

Abstract

**Episodic therapy for genital herpes in sub-Saharan Africa: a pooled analysis from three randomised controlled trials**

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**Background** Acyclovir is not widely used to treat genital herpes in sub-Saharan Africa. Three recent randomised controlled trials evaluated the impact of acyclovir on genital HIV-1 RNA and ulcer healing in Africa. In the South African trial, treatment was associated with faster ulcer healing, but no effect was seen in the other trials.

**Methods** We pooled data on the impact of acyclovir (400mg tid in Ghana, Central African Republic and South Africa; 800mg bid in Malawi) on ulcer healing 7 days after randomisation. Data were stratified by HIV status, ulcer aetiology, ulcer size and duration before presentation. Risk ratios (RR) were estimated with Poisson regression with robust standard errors, and Kaplan-Meier analysis for time to ulcer healing.

**Results** Overall, 1478 genital ulcer patients were included in the trials (928 males, 550 females). The majority (64%) presented with herpetic ulcers (16% with first episode HSV-2 ulcers), 29% unknown aetiology, 3% chancroid, 2% syphilis. 58% were HIV-1 seropositive, and 37% had an AIDS defining condition. Overall, patients on acyclovir were more likely to have a healed ulcer on Day 7 (63% vs 57%, RR=1.10, 95%CI 1.00-1.21) and a shorter time to ulcer healing ( $p=0.04$ ). The benefit of acyclovir was largely confined to patients with HSV-2 ulcers (RR=1.22, 95%CI 1.0-1.4), with little effect among those without HSV-2 ulcers (RR=1.05, 95%CI 0.8-1.3). There was some evidence of a stronger impact among HIV-1 positive than HIV negative patients (RR=1.17, RR=1.02, respectively). Small ulcers (<50mm<sup>2</sup>) responded better to treatment, but there was no difference by time before presentation.

**Discussion** The greatest impact was observed in HIV-1 positive patients, those with HSV-2 ulcers, primary genital herpes and small ulcers. However, these factors did not explain the differential results in South Africa. Genital ulcer patients may provide an entry point for HIV testing and care, and possibly for HSV suppressive therapy.