The AIDS Malignancy Consortium (AMC) is a National Cancer Institute (NCI)-supported clinical trials group, founded in 1995 to support innovative trials for AIDS-associated malignancies. The AMC is composed of 15 main Clinical Trials Sites and their affiliates, and an Operations and Statistical Center. The AMC has three disease-focused working groups: Kaposi’s sarcoma (KS), lymphoma, and human papillomavirus (HPV) working groups. They are responsible for developing and implementing therapeutic protocols for these diseases.

Before 1995, primarily the Adult AIDS Clinical Trials Group (AACTG) conducted multicenter AIDS-related cancer trials. In the mid to late 1990’s, there were large numbers of people with KS as well as lymphoma. However, with the success of anti-retroviral regimens following the approval of protease inhibitors, the incidence of KS and some other cancers declined dramatically, and the health and quality of life of many HIV-positive people improved substantially. Thus, shortly after the creation and funding of the AMC by the NCI, enrolling large numbers of people in HIV-related cancer trials became difficult. Consequently, the last few years have seen declining numbers of people entering AMC trials. While the cause of this trend is great news for people living with HIV, it has impeded the progress of this important research. From a basic science perspective, research into the relationship between cancers and viral infections could lead to developments benefiting many people. For instance, research has clearly shown that KS is associated with infection with a virus from the herpes family, the KS-associated herpes virus (KSHV), also known as human herpesvirus 8 (HHV-8).

As a result of a combination of factors, probably including low study enrollment, problems with tracking samples (particularly pathology specimens), inadequate funding for a centralized data collection and management system, and lack of referrals from community oncologists, the NCI has decided not to continue funding the AMC in its current configuration when the grant expires next year. The NCI is only allowing the AMC to conduct a few trials that may fully enroll within a year, but otherwise no new trials will be developed. This is particularly disappointing because no other funded multi-center network is conducting research for these still very important problems. There remains a need for less toxic initial therapy for KS, as well as therapy for people who fail to obtain good control with the firstline KS treatment options currently available. Also, the field of angiogenesis (new blood vessel growth) inhibition is quite new and, because KS is essentially a cancerous proliferation of blood vessels, opportunities exist to find drugs that inhibit blood vessel growth to treat KS and many other cancers.

The optimal treatment of HIV-associated lymphomas is still unknown. Only about half of people with HIV-associated non-Hodgkin’s lymphoma (NHL) achieve long-term remission with initial therapy. Also, a greater proportion of people with HIV are developing Hodgkin’s disease (HD). The treatment outcome of HD is generally much better than NHL, but whether this is the case for HIV-positive
people is unknown. The treatment outcome of primary brain (CNS) lymphoma is still very poor for most people. For people with relapsed lymphoma, bone marrow transplantation may be an option but many questions remain about the efficacy and safety of this treatment in the HIV-infected population.

As several studies have shown, the safety and efficacy of treatment for HIV-associated lymphomas cannot be assumed the same as for similar types of lymphomas in HIV-negative people. Several years ago, research showed that the higher doses of chemotherapy used in HIV-negative people did not increase cure rates in HIV-positive people and were associated with higher rates of serious side effects. More recently, the AMC trial 010 was unable to show that HIV-positive people benefited from the addition of Rituximab (a monoclonal antibody that attacks cancerous lymphoma cells) to a standard chemotherapy regimen. Also, there was a higher rate of infections observed in the people who received Rituximab than expected. The AMC has recently begun a trial, AMC 034, to see if the outcomes observed using infusional chemotherapy regimens in HIV-negative people with lymphoma will be achieved in HIV-positive people as well.

Thus, much research in these areas is still needed. With the NCI not renewing the AMC, where and how will this research be conducted? As attention shifts to the international arena for the treatment of HIV, consideration must be given to the very high incidence of KSHV in Africa. There remain many questions about the association of KSHV and HIV in Africa and what optimal therapy can be effectively implemented in resource-poor settings. The NCI should consider creating a new cooperative network with maximal flexibility for the effective use of funding and for conducting quality research. Alternatively, the AACTG may need to consider re-entering HIV-associated cancer research and adding this area to its scientific agenda.

Lastly, the human papillomavirus (HPV) working group is a relatively new addition to the AMC, and has initiated the development of several protocols under the leadership of Joel Palefsky. However, only part of the research agenda for HPV is focused on cancer development and treatment. Many questions about HPV infection in HIV-positive people must still be answered, including whether to monitor men and women with routine anal pap smears, what is the natural history of precancerous changes from HPV after effective antiretroviral therapy, and what is the best treatment for precancerous and cancerous changes in the peri-anal area. There is a great need for a national HPV cooperative trials network for gathering the data necessary to address these very important issues.

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Patient Fact Sheet on HIV/AIDS malignancies:
centerforaids.org/rita/facts/malignancy.pdf