, including: participants moving out of area; pregnancies; and time requirements that some participants felt were too great. BOTUSA has taken extensive steps to overcome these challenges, including adding weekend clinic hours, increasing participant reimbursements, and strengthening participant education and retention procedures. While these efforts have resulted in significant improvements in retention, a valid efficacy result could still not be assured.

The trial, however, will provide critical information on safety and adherence to help guide potential implementation planning should PrEP prove effective in other trials.

Next Steps

CDC has developed a proposal for how best to complete the safety and adherence portions of the trial and ensure necessary follow-up and communication to all trial participants.

The original timeline for completion called for participant involvement for 12 months after the study was fully enrolled. It may now be possible to shorten the time requirements for participants while still securing the necessary data to address critical safety and adherence questions. Proposed plans are being discussed and finalized with the Botswana Ministry of Health, as well as with participant and community advisory boards. Final plans will then be submitted for approval to the scientific and ethical review boards in Botswana and the U.S. in January 2010.

CDC's Partnership with Botswana

CDC remains committed to HIV prevention research and to its long-standing partnership with Botswana on critical health issues. CDC expects to complete the safety and adherence analyses from this study by the end of 2010. CDC will also continue its nearly \$60 million commitment to the implementation of HIV prevention and treatment services in Botswana through the U.S. President's Emergency Plan for AIDS Relief (PEPFAR), and will continue other research projects on TB and HIV co-infection.