

# Acyclovir and transmission of HIV-1 from persons infected with HIV-1 and HSV-2.

## Abstract:

Most persons who are infected with human immunodeficiency virus type 1 (HIV-1) are also infected with herpes simplex virus type 2 (HSV-2), which is frequently reactivated and is associated with increased plasma and genital levels of HIV-1. Therapy to suppress HSV-2 reduces the frequency of reactivation of HSV-2 as well as HIV-1 levels, suggesting that suppression of HSV-2 may reduce the risk of transmission of HIV-1. We conducted a randomized, placebo-controlled trial of suppressive therapy for HSV-2 (acyclovir at a dose of 400 mg orally twice daily) in couples in which only one of the partners was seropositive for HIV-1 (CD4 count,  $\geq$  250 cells per cubic millimeter) and that partner was also infected with HSV-2 and was not taking antiretroviral therapy at the time of enrollment. The primary end point was transmission of HIV-1 to the partner who was not initially infected with HIV-1; linkage of transmissions was assessed by means of genetic sequencing of viruses. A total of 3408 couples were enrolled at 14 sites in Africa. Of the partners who were infected with HIV-1, 68% were women, and the baseline median CD4 count was 462 cells per cubic millimeter. Of 132 HIV-1 seroconversions that occurred after randomization (an incidence of 2.7 per 100 person-years), 84 were linked within couples by viral sequencing: 41 in the acyclovir group and 43 in the placebo group (hazard ratio with acyclovir, 0.92, 95% confidence interval [CI], 0.60 to 1.41;  $P=0.69$ ). Suppression with acyclovir reduced the mean plasma concentration of HIV-1 by 0.25 log<sub>10</sub> copies per milliliter (95% CI, 0.22 to 0.29;  $P<0.001$ ) and the occurrence of HSV-2-positive genital ulcers by 73% (risk ratio, 0.27; 95% CI, 0.20 to 0.36;  $P<0.001$ ). A total of 92% of the partners infected with HIV-1 and 84% of the partners not infected with HIV-1 remained in the study for 24 months. The level of adherence to the dispensed study drug was 96%. No serious adverse events related to acyclovir were observed. Daily acyclovir therapy did not reduce the risk of transmission of HIV-1, despite a reduction in plasma HIV-1 RNA of 0.25 log<sub>10</sub> copies per milliliter and a 73% reduction in the occurrence of genital ulcers due to HSV-2. (ClinicalTrials.gov number, NCT00194519.)