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Articles

Daily and non-daily pre-exposure prophylaxis in African women (HPTN 067/ADAPT Cape Town Trial): a randomised, open-label, phase 2 trial

Prof Linda-Gail Bekker MD [a], Surita Roux MBChB [b], Elaine Sebastien RNRM [a], Ntando Yola PgDPH [a], K Rivet Amico PhD [c], Prof James P Hughes PhD [d, k], Mark A Marzinke PhD [e, j], Craig W Hendrix MD [e], Prof Peter L Anderson PharmD [f], Vanessa Elharrar MD [g], Michael Stirratt PhD [h], James F Rooney MD [i], Estelle Piwowar-Manning MT(ASCP) [j], Prof Susan H Eshleman MD [j], Laura McKinstry MPH [k], Maoji Li MMath [k], Bonnie J Dye MPH [l], Robert M Grant MD [m], HPTN 067 (ADAPT) study team

Summary

Background

The relative feasibility and acceptability of daily versus non-daily dosing of oral HIV pre-exposure prophylaxis (PrEP) among women are unknown. We aimed to investigate the feasibility of non-daily PrEP regimens in adult women.

Methods

We did a randomised, open-label, phase 2 clinical trial (HPTN 067/ADAPT) of oral PrEP with emtricitabine plus tenofovir disoproxil fumarate at a research centre in Cape Town, South Africa. Participants were adult women (age ≥18 years) who received directly observed dosing once a week for 5 weeks followed by random assignment (1:1:1) at week 6 to one of three unblinded PrEP regimens for self-administered dosing over 24 weeks: daily; time-driven (twice a week plus a post-sex dose); or event-driven (one tablet both before and after sex). Primary outcomes were PrEP coverage (at least one dose within the 4 days before sex and one dose within 24 h after sex), pills needed or used to achieve regimen-specific adherence and coverage, and symptoms and side-effects. All analyses were by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT01327651; the trial is completed and this report presents the final analysis.

Findings

Between Sept 12, 2011, and Oct 3, 2012, 191 women were enrolled to the trial. 178 (93%) completed directly observed dosing and were randomly assigned one of the three PrEP regimens for the self-administered phase: 59 were allocated the daily regimen, 59 the time-driven regimen, and 60 the event-driven regimen. Median age of women was 26 years (IQR 21–37; range 18–52). In women allocated the daily regimen, 1459 (75%) of 1952 sex events were covered by PrEP, compared with 599 (56%) of 1074 sex events among those assigned the time-driven regimen (odds ratio [OR] 2·35, 95% CI 1·43–3·83; p=0·0007) and 798 (52%) of 1542 sex events among those allotted the event-driven regimen (2·76, 1·68–4·53; p<0·0001). Fewer pills were needed for complete adherence in women allocated non-daily regimens (*vs* daily regimen, relative mean 2·53 [95% CI 2·39–2·69] for the time-driven regimen and 4·16 [3·59–4·82] for the event-driven regimen; p<0·0001). Side-effects were uncommon. Eight HIV seroconversions occurred overall, with four documented during the self-administered phase (two with the time-driven regimen and two with the event-driven regimen). Adherence to the assigned regimen was 75% (7283 of 9652 doses taken) for women allocated the daily regimen compared with 65% for those assigned the time-driven regimen (2367 of 3616 doses taken; p=0·0028) and 53% for those allotted the event-driven regimen (1161 of 2203 doses taken; p<0·0001). When sex was reported in the previous week, PrEP drugs were detected (above the lower limits of quantification) more frequently in women assigned the daily regimen (73 [68%] of 107 samples) than in those allocated the time-driven regimen (42 [58%] of 72 samples) and the event-driven regimen (41 [41%] of 99 samples).

Interpretation

Daily PrEP dosing resulted in higher coverage of sex events, increased adherence to the regimen, and augmented drug concentrations than did either time-driven or event-driven

dosing. These findings support recommendations for daily use of PrEP with oral emtricitabine plus tenofovir disoproxil fumarate in women.

Funding

HIV Prevention Trials Network.

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