Tenofovir Prevents Acquisition of, but does not Treat HSV-2

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Herpes simplex virus 2 (HSV-2) is the leading cause of genital ulcers worldwide. The lack of symptoms in a high percentage of infected individuals makes it difficult to accurately determine the extent of the epidemic, but estimates range from 10 to 80% infected individuals depending on the country. While in the US HSV-2 infections affect 20-30% of the adult population, the burden is much higher in developing countries. The lack of a vaccine and the frequent lifelong asymptomatic reactivation of the virus complicate the effort to reduce its spread.

Very few therapeutic tools, mainly nucleoside analogues, are available for HSV-2 therapy. Interestingly, it has been shown that the use of tenofovir for pre-exposure prophylaxis (PrEP), a highly effective method of preventing HIV acquisition, is able to reduce HSV-2 acquisition as well. In the CAPRISA 004 study, the efficacy of pericoital use of a gel preparation containing tenofovir to prevent HIV in highly exposed women was tested and a 51% reduction in HSV-2 acquisition was observed along with a 39% reduction in HIV acquisition. Given the anti-HSV-2 activity of tenofovir, Dr. Rachel Bender Ignacio from the Vaccine and Infectious Disease Division (VIDD) at Fred Hutch evaluated the efficacy of tenofovir on reducing HSV-2 shedding and symptomatic genital lesions in
HSV-2 infected women. The results of this study were published last month in the Journal of Infectious Diseases.

The study evaluates viral shedding of viral DNA and lesion rate in 64 women enrolled through the University of Washington Virology Research Clinic during a four-week lead-in phase (where they did not receive treatment) and a five week trial of oral tenofovir, vaginal topical tenofovir or placebo. No statistically significant differences were observed before and during treatment in the oral tenofovir arm overall. However, in highly adherent women, the oral formulation reduced symptomatic and asymptomatic shedding and lesions by about 25%, while both the oral and vaginal gel products reduced viral DNA shed by half a log.

Dr. Bender Ignacio provided the following interpretation of her results: "Despite having evident biologic activity in our study and in prior in vitro studies, neither route of administration of tenofovir resulted in substantial decrease in shedding of transmissible virus nor symptomatic lesions. Systemic toxicities prevent trials of higher doses of oral tenofovir than currently in use for HIV infection; the vaginal applications of tenofovir far exceed the required inhibitory concentrations (IC50) for HSV-2, but still do not prevent viral shedding, likely because herpes reactivation events are initiated in the sacral ganglia, far upstream of where high mucosal drug levels are present. We would therefore support the continued use of tenofovir for prevention of acquisition of HIV and HSV-2 by persons who are uninfected (PrEP), but cannot advocate further study or use of tenofovir to prevent HSV-2 transmission or symptoms in those who are already infected based on these results. Therefore highly efficacious anti-herpes agents such as acyclovir, valacyclovir, or pritelivir, should be studied and considered for clinical use in combination with tenofovir for persons who are HSV-2 infected but desire HIV PrEP. Our findings, despite being largely negative, help us better understand the limitations of the clinical utility of either formulation of tenofovir product."

Given the frequency of HIV and HSV-2 infection and the need for new therapeutic approaches for HSV-2, answering the question of whether a single agent can be used for HIV and HSV therapy was essential. Unfortunately, the results do not support such a use for tenofovir. More research is needed in order to find an effective approach for HIV and HSV-2 co-infections.