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High Cancer-Related Mortality in an Urban, Predominantly African-American, HIV-Infected Population

David J. Riedel, MD^a, Evelyn Ivy W. Mwangi, MBChB, MPH, Lori E. Fantry, MD, MPH, Carla Alexander, MD, Mian B. Hossain, PhD, C. David Pauza, PhD, Robert R. Redfield, MD, and Bruce L. Gilliam, MD

Institute of Human Virology and Division of Infectious Diseases, University of Maryland School of Medicine, Baltimore, MD, USA 21201

Abstract

Objective—To determine mortality associated with a new cancer diagnosis in an urban, predominantly African-American, HIV-infected population.

Design—Retrospective cohort study.

Methods—All HIV-infected patients diagnosed with cancer between January 1, 2000 and June 30, 2010 were reviewed. Mortality was examined using Kaplan Meier estimates and Cox proportional hazards models.

Results—There were 470 cases of cancer among 447 patients. Patients were predominantly African-American (85%) and male (79%). Non-AIDS-defining cancers (NADC, 69%) were more common than AIDS-defining cancers (ADC, 31%). Cumulative cancer incidence increased significantly over the study period. The majority (55.9%) were taking antiretroviral therapy (ART) at cancer diagnosis or started afterwards (26.9%); 17.2% never received ART. Stage 3 or 4 cancer was diagnosed in 67%. There were 226 deaths during 1,096 person years of follow up, yielding an overall mortality rate of 206 per 1,000 person years. The cumulative mortality rate at 30 days, one year, and two years was 6.5%, 32.2%, and 41.4%, respectively. Mortality was similar between patients on ART whether they started before or after the cancer diagnosis but was higher in patients who never received ART. In patients with a known cause of death, 68% were related to progression of the underlying cancer.

Conclusions—In a large cohort of urban, predominantly African-American patients with HIV and cancer, many patients presented with late stage cancer. There was substantial 30-day and two-year mortality, although ART had a significant mortality benefit. Deaths were most often caused by progression of cancer and not from another HIV- or AIDS-related event.

Keywords

HIV; AIDS; cancer; mortality; non-AIDS defining cancer; AIDS-defining cancer; malignancy; urban

Introduction

HIV infection increases the risk of certain malignancies [1-4]. Three cancers (Kaposi sarcoma, non-Hodgkin lymphoma, and invasive cervical cancer) are considered AIDS-

^aCorresponding Author: David J. Riedel, MD, Institute of Human Virology and Division of Infectious Diseases, University of Maryland School of Medicine. Program in Oncology, University of Maryland Marlene and Stewart Greenebaum Cancer Center, 725 W. Lombard St., N552, Baltimore, MD, 21201, Tel: 410-706-5665, Fax: 410-706-4619, driedel@ihv.umaryland.edu.

defining illnesses [5] and are characterized as AIDS-defining cancers (ADC). With the advent of effective antiretroviral therapy (ART), the incidence of ADCs has declined [6, 7], yet incidence rates remain many times higher than in the non-HIV-infected population [8].

More recently, HIV-infected patients have also been observed to be at higher risk for non-AIDS-defining cancers (NADC) [6, 7, 9, 10]. NADCs include but are not limited to cancers of the lung, liver, oral cavity, anus and Hodgkin lymphoma. These NADCs are increasingly important causes of morbidity and mortality in HIV-infected patients [11-16]. Many cohorts to date have had a small percentage of African-Americans and have not focused on describing causes of death. In order to understand the impact of cancer on survival, it is essential to distinguish between cancer, AIDS-related opportunistic infections (OIs), or other causes of death in these patients.

Despite representing a small proportion (13.6%) of the general U.S. population, African-Americans accounted for 50.3% of new HIV infections during 2005-2008 [17]. In Baltimore city, 85% of HIV/AIDS patients are African-American, and there is a high percentage of late presenters to care (22.1%) [18]. Historically, inferior cancer treatment outcomes have been described both for African-Americans [19-22] and for HIV-infected patients [11]. The impact of cancer on urban, predominantly African-American, HIV-infected patients in the era of highly active antiretroviral therapy (HAART) is understudied, and it is unclear whether cancer screening protocols are adequate for HIV-infected patients from underserved minorities.

The purpose of this study was to characterize the numbers and types of cancers, patient characteristics, mortality, and causes of death among HIV-infected patients in an urban, predominantly African-American population.

Methods

Study Population

The Institute of Human Virology (IHV) provides comprehensive care to approximately 5,000 HIV-infected patients per year at the University of Maryland Medical Center's HIV clinic (UMMC), the IHV Jacques Initiative, Maryland General Hospital (MGH), and Baltimore Veterans Affairs (VA) Medical Center. The outpatient UMMC clinic population is largely African-American (88%; 82% at VA) and predominantly male (56%; 95% at VA). Incidence was calculated for the two largest clinic sites (UMMC and VA), which together comprised 70% of all cancers. The University is a tertiary/quaternary care referral center for patients diagnosed with cancer from around the state of Maryland and surrounding areas. Consequently, cancer incidence could not be calculated because some inpatient cases receive primary HIV care outside our system.

We reviewed all HIV-infected patients diagnosed with invasive cancer from January 1, 2000 to June 30, 2010 at the University and its clinics. Cases were identified by searching electronic clinic records for diagnoses of "cancer," "neoplasm," "malignancy," "tumor," and "lymphoma." The University Clinical Data Repository (CDR) was also searched using ICD9 codes for HIV or AIDS and for any neoplasm. At the VA, the clinical case registry of HIV-infected patients was searched by ICD9 codes for any neoplasm. Institutional Review Boards at each site approved the protocol.

Data Abstraction

Cancer diagnoses were confirmed by pathology or clinician reports and were categorized as ADCs or NADCs. ADCs included Kaposi sarcoma, invasive cervical cancer, and non-Hodgkin lymphomas. NADCs were all other cancers. Subjects diagnosed with incident

cancer as the presenting manifestation of HIV infection were included (i.e. subjects tested for HIV as a result of a new cancer diagnosis); subjects diagnosed with cancer prior to being diagnosed with HIV were excluded (N = 4). Cancer treatments included chemotherapy, radiation, or surgery. When more than one cancer was diagnosed in the same patient (N = 23), only the first cancer was analyzed further.

Demographic and clinical data were abstracted from medical charts. The HIV diagnosis date was defined as either the first positive HIV screening test or clinical documentation of known HIV positivity; if neither was available in the record, the date of the first HIV-specific test (CD4 or RNA viral load) was used. HIV viral load suppression was defined as any HIV viral load less than or equal to 400 copies/ml (assays used over time had varying detection limits from 48 to 400 copies/ml).

Subject status as of June 30, 2010 was recorded as alive, dead or unknown. Survival was calculated from the date of cancer diagnosis to the conclusion of the follow up period (June 30, 2010). Dates and causes of death were recorded if known. Causes of death were obtained from death certificates when patients died in the hospital; causes of death for patients with progressive, metastatic or untreatable cancer who died after hospital discharge to hospice were attributed to the underlying cancer. Social security death index records were checked to ascertain status for patients lost to follow up.

Statistical Analysis

The primary endpoint was mortality after cancer diagnosis. Categorical variables were analyzed using student's t test with a p value of less than 0.05 deemed significant. Survival analysis was conducted using Kaplan-Meier estimates and Cox proportional hazards models for all-cause mortality. Survival curves were compared using log-rank tests. All statistical analyses including data management were carried out using Stata 11.0 (Stata Corporation, College Station, Texas, USA 2009).

Results

A total of 470 cases of cancer were identified among 447 patients (Table 1). The median age at the time of first cancer diagnosis was 50 years (0.2% < 20 years; 4.3% 20-29 years; 12.8% 30-39 years; 31.3% 40-49 years; 37.1% 50-59 years; 14.3% > 60 years). The majority of patients were male (79%) and African-American (85%). The most common risk factor for HIV acquisition was injection drug use (IDU) (39.4%), although heterosexual (30%) and homosexual (17%) contact were also common. The median time from HIV diagnosis to cancer diagnosis was 7 years (range 0-25 years). Thirty-nine patients (8.9%) were diagnosed with HIV within 30 days of their cancer diagnosis; this happened more frequently among patient with ADCs (25 (19.2%)) than among those with NADCs (14 (4.6%)) (P < 0.001).

IDUs were more likely to have NADCs than ADCs (P = 0.004) while men who have sex with men (MSM) were more likely to have ADCs (P = 0.014). Smoking (both current and former) was significantly more frequent in patients with NADCs than ADCs (P = 0.011 for current and 0.017 for former smokers). Hepatitis C infection was more common in NADCs (48.7%) than in ADCs (31.7%) (P < 0.001).

The median CD4 cell count nadir prior to cancer diagnosis was 172 cells/mm³ (Table 1). At the time of cancer diagnosis, the median CD4 cell count was 268.5 cells/mm³, and the median HIV RNA load was 740.5 copies/ml. Patients with ADCs were much more likely to have a CD4 < 200 cells/mm³ and a VL > 100,000 copies/ml than those with NADCs (P < 0.001 for both). The majority of patients (55.9%) were taking ART at the time of cancer diagnosis; ART was started after the cancer diagnosis in 26.9%. However, a substantial

minority (17.2%) never received ART. Patients with NADCs were more likely to be taking ART at the time of cancer diagnosis ($P < 0.001$), whereas patients with ADC were more likely to be initiated on ART after cancer diagnosis ($P < 0.001$).

The distribution of cancers and related HIV characteristics are displayed in Table 2. NADCs (69%) were more common than ADCs (31%). The median CD4 for NADCs was higher than that of ADCs (343 vs. 103 cells/mm³, respectively). The median VL for NADCs was lower than that of ADCs (400 vs. 42,163 copies/ml, respectively).

The cumulative cancer incidence increased over time at both the VA and UMMC clinics (combined in Figure 1); both trends were significant over the ten year time period ($P < 0.05$). Comparison of combined incidence for these two clinics in the first 5 years of the study period (2000-2004) to the second half of the period (2005-2009) showed a 15% increase in cancers ($P = 0.72$). NADCs outnumbered ADCs each year.

The median cancer stage at the time of diagnosis in 313 patients with documented staging was Stage 3; 67% of patients were Stage 3 or 4 (no stage information for Kaposi sarcoma and missing for others).

Overall, 76% of patients received some form of cancer treatment, 22% received no cancer treatment, and 2% were not clearly documented. Cancer treatments included chemotherapy (50%), radiation therapy (37%), and surgery (25%) (categories were not mutually exclusive). There were no overall differences in the percentage of patients with ADCs vs. NADCs who received any cancer treatment. However, surgery and radiation were more frequently utilized in NADCs than ADCs ($P < 0.001$ for each), while chemotherapy was more commonly used in ADCs ($P < 0.001$).

Mortality

Death was associated with progression of the underlying cancer in 68% of cases with a known cause of death (Table 3). Of 30 deaths attributed to HIV/AIDS, 29 were caused by the ADC. Only 5% of total deaths were attributed to infection. Of the patients who died, those with NADCs were more likely to die from their cancer than those with ADCs ($P = 0.001$).

Among the 447 patients diagnosed with cancer, there were 226 deaths during 1,096 person years of follow up time. The overall mortality rate was 206 per 1,000 person years. The cumulative mortality rate within 30 days, at one year, and at two years was 6.5%, 32.2%, and 41.4%, respectively. The 30-day mortality rate was highest for pancreatic cancer (42.9%), cancer of unknown primary (37.5%), Hodgkin lymphoma (22.2%), and liver cancer (21.7%). The two most common cancers (NHL and lung cancer) had high two-year cumulative mortality of 47.1% and 73.4%. The highest two-year cumulative mortality was found in pancreatic cancer (100%), cancer of unknown primary (87.5%), and liver cancer (82.6%). Mortality rates for multiple myeloma and prostate, thyroid, and non-melanoma skin cancer were the lowest throughout the study period.

Mortality was analyzed using both Kaplan-Meier (KM) estimates and Cox proportional hazards models. Mortality was not significantly different whether patients had an ADC compared to an NADC (Figure 2a). KM analysis of ADC mortality with and without no statistical difference from the original analysis depicted in Figure 2a (data not shown). By KM estimates, patients who never received ART were at higher risk for mortality than those who were either on ART at the time of cancer diagnosis or started on ART after cancer diagnosis (Figure 2b). When this data was analyzed for ADCs and NADCs separately, patients not on ART remained at higher risk of mortality ($P = 0.012$ and $P = 0.002$,

respectively) (KM graphs not shown). Similarly, patients with a suppressed VL at the time of cancer diagnosis had lower mortality than those with uncontrolled viral replication (Figure 2c).

In univariate analysis (Table 4), alcohol use, current IDU, HIV VL > 100,000 copies/ml, and both the VA and primary HIV care site outside the University were all significantly associated with mortality. Sex, race, age, smoking, HBV and HCV status, CD4, and type of cancer (ADC vs. NADC) were not associated with increased risk of mortality. Patients who ever had ART had significantly lower mortality than those who never received ART. In the multivariate model, an HIV RNA VL > 100,000 copies/ml remained significantly associated with mortality (adjusted hazard ratio, 2.22; 95% confidence interval (1.31-3.77)). Patients receiving care at other/outside HIV care sites remained at higher risk of mortality (adjusted hazard ratio, 2.38; 95% CI (1.52-3.71)). Ever ART use, current IDU status, and VA site of HIV care were no longer significant in the multivariate analysis.

Eleven percent (50) of patients were lost to follow up (LTFU) before June 30, 2010. These patients were demographically similar (sex, race, and age) compared to the rest of the cohort; however, LTFU patients were more likely to have ADCs and to be followed at outside HIV clinics. Patients with NADCs and those in the VA system were less likely to be LTFU.

Discussion

In this urban, mainly African-American, HIV-infected population from 2000 to mid-2010, there was a trend toward an increasing incidence of cancer. These cancers were more frequently NADCs than ADCs. However, ADCs, and especially NHL, continue to be regularly diagnosed, even in the late HAART era (after 2005). The study population was 85% African-American with a high percentage of IDU (45.6%), a demographic disproportionately affected by the HIV epidemic in the U.S. [17] and often suffering disparate cancer survival outcomes [19].

A significant proportion (8.9%) of the cohort was diagnosed with HIV at the time of cancer diagnosis (usually ADCs). Late presentation of HIV infection has been a persistent problem in the U.S. and is often associated with poor treatment outcomes [23]. Concurrent diagnosis of HIV/AIDS and an ADC can be prevented, underlining the CDC's recommendation to expand HIV screening in the general population [24]. With two-thirds of patients presenting with late stage cancers, HIV providers may need to consider being more aggressive with cancer screening.

The causes of mortality in HIV-infected patients have transitioned from AIDS-related infections and complications of the pre-ART and early ART era of the 1980s and 1990s to primarily non-AIDS events during the HAART era of the late 1990s and 2000s. Malignancy is increasingly recognized as one of the most common causes of death among HIV-infected patients in the later HAART era [14, 26]. In this study, mortality in patients dually diagnosed with HIV and cancer was high: 6.5%, 32.2%, and 41.4%, within 30 days, at one year, and at two years, respectively. The observation that 6.5% of patients died within 30 days of their initial cancer diagnosis likely relates to advanced cancer stage at presentation (67% at stage 3 or 4). Late stage cancer patients are often poor candidates for chemotherapy, referred directly to hospice, or may suffer potentially fatal treatment complications (e.g. tumor lysis syndrome).

The overall 2-year survival of 58.6% in this study was similar to that reported by Achenbach et al [15] in ART-treated patients drawn from a cohort from eight U.S. sites between 1996 and 2009. However, their population was mainly white (52%), and nonwhites had a

statistically nonsignificant higher hazard ratio for death. The University's urban clinics are largely African-American and of lower socioeconomic status with higher rates of substance abuse and hepatitis C infection, a population that often suffers disparate cancer outcomes [20-22]; despite this fact and including some patients who never took ART or received cancer-specific therapy, 2-year survival was comparable to that of patients on ART with cancer around the country [15]. Previous work has demonstrated that racial disparities in cancer outcomes may be mitigated when cancer treatment and medical care is comparable [27]. It is possible that this cohort had similar outcomes due to high engagement in care and multidisciplinary coordination among HIV providers, oncologists, and others.

HIV-infected patients diagnosed with cancer are at high risk of death from a variety of causes, including progression of the underlying cancer, toxic effects related to cancer treatment, infections resulting from cancer treatment-related immunosuppression, as well as AIDS-related opportunistic infections. Accurate determination of the cause of death has important implications for both HIV and cancer management programs. Although a number of studies have documented high rates of mortality from cancer in HIV-infected patients [14, 28] and high mortality rates in dually affected patients with HIV and cancer [7, 15, 29], actual causes of death in dually affected individuals are not well documented. Recently, Worm et al reported from the D:A:D cohort that 88% of deaths in patients with NADC were caused by the underlying cancer [30]. Simard et al have also shown high mortality risk attributable to a cancer diagnosis in AIDS patients at a population level [16]. In the current study, the majority of deaths with a known cause were associated with progression of the underlying cancer. Fewer than 5% of total deaths were attributed to infectious causes. Data was incomplete on a number of patients, which limits the generalizability of this observation. With a better understanding of the natural history of dually diagnosed patients, clinicians can focus on cancer treatment and maintaining ART as keys to prolonging survival.

This study has several limitations. Some malignancies in our clinics may have been missed with retrospective identification of cases; however, by searching both clinic and hospital databases, we increased the probability of including nearly all cases. We excluded non-invasive cancers such as breast ductal carcinoma in situ, anal carcinoma in situ, and cervical intraepithelial neoplasia in order to strengthen the mortality analyses. Since some patient outcomes were unknown, the significance of the Cox proportional hazards model results may be affected by missing data.

Although cases reported here are from a single institution, the outcomes may be representative of urban HIV-infected populations with high numbers of African-Americans and IDUs. Because the University is a referral center and some patients were followed in outside clinics, it was not possible to calculate overall cancer incidence and prevalence rates. Still, in the two main HIV clinics served, there was a significant trend of increasing overall cancer diagnoses over this time period. Factors contributing to an increasing incidence of cancer in our population may include the aging of the general HIV population, older age of the VA HIV population [31], high rates of behavioral cancer risk factors (e.g. smoking) in HIV-infected patients [32], and increased duration of HIV infection with longer periods of HIV viremia [33-35] and immune activation.

In conclusion this study describes the cancers and subsequent outcomes in an urban, predominantly African-American, HIV-infected population. Outcomes were similar to those reported from a national cohort of predominantly white, ART-treated patients. However, the findings reinforce the CDC's recommendation to make HIV screening routine so that patients do not present late with undiagnosed HIV and an AIDS-defining cancer. With two-thirds of patients presenting with stage 3 and 4 disease, it raises the question of whether

cancer screening practices should be the same for HIV-infected patients as for the general population. The data also suggest a survival benefit for patients on ART, which mandates that HIV providers and oncologists work together closely to co-manage these complex patients. With the aging of the HIV population, cancer screening, diagnosis, and treatment will assume increased significance in the years ahead.

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Figure 1. Combined annual cumulative cancer incidence at two HIV clinics (UMMC and VA), by year of diagnosis and ADC vs. NADC.

Figure 2a.
Survival analysis for ADC vs. NADC ($P = 0.477$)

Figure 2b.

Survival analysis comparing patients on ART prior to cancer diagnosis, those started on ART after cancer diagnosis, and those who did not receive ART ($P = 0.0001$).

Figure 2c.

Survival analysis comparing those with suppressed VL (< 400 copies/ml) to those not suppressed (> 400 copies/ml) ($P = 0.004$).

Table 1

Demographic and clinical characteristics at the time of cancer diagnosis (P value tests ADC versus NADC).

Characteristic	Total (N = 447)	ADC (N = 139)	NADC (N = 308)	P value
Median age [years (range)]	50 (19, 77)	42 (19, 67)	52 (25, 77)	
Sex [N (%)]				
Male	354 (79.2)	111 (79.9)	243 (78.9)	0.817
Female	93 (20.8)	28 (20.1)	65 (21.1)	0.817
Race [N (%)]				
African-American	381 (85.2)	115 (82.7)	266 (86.4)	0.317
Caucasian	62 (13.9)	22 (15.8)	40 (13.0)	0.421
Hispanic	4 (0.9)	2 (1.4)	2 (0.6)	0.412
HIV transmission risk factor [N (%)] *				
Heterosexual	134 (30.0)	40 (28.8)	94 (30.5)	0.710
Injection drug use	176 (39.4)	41 (29.5)	135 (43.8)	0.004
MSM	74 (16.6)	32 (23.0)	42 (13.6)	0.014
Transfusion	1 (0.2)	0 (0)	1 (0.3)	0.501
Median duration of HIV infection before cancer diagnosis [years (range)] *	7 (0, 25)	4 (0, 24)	9 (0, 25)	
Site of primary HIV care				
UMMC	192 (43.0)	71 (51.1)	121 (39.3)	0.020
Jacques Initiative	2 (0.5)	0 (0)	2 (0.7)	0.341
Maryland General Hospital	13 (2.9)	4 (2.9)	9 (2.9)	0.979
Baltimore VA Medical Center	119 (26.6)	16 (11.5)	103 (33.4)	<0.001
Outside/Other	121 (27.1)	48 (34.5)	73 (23.7)	0.017
Smoking [N (%)] *				
Current	277 (62.0)	74 (53.2)	203 (65.9)	0.011
Former	84 (18.8)	17 (12.2)	67 (21.8)	0.017
Never	83 (18.6)	45 (32.4)	38 (12.3)	<0.001
Alcohol [N (%)] *				
Current	63 (14.1)	15 (10.8)	48 (15.6)	0.178
Former	157 (35.1)	32 (23.0)	125 (40.6)	<0.001
Never	224 (50.1)	89 (64.0)	135 (43.8)	<0.001
Injection drug use [N (%)] *				
Current	34 (7.6)	12 (8.6)	22 (7.1)	0.582
Former	170 (38.0)	36 (25.9)	134 (43.5)	<0.001
Never	241 (53.9)	89 (64.0)	152 (49.4)	0.004
Hepatitis B infection [N (%)]	36 (8.1)	14 (10.1)	22 (7.1)	0.292

Characteristic	Total (N = 447)	ADC (N = 139)	NADC (N = 308)	P value
Hepatitis C infection [N (%)]	194 (43.4)	44 (31.7)	150 (48.7)	0.001
CD4 cell count (cells/mm ³) [N (%)]				
Median	268.5	103	343	
200	132 (29.5)	69 (49.6)	63 (20.4)	<0.001
201-500	147 (32.9)	34 (24.5)	113 (36.7)	0.011
> 500	65 (14.5)	3 (2.2)	62 (20.1)	<0.001
None recorded	103 (23.0)	33 (23.7)	70 (22.7)	0.814
VL (copies/ml) [N (%)] Median	740.5	42,163	400	
400	141 (31.5)	23 (16.5)	118 (38.3)	<0.001
401-10,000	55 (12.3)	10 (7.2)	45 (14.6)	0.027
10,001-100,000	59 (13.2)	23 (16.5)	36 (11.7)	0.160
> 100,000	49 (11.0)	33 (23.7)	16 (5.2)	<0.001
None recorded	143 (32.0)	50 (36.0)	93 (30.2)	0.226
Antiretroviral therapy				
Taking at time of cancer diagnosis	250 (55.9)	55 (39.6)	195 (63.3)	<0.001
Initiated after cancer diagnosis	120 (26.9)	67 (48.2)	53 (17.2)	<0.001
Never taking	77 (17.2)	17 (12.2)	60 (19.5)	0.060
Cancer treatment				
Any	341 (76.3)	105 (75.5)	236 (76.6)	0.803
Chemotherapy	222 (49.7)	94 (67.6)	128 (41.6)	<0.001
Radiation	163 (36.5)	31 (22.3)	132 (42.9)	<0.001
Surgery	111 (24.8)	8 (5.8)	103 (33.4)	<0.001

MSM, men who have sex with men;

UMMC, University of Maryland Medical Center;

VA, Veteran's Affairs;

VL, HIV-1 RNA viral load

* Missing observations: transmission (62), duration (9), smoking (3), alcohol (3), injection drug use (2).

Table 2

HIV characteristics of patients by specific ADC and NADC at the time of cancer diagnosis.

Cancer type	Observed N=447	Median Age (years)	Median CD4 (cells/mm ³)	Median VL (copies/ml)
<i>AIDS-defining cancer</i>	<i>139 (31.1)</i>	<i>42</i>	<i>103</i>	<i>42,163</i>
Kaposi's sarcoma	44 (9.8)	39.5	93	28,416
Non-Hodgkin lymphoma	90 (20.1)	44	100	74,816
Diffuse large B cell lymphoma	47 (10.5)	44	78	14,992
Primary CNS lymphoma	7 (1.6)	42	6	135,020
Burkitt's lymphoma	23 (5.2)	46	178	131,000
Plasmablastic lymphoma	6 (1.3)	46	256	230,545
Primary effusion lymphoma	1 (0.2)	27	33	-
Castleman's disease	1 (0.2)	38	495	400
Other/unspecified lymphatic	5 (1.1)	46	202	219,000
Invasive cervical	5 (1.1)	45	252	8,796
<i>Non-AIDS-defining cancer</i>	<i>308 (68.9)</i>	<i>52</i>	<i>343</i>	<i>400</i>
Lung	64 (14.3)	54	313	1,958
Small cell	4 (0.9)	55	276	9,519
Adenocarcinoma	22 (4.9)	52	282	2,560
Squamous cell	23 (5.2)	56	375	423
Bronchoalveolar	1 (0.2)	42	579	498
Other non-small cell [*]	14 (3.1)	51.5	239	43,800
Prostate	37 (8.3)	58	447	400
Head and neck	34 (7.6)	52	230.5	554
Liver	23 (5.2)	54	351	400

Cancer type	Observed N=447 (%)	Median Age (years)	Median CD4 (cells/mm ³)	Median VL (copies/ml)
Anal	22 (4.9)	46.5	212.5	494
Hodgkin lymphoma	18 (4.0)	43.5	189	422
Lower gastrointestinal ^{**}	18 (4.0)	51.5	340.5	400
Breast	16 (3.6)	48	445	400
Kidney/Bladder	13 (2.9)	54	417	400
Penis	8 (1.8)	56	332.5	400
Non-melanoma skin	8 (1.8)	46	448.5	400
Cancer of unknown primary	8 (1.8)	53	260.5	4,813
Leukemia	8 (1.8)	50	209.5	428.5
Pancreas	7 (1.6)	51	389	400
Vulvar/vaginal	3 (0.7)	42	17	562
Multiple myeloma	3 (0.7)	50	429	400
Upper gastrointestinal ^{**}	2 (0.4)	52.5	301	400
Thyroid	2 (0.4)	51.5	342	400
Ovarian	2 (0.4)	51	199	1,740
Other [†]	12 (3.8)	53	462	400

* Other non-small cell had no defined subtype.

** Lower gastrointestinal includes colon and rectal cancer; upper gastrointestinal includes stomach and esophageal cancer.

[†] Only one cancer of each type in this category: ureter, leiomyosarcoma, granular cell tumor of hypopharynx, gastrointestinal stromal tumor, appendix, mucinous appendix, esthesioneuroblastoma, carcinoid tumor, and squamous cell cancers of a wound and the perineum.

Table 3

Documented causes of death among HIV-infected patients with cancer who died.

Cause of Death	Observed (%)	ADC	NADC	P value
Cancer	108 (47.8)	0 (0)	108 (67.9)	<0.001
Infection	11 (4.9)	7 (10.5)	4 (2.5)	0.011
HIV/AIDS	1 (0.4)	30 (44.8)	0 (0)	<0.001
Cardiovascular	1 (0.4)	0 (0)	1 (0.6)	0.515
Pulmonary	5 (2.2)	3 (4.5)	2 (1.3)	0.133
Liver	3 (1.3)	1 (1.5)	2 (1.3)	0.888
Other*	1 (0.4)	0 (0)	1 (0.6)	0.515
Unknown	67 (29.7)	26 (38.8)	41 (25.8)	0.050
Total	226 (100)	67 (100)	159 (100)	

* cause of death documented as internal bleeding.

Table 4

Univariate and multivariate Cox proportional hazards models of mortality at cancer diagnosis.

	Hazard ratio (95% CI)	P value	Adjusted Hazard ratio	P value
Age				
40 years (reference)	1.0	—	1.0	—
40-49 years	1.06 (0.73-1.54)	0.77	0.83 (0.49-1.39)	0.48
> 50 years	1.32 (0.93-1.86)	0.12	1.20 (0.69-2.10)	0.52
Sex				
Male (reference)	1.0	—	1.0	—
Female	0.88 (0.65-1.20)	0.40	0.90 (0.58-1.41)	0.66
Race				
White (reference)	1.0	—	1.0	—
Non-White	1.06 (0.74-1.52)	0.75	0.86 (0.52-1.42)	0.55
Site of primary HIV care				
UMMC	1.0	—	1.0	—
JI/MGH *	0.95 (0.37-2.42)	0.91	1.55 (0.39-6.12)	0.53
Baltimore VA Medical Center	1.45 (1.06-1.99)	0.02	1.11 (0.67-1.82)	0.68
Outside/Other	1.85 (1.36-2.52)	<0.01	2.38 (1.52-3.71)	<0.01
Alcohol use				
Never (reference)	1.0	—	1.0	—
Current	1.38 (0.98-1.94)	0.06	0.98 (0.59-1.64)	0.94
Former	1.33 (1.00-1.78)	0.05	1.25 (0.82-1.91)	0.31
Smoking				
Never (reference)	1.0	—	1.0	—
Current	1.38 (0.96-2.00)	0.08	1.54 (0.89-2.73)	0.14
Former	1.02 (0.63-1.65)	0.95	1.12 (0.54-2.31)	0.76
Injection drug use				
Never (reference)	1.0	—	1.0	—
Current	1.64 (1.09-2.45)	0.02	1.14 (0.56-2.30)	0.72
Former	1.27 (0.97-1.67)	0.09	1.19 (0.76-1.84)	0.45
Hepatitis B	1.01 (0.61-1.69)	0.96	1.06 (0.46-2.45)	0.88
Hepatitis C	1.15 (0.89-1.48)	0.30	0.82 (0.53-1.28)	0.39
CD4				
200	1.38 (0.92-2.07)	0.11	1.48 (0.83-2.65)	0.19
201-500	0.84 (0.55-1.27)	0.41	0.83 (0.48-1.43)	0.50
500 (reference)	1.0	—	1.0	—
HIV-1 RNA				

	Hazard ratio (95% CI)	P value	Adjusted Hazard ratio	P value
400	1.0 (ref)	–	1.0	–
401-10,000	1.68 (1.12-2.52)	0.01	1.76 (1.12-2.77)	0.01
10,001-100,000	1.07 (0.70-1.62)	0.75	1.09 (0.65-1.85)	0.74
> 100,000	2.39 (1.54-3.72)	<0.01	1.88 (1.09-3.25)	0.02
Ever on antiretroviral therapy	0.67 (0.46-0.98)	0.04	0.76 (0.41-1.38)	0.36
Cancer type				
NADC (reference)	1.0		1.0	–
ADC	0.93 (0.69-1.23)	0.60	0.86 (0.54-1.37)	0.53

UMMC, University of Maryland Medical Center;

JJ, Jacques Initiative;

MGH, Maryland General Hospital;

VA, Veteran's Affairs

* The two sites were analyzed together in the model due to a low number of patients from each site.