ABSTRACT

Abstract BACKGROUND: Antiretroviral pre-exposure prophylaxis (PrEP), with daily oral tenofovir disoproxil fumarate or tenofovir disoproxil fumarate in combination with emtricitabine, has been shown to be efficacious for HIV-1 prevention. Although the use of more than one antiretroviral agent is essential for effective HIV-1 treatment, more than one agent might not be required for effective prophylaxis. We assessed the efficacy of single-agent tenofovir disoproxil fumarate relative to combination emtricitabine plus tenofovir disoproxil fumarate as PrEP. METHODS: We did a randomised, double-blind, placebo-controlled three-group phase 3 trial of daily oral tenofovir disoproxil fumarate and emtricitabine plus tenofovir disoproxil fumarate PrEP in HIV-1 uninfected individuals in heterosexual HIV-1 serodiscordant couples from Kenya and Uganda. After an interim review, the trial's placebo group was discontinued and thereafter the active groups were continued, and participants initially randomly assigned to placebo were offered rerandomisation in a 1:1 ratio to tenofovir disoproxil fumarate or emtricitabine plus tenofovir disoproxil fumarate as PrEP. The primary endpoints were HIV-1 seroconversion and safety. This trial is registered with ClinicalTrials.gov, number NCT00557245. FINDINGS: 4410 (99·6%) of 4427 couples received tenofovir disoproxil fumarate or emtricitabine plus tenofovir disoproxil fumarate and were followed up for HIV-1 acquisition. Of 52 incident HIV-1 infections, 31 occurred in individuals assigned tenofovir disoproxil fumarate (incidence 0·71 cases per 100 person-years) and 21 were in those assigned emtricitabine plus tenofovir disoproxil fumarate (0·48 cases per 100 person-years); HIV-1 incidence in the placebo group until discontinuation was two cases per 100 person-years. HIV-1 prevention efficacy with emtricitabine plus tenofovir disoproxil fumarate was not significantly different from that of tenofovir disoproxil fumarate alone (hazard ratio [HR] 0·67, 95% CI 0·39-1·17; p=0·16). Detection of tenofovir in plasma samples, compared with no detection and as measured in seroconverters and a subset of non-seroconverters, was associated with an 85% relative risk reduction in HIV-1 acquisition for the tenofovir disoproxil fumarate group (HR 0·15, 95% CI 0·06-0·37; p<0·0001) and 93% for the emtricitabine plus tenofovir disoproxil fumarate group (0·07, 0·02-0·23; p<0·0001). No significant differences were noted in the frequency of deaths, serious adverse events, or serum creatinine and phosphorus abnormalities between the two groups. INTERPRETATION: These results do not rule out the potential for a slight difference in HIV-1 protection with tenofovir disoproxil fumarate compared with emtricitabine plus tenofovir disoproxil fumarate, but show that once-daily oral tenofovir disoproxil fumarate or emtricitabine plus tenofovir disoproxil fumarate regimens both provide high protection against HIV-1 acquisition in heterosexual men and women.