

Incidence of genital ulcers and HSV+ genital ulcers in trial of HSV-2 suppression to prevent HIV acquisition (HPTn 039)

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Background: Limited data are available on the response of HSV-2 to acyclovir in resource-poor countries. We analyzed the effect of daily standard dose acyclovir on genital ulcers in a randomized, placebo-controlled trial of HSV-2 suppression to reduce HIV acquisition among women in Africa and MSM in the Americas.

Methods: HIV-negative, HSV-2 seropositive participants were randomized to acyclovir 400 mg bid or placebo with monthly visits for 12-18 months for drug dispensation, adherence and risk reduction counselling, quarterly HIV testing, and HSV DNA Taqman PCR testing of genital ulcer (GU) swabs.

Results: 3172 participants were enrolled: 1814 MSM from US and Peru sites and 1358 women from Zimbabwe, Zambia, and South Africa. At enrolment, 17% of US, 29% Peru MSM, and 26% of women reported genital herpes symptoms in the past 3 months; 3% of men and 21% of women were diagnosed with GU on exam. Over follow-up, HSV-2 DNA was detected in 876/1890 ulcers. Overall GU by exam and history were reduced in the acyclovir arm, RR=0.63, with significant regional differences (RR: 0.51 US, 0.61 Peru, 0.68 Africa). RR for HSV-2 positive GU episodes was 0.36, with significant regional differences (US 0.12; Peru 0.38, Africa 0.41). Reduction in HSV quantity in ulcers was only observed among US MSM. HIV incidence was 3.9/100 person yrs in the acyclovir arm (75 events) and 3.3/100 person-yrs in the placebo arm (64 events), HR=1.16 (95% CI 0.83, 1.62), with no significant difference in HR by past GU history, risk group, or region.

Conclusions: With excellent retention and high drug adherence, standard doses of acyclovir suppressive therapy reduced incidence of GU and HSV-2+ GU, but less than in previous studies and with significant differences by population and region, and did not reduce HIV acquisition. Further work is needed to clarify the etiology of GU and response of HSV-2 to standard therapy in different populations.

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