

Abstract

BACKGROUND: Most people infected with HIV-1 are dually infected with herpes simplex virus type 2. Daily suppression of this herpes virus reduces plasma HIV-1 concentrations, but whether it delays HIV-1 disease progression is unknown. We investigated the effect of acyclovir on HIV-1 progression.

METHODS: In a trial with 14 sites in southern Africa and east Africa, 3381 heterosexual people who were dually infected with herpes simplex virus type 2 and HIV-1 were randomly assigned in a 1:1 ratio to acyclovir 400 mg orally twice daily or placebo, and were followed up for up to 24 months. Eligible participants had CD4 cell counts of 250 cells per mL or higher and were not taking antiretroviral therapy. We used block randomisation, and patients and investigators were masked to treatment allocation. Effect of acyclovir on HIV-1 disease progression was defined by a primary composite endpoint of first occurrence of CD4 cell counts of fewer than 200 cells per microL, antiretroviral therapy initiation, or non-trauma related death. As an exploratory analysis, we assessed the endpoint of CD4 falling to <350 cells per microL. Analysis was by intention to treat. The trial is registered with ClinicalTrials.gov, number NCT00194519.

FINDINGS: At enrollment, the median CD4 cell count was 462 cells per microL and median HIV-1 plasma RNA was 4.1 log(10) copies per microL. Acyclovir reduced risk of HIV-1 disease progression by 16%; 284 participants assigned acyclovir versus 324 assigned placebo reached the primary endpoint (hazard ratio [HR] 0.84, 95% CI 0.71-0.98, p=0.03). In those with CD4 counts \geq 350 cells per microL, aciclovir delayed risk of CD4 cell counts falling to <350 cells per microL by 19% (0.81, 0.71-0.93, p=0.002)

INTERPRETATION: The role of suppression of herpes simplex virus type 2 in reduction of HIV-1 disease progression before initiation of antiretroviral therapy warrants consideration.

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