Today AIDS-associated Burkitt's lymphoma (BL) and atypical BL remain a significant cause of morbidity and mortality in HIV-infected patients the world over and especially in sub-Saharan Africa. While the overall incidence of BL appears to be stable in the backdrop of HIV infection in the current antiretroviral therapeutic era, there is clearly a trimodal age peak that is now observed and is clearly reflective of AIDS association, a predominance of males persists, and improved understanding of pathogenic mechanisms may shed new light on the disease process especially in HIV-infected patients. Importantly, it is clinically well recognized that it is no longer appropriate to consider AIDS-related non-Hodgkin's lymphoma as a single disease entity and rather treatment of AIDS lymphoma needs to be tailored to lymphoma subtype. While intensive therapeutic strategies in the western world are clearly improving outcome, in AIDS epicenters of the world and especially sub-Saharan Africa more pragmatic and risk-adapted approaches are clearly needed. We are also likely entering the era of viral-targeted therapeutic approaches that may be impactful in resource-challenged areas of the world and provide new strategies for disease prevention altogether.