



In sub-Saharan Africa, the intersection between the HIV epidemic and the endemic nature of Kaposi's sarcoma-associated herpesvirus (KSHV) infection has caused Kaposi's sarcoma (KS) to become the most common malignancy in the region. In places where highly active antiretroviral therapy (HAART) is readily available (e.g., in the U.S.), use of HAART often causes regression of KS even in the absence of conventional chemotherapy. While little is known about which specific antiretroviral drugs are critical to convey HAART's effect on KS, recent data from *in vitro* systems and animal models suggest that protease inhibitors (PIs), originally developed to block the active site of HIV aspartyl protease, also have direct anti-KS effects above and beyond their effect on HIV.

To address the hypothesis that PI-containing HAART is superior to PI-sparing HAART in promoting KS regression, investigators at the Infectious Diseases Institute and Uganda Cancer Institute in the Mulago Hospital Complex in Kampala, Uganda, in collaboration with the University of California, San Francisco, are conducting an NCI-sponsored randomized trial. This study is comparing a PI-based HAART regimen (lopinavir/ritonavir plus emtricitabine/tenofovir) to a non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimen (efavirenz plus emtricitabine/tenofovir) for the ability to promote the regression of KS in persons with AIDS-related KS. Subjects are followed at four-week intervals for 48 weeks, and the primary outcome is change in KS tumor burden as assessed using the established metric from the NCI-sponsored AIDS Malignancy Consortium.

The study also has several fruitful observational components including to: a) evaluate which pre-treatment parameters are predictive of KS regression on HAART in the African context; b) examine the effect of HAART on KSHV-related virologic activity and host immune response to KSHV, including whether HAART reduces levels of KSHV shedding and infectiousness; and c) investigate KS-associated immune reconstitution inflammatory syndrome (IRIS). The work therefore encompasses the investigation of three entities – KS, KSHV, and HIV – about any of which the scholar can focus his/her research. In addition to the research components, the trial has the primary clinical responsibility for the over 200 participants with HIV and KS, and thus the scholar has the opportunity to observe clinically how antiretroviral drugs can have a powerful impact on individual patients. A scholar is sought to have a high level of responsibility in study implementation, working side-by-side with Ugandan physicians and managing the day-to-day field work.

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