



Making the Case for an HIV Oncology Clinic

Though the incidence of AIDS-defining cancers (Kaposi's sarcoma, non-Hodgkin lymphoma, and invasive cervical carcinoma) has decreased with the use of antiretroviral therapy, numerous studies suggest that non-AIDS-defining cancers (cancers not previously associated with HIV and AIDS) appear to be increasing in incidence.¹⁻⁵ These malignancies have increased as has the proportion of mortality associated with non-AIDS-defining malignancies in patients with HIV.⁶ In fact, cancer prevalence ranges from 7 percent to 15 percent as a cause of mortality in the population with HIV.⁷ It appears that these conditions have an earlier onset and worse prognosis in patients with HIV than in the general cancer population.⁶

Some studies have shown that HIV increases susceptibility to cancers through the direct effects of the virus (genetic instability and increased susceptibility to carcinogens, for instance) and long-term immunosuppression.^{6,8} Other possible contributors to the increased prevalence of non-AIDS-defining cancers are greater prevalence of co-infection with viruses that have etiologic roles in cancer and endothelial cell abnormalities, including the elaboration of angiogenic factors, which could serve to facilitate tumor growth.⁶

Several studies have shown that among the different non-AIDS-defining cancers, solid tumors and hematologic malignancies may be more prevalent in patients with HIV.⁶ A recent review found that the incidence of anal carcinoma, Hodgkin lymphoma, liver cancer, lung cancer, melanoma, oropharyngeal carcinoma, leukemia, colorectal cancer, and renal cancer are greater than in the general population.⁹

A multidisciplinary approach is recommended when treating HIV-positive patients affected with cancer. Pilot projects have been developed and are underway to determine the best approach to efficiently and comprehensively combine the care of the two medical conditions.

It has also been suggested that neither T cell count at the time of diagnosis nor T cell count nadir was predictive of non-AIDS-associated malignancy.⁶ Viral load has also been studied and its influence does not appear to be significant in relation to prevalence of non-AIDS-defining cancers.⁶ Other reviews have revealed that there might be a role for T cell count nadir.^{8,10}

Current studies suggest that patients with HIV-associated non-AIDS-defining cancers, particularly those with robust CD4 counts, should be treated with similar approaches to their HIV-negative counterparts.⁸ However, as discussed below, information on this topic is scarce.⁸

Highly active antiretroviral therapy (HAART), the use of multiple drugs that act on different viral targets, appears to be a protective factor against the appearance of certain non-AIDS-defining cancers (other than Kaposi sarcoma, non-Hodgkin lymphoma, and invasive cervical carcinoma).^{6,8,11} Based on these results, some researchers have suggested that, in view of the fact that newer antiretroviral regimens have more favorable toxicity and better resistance profiles than prior regimens, initiating therapy at higher CD4 cell counts may be a better option for adjuvant treatment.

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Epidemiology

A number of reports indicate that certain types of non-AIDS-defining cancers are higher among persons with HIV than among the general population.^{9,12} The incidence of non-AIDS-defining cancers has increased significantly over the past 10 years and has now surpassed that of AIDS-defining cancers in patients with HIV.¹³ Several malignant conditions, including Hodgkin lymphoma, anal cancer, soft tissue cancer, and multiple myeloma, have been found in increased numbers in patients with HIV.¹² Other reports indicate that anal carcinoma, head and neck carcinoma, testicular cancer, and cancer of lung, colon, skin (basal cell skin carcinoma, squamous cell carcinoma, cell skin carcinoma, and melanoma) have also increased in patients with HIV.^{1,11} Research around other malignancies, such as prostate, breast, and bladder cancer is mixed, with some reporting that these cancers appear to have decreased in the HIV community,⁶ whereas others indicate that these neoplasms appear to have increased in patients with HIV.⁸ Obviously more research and data are needed in relation to the epidemiology of certain types of malignancies.⁸ Table 1, right, is a comparison of standardized incidence rates for non-AIDS-defining malignancies between patients with HIV patients and the general population.¹⁰

Our Program At-a-Glance

Since its inception in 1953, Memorial Healthcare System (mhs.net) has been a leader in providing high-quality healthcare services to South Florida residents. Today, it is one of the largest public

healthcare systems in the nation and highly regarded for its exceptional patient- and family-centered care. Memorial's patient, physician, and employee satisfaction rates are some of the most admired in the country, and the system is recognized as a national leader in quality healthcare.

Memorial Regional Hospital is the flagship facility of the healthcare system and one of the largest hospitals in the state. Memorial Regional Hospital offers extensive and diverse healthcare services that include Memorial Cardiac and Vascular Institute; Memorial Cancer Institute, which treats more inpatients than any other in Broward County; and Memorial Neuroscience Institute.

Memorial Regional Hospital and Memorial Regional Hospital South, both located in Hollywood, Fla., offer a variety of medical and surgical services. Joe DiMaggio Children's Hospital at Memorial provides a comprehensive array of pediatric services and is the leading children's hospital in Broward and Palm Beach counties. Memorial Hospital West, Memorial Hospital Miramar, and Memorial Hospital Pembroke serve the communities of western Broward County and others in South Florida. Memorial Home Health Services, Memorial Manor nursing home, and a variety of ancillary healthcare facilities round out the system's wide-ranging health services.

Memorial Regional Hospital and Memorial Regional Hospital South, both located in Hollywood, Fla., offer a variety of medical and surgical services. The Infectious Disease program, located at Memorial Regional Hospital, offers comprehensive services for the treatment of HIV/AIDS, hepatitis B and C, and other healthcare or travel-related illnesses. The Ryan White Program is also part of the Infectious Diseases services at Memorial Healthcare System.

Our Community At-a-Glance

Broward County is in the southeastern part of Florida. As of 2016, the population was 1,909,632, making it the second most populous county in Florida and the 17th most populous in the United States. Its county seat is Fort Lauderdale. Broward County is part of the Miami metropolitan area, which was home to an estimated 6,012,331 people at the 2015 census.¹⁴

Broward County includes 31 municipalities, 5 of which are home to more than 100,000 residents. A diverse county in which racial and ethnic minorities are most of the population, the racial and ethnic breakdown includes 40 percent white or Caucasian, 29 percent black or African American, 27 percent Latino or Hispanic (including individuals of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish descent), and 4 percent categorized as other races. This diverse population represents more than 200 different countries and 130 different languages. One-third (31.8 percent) of Broward's residents are foreign-born, which is a higher rate than the Florida average. In addition, 44.3 percent of foreign-born residents are not U.S. citizens.¹⁴

According to the U.S. Census Bureau's 2014 American Community Survey, the Broward County median household income was \$51,608.¹⁴ The percentage of families whose income was

Table 1. Comparison of Standardized Incidence Rates for Non-AIDS-Defining Malignancies Between Patients with HIV and the General Population⁹

Malignancy	Patients with HIV (Standardized Incidence Rate per 100,000 Person-Years; 2000–2003)	General Population (Standardized Incidence Rate per 100,000 Person-Years; 2000–2003)
Anal carcinoma	78.2	1.3
Colorectal cancer	66.2	21.1
Hodgkin lymphoma	64.4	3.6
Liver cancer	35.4	4.7
Lung cancer	84.9	23.4
Melanoma	37.5	9.9
Oropharyngeal cancer	36.9	11.7

below the poverty level in the past 12 months was 11.3 percent. Almost one-fifth (18.8 percent) of Broward residents 18-24 years of age earned less than a high school diploma. Eighty-eight percent of persons aged 25 and older attained a high school diploma or higher and 30.5 percent attained a bachelor's degree or higher. Overall, 18 percent of Broward residents had no health insurance coverage in 2014; 10 percent of those were 18 years of age or younger, and 24 percent were 18-64 years of age. The 2014 American Community Survey reports that 59.5 percent of Broward residents have private health insurance, 19.7 percent have either Medicare or Medicaid, and 18 percent are uninsured.¹⁴

According to the CDC 2014 HIV Surveillance Report, Florida ranked second among states in the number of HIV infection cases with 5,332 estimated cases reported.¹⁵ Broward County is part of the Miami-Fort Lauderdale-West Palm Beach, Fla., metropolitan service area, which accounts for 47.5 percent of Florida's HIV infection cases. When examining the service area by HIV infection case rate per 100,000 persons, Broward ranks second in the United States (44.7) just behind Miami (49.9), which ranks first. HIV prevention and service funds have not been equitably distributed to Broward. Though the Centers for Disease Control and Prevention, HIV/AIDS Bureau, and other federal agencies have targeted funds to address the Miami-Dade HIV epidemic, Broward's epidemic receives limited funding, reflecting a lack of understanding of the impact of the HIV epidemic in Broward and the need for targeted funds to address prevention and care efforts. Broward's proximity and juxtaposition between Miami and Palm Beach counties allow for cross-county social networking that can increase this region's risk of HIV transmission. Broward's population of people living with HIV/AIDS differs from the rest of the state, with a larger percentage of men who have sex with

men living with HIV (56 percent) compared to the state of Florida (48 percent). These data support the need to have and evaluate targeted programs and interventions designed for the diverse gay and bisexual community of Broward County.¹⁴

A Changing Demographic in Our Community

Over the past 10 years, the proportion of newly diagnosed adult HIV cases has increased among those aged 20-29 by 10 percentage points. HIV infection trends show that adults 50 years or older are the fastest growing segment of the adult population of Broward living with HIV/AIDS. The aging population, immigration of males who have sex with males, and Broward County's popularity as a retirement community contribute to the rate of older people living with HIV/AIDS as evidenced by a 9 percentage point increase from 2005 to 2014 among the 50 and over age group. In contrast, the proportion of newly diagnosed adult HIV cases among those aged 30-39 and 40-49 decreased by 9 and 11 percentage points, respectively, over the same period. The 13-19 age group remained relatively level during this time, with a 1 percentage point increase from 2005 to 2014.¹⁵

Models of Care in HIV Oncology

In a systematic review, Sigfrid and colleagues looked at the experience of pilot programs integrating HIV and oncology services for cervical cancer patients infected with HIV.¹⁶ The authors identified three distinct models of integration:

1. Integration within the same clinic through training of existing staff
2. Integration through co-location of services
3. Integration through complex coordination across the care pathway.

However, several barriers were reported, including high loss to follow-up for further treatment, limited human resources, and logistical and supply chain management support.¹⁶ Complex integration in a single visit was shown to reduce loss to follow-up. The use of existing health infrastructure and funding together with comprehensive staff training and supervision, community engagement, and digital technology were some of the many other facilitators for integration reported across models.¹⁶ However, the descriptive nature of most papers and lack of data on the effect on long-term outcomes for HIV or cervical cancer limits the inference on the effectiveness of the integrated programs. There is a need for strengthening of health systems across the care continuum and for high-quality studies evaluating the effect of integration on HIV as well as cervical cancer outcomes.

The Infectious Disease Clinic at Memorial Regional Hospital started the screening process of identifying patients with malignancies and cancer in September 2017. The number of patients currently served by this clinic is approximately 1,000 patients.

In another review, Haldane et al. included studies that reported service integration for HIV and/or AIDS with coronary heart diseases, chronic cardiovascular disease, cerebrovascular diseases (stroke), hypertension, or diabetes.¹⁷ Models looked at integration from micro (patient-focused integration) to macro (system-level integration). Most reported integration of hypertension and diabetes with HIV and AIDS services and described multidisciplinary collaboration, shared protocols, and incorporating screening activities into community campaigns.¹⁷ Integration took place exclusively at the mesolevel (institution), with no microlevel (patient) or macrolevel (systems) integrations described. Integration should build on existing protocols and use the community as a locus for advocacy and health services, while promoting multidisciplinary teams, including greater involvement of pharmacists. There is a need for robust and well-designed studies at all levels—particularly macrolevel studies, research looking at long-term outcomes of integration, and research in a more diverse range of countries.¹⁷

In another study conducted in Uganda, Kumakech and colleagues identified healthcare provider perceptions in relation to integrating cancer screening services in HIV/AIDS clinics. Three themes emerged from these data¹⁸:

1. Appreciating benefits of integration
2. Worrying about the limited health system capacity and potential consequences of integration

3. Feeling optimistic about integration under improved health system conditions.

There were also worries that HIV stigma and shortage of health-care workers would affect the effective delivery of the integrated program.¹⁸

Another example is provided by Haberlen et al., who reviewed the logistics of integrating family planning services in patients with HIV. A body of evidence supports the feasibility, benefits, and potential cost-effectiveness of integrating family planning into HIV care and treatment services in a range of settings. However, the quality of the evidence of effectiveness is modest. Furthermore, some integration efforts demonstrate that improving access is not sufficient to improve the uptake of more effective contraceptive methods among women living with HIV who want to avoid pregnancy. Integration, particularly in contexts where the use of effective contraception is low, must address the cultural and gender norms that impact women's decision making regarding family planning alongside improving access to family planning information and services within routine HIV care.¹⁹

Starting Up an HIV Oncology Clinic

With these studies and experiences as a foundation, in 2016 Memorial Healthcare System established a working group comprised of representatives from the Oncology and Infectious Diseases departments, physician managers, administrators, and patient advocates. Based on historical cohorts of patients with HIV, the prevalence of cancer, and the patient population seen in Memorial Regional Hospital's Infectious Disease Clinic, the working group expected and found a significant number of oncology and hematology patients being treated at the clinic. Another reason these numbers were so high: Memorial's Infectious Disease Clinic is a referral center.

The working group surveyed these patients and found that they welcomed the idea of having a multidisciplinary HIV Oncology Clinic in the Infectious Disease Clinic. A provider survey also showed that an interdisciplinary approach would be beneficial in the treatment of this patient population. Based on these survey results, the working group was able to meet with and obtain buy-in from senior physician group administrators. Next, a series of group discussions was held with providers, patients, administrators, and executives, so that these stakeholders could provide input and help guide the working group in the development and implementation of the HIV Oncology Clinic.

The Infectious Disease Clinic at Memorial Regional Hospital started the screening process of identifying patients with malignancies and cancer in September 2017. The number of patients currently served by this clinic is approximately 1,000 patients. Patient demographics include 62 percent male patients and 38 percent female patients; approximately 25 percent of newly diagnosed patients are over 50. To date, 30 patients have been identified as having both HIV and malignancies and/or cancer. The distribution of cases includes 70 percent of patients with hematologic malignancies (six cases of Burkitt lymphoma, eight cases of diffuse large B cell lymphoma, five patients with Hodgkin lymphoma, and two patients with multiple myeloma) and 30 percent of patients with solid malignancies (seven patients with

lung cancer, one patient with colon cancer, and one patient with breast cancer).

The HIV Oncology Clinic devotes one half-day clinic to the care of these patients in Memorial Regional Hospital's Infectious Disease Clinic every Friday. In addition to traditional oncology care, these patients also receive education on HIV infections and cancer—basic information on staging, prognosis, chemotherapy agents, and targeted therapy.

The HIV Oncology Clinic is staffed by an infectious disease provider, a hematologist/oncologist, an infectious disease nurse practitioner, a medical assistant case manager, social services, psychology, and office clerks. This half-day clinic offers patients the opportunity to meet with a multidisciplinary cancer care team. At this point in time, social work, case management, psychology, and navigators are available to patients. Imaging studies and cancer registry is also available if needed. Between four to six patients are seen in the half-day HIV Oncology Clinic. New patients are allotted one-hour slots; follow up patients are scheduled for 30 minutes.

Family members are allowed and encouraged to attend. The medical assistant and office staff gather patient medical records and identify and upload necessary medical documentation, including imaging studies, labs, etc. At the half-day HIV Oncology Clinic, the multidisciplinary team conducts patient management and treatment. If chemotherapy interventions are needed, these are scheduled at Memorial Regional Hospital Cancer Institute or Memorial Hospital West Cancer Institute. (The Memorial Regional Cancer Institute is located one block from the HIV Oncology Clinic.)

After their visit to the HIV Oncology Clinic, patients are followed by navigators and non-physician providers (the nurse practitioner and medical assistant) to ensure that appropriate studies are completed; for example, imaging studies or laboratory workup. Nurse practitioners and medical assistants at Memorial Regional Cancer Institute or Memorial West Cancer Institute also help follow up with these patients, when necessary.

Radiation oncology services are provided at both Memorial Regional Cancer Institute and Memorial West Cancer Institute. Care coordination between radiation oncology services and the HIV Oncology Clinic is smooth, with active communication around patient scheduling, follow-up, and management. Surgical oncology is also involved in the HIV Oncology Clinic as needed.

Two case studies below better illustrate the flow of the HIV Oncology Clinic.

HIV Oncology Clinic Case Studies

A 42-year-old patient with a diagnosis of HIV infection in the past (more than five years ago) with no active treatment presented to the Infectious Disease Clinic. In the initial assessment, the patient complained of constitutional symptoms (fever, night sweats, and weight loss) accompanied by a 5-cm neck mass with many 2- to 3-cm neck masses. After evaluation by an infectious disease provider, the patient was evaluated by a hematologist/oncologist. The patient was subsequently admitted to the Memorial Hospital West Emergency Room for workup.

The patient was found to have advanced stage highly aggressive lymphoma (double hit lymphoma) with an International Prognostic Index score of 3. The patient was started on chemotherapy with DA-EPOCH-R during the same hospitalization with intrathecal chemotherapy. Discharged home, the patient's treatment plan is to finish six cycles of chemotherapy with central nervous system prophylaxis followed by an autologous bone marrow transplant.

More studies are needed to assess risk and associated factors for non-AIDS-defining cancers. The frequency of these conditions in the population with HIV needs to be accurately determined to direct efforts for decreasing prevalence.

This case illustrates the multidisciplinary approach in the HIV Oncology Clinic. The patient was seen expeditiously the same day and a clinical decision to expedite care was done immediately. The patient benefited from the rapid intervention and hospitalization to initiate treatment. HIV therapy was also started while the patient was in the hospital.

In our second case study, a 55-year-old female patient (an established patient in the Infectious Disease Clinic) was seen at the HIV Oncology Clinic for persistent cough for two months, no constitutional symptoms, and occasional chest discomfort. After evaluation by the hematologist/oncologist, imaging studies were immediately ordered. A mass in the lung with mediastinal lymphadenopathy was found. A biopsy was scheduled and an evaluation by radiation oncology was requested. The biopsy showed adenocarcinoma of lung, stage IIIB. Chemoradiation was promptly started. The patient is currently followed up in the HIV Oncology Clinic.

This seamless and rapid care coordination with radiology, pathology, and radiation oncology is another example of the multidisciplinary approach of the HIV Oncology Clinic.


Future Research and Directions

More studies are needed to assess risk and associated factors for non-AIDS-defining cancers. The frequency of these conditions in the population with HIV needs to be accurately determined to direct efforts for decreasing prevalence.

Effective screening and treatment options need to be established. It is crucial that we get a better understanding of the interactions among chemotherapy, HAART, and other medications used by patients with HIV. The role of more aggressive chemotherapy regimens and an earlier start of HAART therapy in patients who have non-AIDS-defining cancers needs to be clarified. Whether the same chemotherapy regimens could be applied with

success in the population with HIV is still debatable. The role of a higher relapse rate in patients with HIV needs to be verified with inclusion of patients with HIV in clinical trials.

Immunotherapy has been recently added in the armamentarium of melanoma and lung cancer. Reports of the treatment of patients with HIV with immunotherapy showed benefit in this population. Clinical trials of checkpoint inhibitors in melanoma and lung cancer and patients with HIV are undergoing. Good responses to these agents have been documented in non-small cell lung cancer and HIV infection. The use of immunotherapy opens many opportunities for use of targeted therapy in populations with HIV.

As we progress in our study of the frequency of non-AIDS-defining malignancies, prevention will be an important tool against these problems. The creation of integrated oncology and infectious diseases working groups for clinical and research purposes is one possible approach to this problem. Another avenue for exploration could be the formulation of specific guidelines for this patient population. When it comes to the aging population with HIV, these suggestions may be even more important because these patients may be at a higher risk of developing these malignancies. Bottom line: research into these issues is needed to prepare for what could be a new epidemic. 

Marco A. Ruiz, MD, is an attending physician, Hematology Oncology, Bone Marrow Transplant at Moffit at Memorial Healthcare System, Hollywood, Fla.

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