ABSTRACT

Importance Antiretroviral preexposure prophylaxis (PrEP), using tenofovir disoproxil fumarate (TDF) and combination emtricitabine/tenofovir disoproxil fumarate (FTC+TDF), is efficacious for prevention of human immunodeficiency virus (HIV) acquisition. PrEP could reduce periconception HIV risk, but the effect on pregnancy outcomes is not well defined.

Objective To assess pregnancy incidence and outcomes among women using PrEP during the periconception period.

Design, Setting, and Participants Randomized trial among 1785 HIV-serodiscordant heterosexual couples (the Partners PrEP Study) in which the female partner was HIV uninfected that demonstrated that PrEP was efficacious for HIV prevention, conducted between July 2008 and June 2013 at 9 sites in Kenya and Uganda.

Interventions Daily oral TDF (n = 598), combination FTC+TDF (n = 566), or placebo (n = 621) through July 2011, when PrEP demonstrated efficacy for HIV prevention. Thereafter, participants continued receiving active PrEP without placebo. Pregnancy testing occurred monthly and study medication was discontinued when pregnancy was detected.

Main Outcomes and Measures Pregnancy incidence, birth outcomes (live births, pregnancy loss, preterm birth, congenital anomalies), and infant growth.

Results A total of 431 pregnancies occurred. Pregnancy incidence was 10.0 per 100 person-years among women assigned placebo, 11.9 among those assigned TDF (incidence difference, 1.9; 95% CI, −1.1 to 4.9 [$P = .22$ vs placebo]), and 8.8 among those assigned FTC+TDF (incidence difference, −1.3; 95% CI, −4.1 to 1.5 [$P = .39$ vs placebo]). Before discontinuation of the placebo treatment group in July 2011, the occurrence of pregnancy loss (96 of 288 pregnancies) was 42.5% for women receiving FTC+TDF compared with 32.3% for those receiving placebo (difference for FTC+TDF vs placebo, 10.2%; 95% CI, −5.3% to 25.7%; $P = .16$) and was 27.7% for those receiving TDF alone (difference vs placebo, −4.6%; 95% CI, −18.1% to 8.9%; $P = .46$). After July 2011, the frequency of pregnancy loss (52 of 143 pregnancies) was 37.5% for FTC+TDF and 36.7% for TDF alone (difference, 0.8%; 95% CI, −16.8% to 18.5%; $P = .92$). Occurrence of preterm birth, congenital anomalies, and growth throughout the first year of life did not differ significantly for infants born to women who received PrEP vs placebo.

Conclusions and Relevance Among HIV-serodiscordant heterosexual African couples, differences in pregnancy incidence, birth outcomes, and infant growth were not statistically different for women receiving PrEP with TDF alone or combination FTC+TDF compared with placebo at conception. Given that PrEP was discontinued when pregnancy was detected and that CIs for the birth outcomes were wide, definitive statements about the safety of PrEP in the periconception period cannot be made. These results should be discussed with HIV-uninfected women receiving PrEP who are considering becoming pregnant.