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Time for Oncologists to Opt-In for Routine Opt-Out HIV testing?

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Abstract

Human immunodeficiency virus (HIV) infected individuals are at high risk for malignancies. However, it is not currently standard of care to test routinely all cancer patients for HIV. In 2006, the Centers for Disease Control (CDC) recommended HIV testing in all healthcare settings, calling for standard non-targeted “opt-out” HIV screening. For a variety of reasons, routine opt-out HIV testing is still not widely utilized in the United States. Although many barriers to routine opt-out HIV testing have been addressed, such opt-out HIV testing continues to be conducted primarily in venues which target specific patient populations such as pregnant women. Although opt-out testing has been piloted in emergency departments, less emphasis has been placed on opt-out HIV testing in other clinical settings. We describe the background, rationale, and evidence for supporting opt-out HIV testing as routine care for cancer patients, and discuss evidence for its potential to improve clinical outcomes by facilitating appropriate HIV management during cancer treatment for those individuals who are found to be HIV positive.

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Introduction

Over 1 million individuals in the United States (U.S.) are infected with human immunodeficiency virus (HIV), of which approximately one-quarter are unaware of their HIV status. Surveillance data have consistently shown that HIV infected individuals in the U.S. are diagnosed late in their course of HIV infection, as almost 40% of newly-diagnosed patients progress to clinical acquired immune deficiency syndrome (AIDS) within one year.[1] These statistics are particularly worrisome for cancer patients who are initiating anti-cancer therapies including, surgery, chemotherapy, and radiation. For these patients, because undiagnosed HIV infection may lead to increased cancer treatment-related morbidity and mortality, it would be important to identify them early in their management.

In 2006, the Centers for Disease Control (CDC) released revised recommendations for HIV testing in all health care settings, calling for routine, non-targeted “opt-out” screening for adolescents and adults aged 13 to 64. According to these recommendations, HIV testing would be performed as part of routine medical care unless the patient declined. Specifically, the recommendations call for an end to separate written informed consent for HIV testing and uncouples pre-test HIV prevention counseling from HIV testing.[2] Many physician groups support this approach, including the American College of Physicians (ACP) and American Medical Association (AMA).[3, 4]

In practice, however, this recommendation has not been widely adopted.[5] While certain patient populations, such as pregnant women and more recently, patients presenting for emergency department care, have been targeted for opt-out testing, a routine opt-out approach to HIV testing in general primary care has not yet been realized. We argue that until the practice of opt-out HIV testing is more broadly utilized in the U.S., patients diagnosed with cancer should be included as another targeted group because of the potential to decrease morbidity and mortality by appropriate HIV prophylaxis and treatment. In this article, we review the background for opt-out HIV testing, some of the barriers to its implementation, and its success in specific clinical settings. We then present data to support the argument for routine opt-out HIV testing in patients with cancer.

Revised CDC guidelines for opt-out HIV testing

As stated above, the revised CDC guidelines for HIV testing published on September 22, 2006 recommend that HIV testing be integrated into the general consent for medical evaluation and care, but allows a patient to decline specifically HIV testing.[2] The CDC cited several reasons for revising their HIV testing recommendations. First, risk-based testing for HIV has proven ineffective. Despite multiple encounters with emergency rooms, hospitals, acute care clinics and sexually transmitted disease clinics, persons with HIV infection have been shown to receive HIV testing late in the course of their disease.[2] Early diagnosis of HIV infection is beneficial given the overwhelming evidence for improved survival when highly active antiretroviral therapy (HAART) is initiated early in the course of HIV disease. [6, 7] Second, the CDC noted that universal routine opt-out HIV testing of pregnant women and mandatory HIV-testing of donated blood products substantially decreased the rate of perinatal HIV infection and nearly eradicated transfusion-related HIV infection. Finally, the rate of new HIV diagnoses in the U.S. has not decreased in nearly a decade. Given the evidence that most people substantially reduce risky behaviors when they become aware of their HIV infection, [8] and that HIV transmission risk is reduced in treated patients with virologic suppression,[9] increasing the number of individuals aware of their HIV infection and who have achieved virologic suppression on HAART could decrease HIV transmission rates. Thus, although routine opt-out HIV testing represents an important policy shift, realizing these health benefits will depend on its successful implementation.

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Barriers to routine opt-out HIV Testing

Many barriers have hindered routine widespread implementation of opt-out HIV testing in the U.S.[3] In the past, these have included low levels of physician awareness, lack of reimbursement, as well as state and local laws. Lately, several of these barriers have been removed, including the recent decision by the Centers for Medicare and Medicaid Services (CMS) to reimburse routine HIV testing. In addition, many states have changed, or are in the process of altering, state laws that restrict opt-out testing because of the requirement for separate consent.

However, other obstacles exist. Physician attitudes, logistic problems, and funding issues associated with the extra personnel and effort associated with opt-out testing (e.g. properly obtaining consent, laboratory quality control and management, and communication of test results) continue to threaten the long-term sustainability of many opt-out HIV testing programs.[3] In 17 published studies evaluating barriers to routine opt-out HIV testing, U.S. physicians reported 41 different barriers.[5] Although many were specific to a particular practice setting, four non-policy barriers were identified in all practice settings: insufficient time, lack of knowledge or training, perceived lack of patient acceptance, and competing priorities [5]

However, many of these barriers can and have already been addressed. For example, implementing an opt-out approach obviates the need for pretest counseling or obtaining separate consent, thereby eliminating the time consumed by these procedures. In addition, Burke et al[5] have suggested that establishing reminder systems for HIV testing, similar to other routine health maintenance practices such as immunization, would eliminate the issue of competing priorities. Finally, despite the perception that patients may have a negative opinion about opt-out HIV testing, in one survey study, patient acceptance rates for the concept of opt-out testing were 100% in the prenatal setting and 91% in the hospital setting.[10]

Indeed, several successful large scale opt-out HIV testing programs are ongoing in the U.S. Sponsored by the CDC, City of Houston, and Harris County Hospital District, an opt-out HIV testing program was implemented in the emergency center at the Ben Taub General Hospital, in Houston Texas, in October 2008. This program uses standard blood testing rather than rapid testing, and currently tests about 3000 patients per month, with over 40,000 tests completed. The new HIV positivity rate is about 0.8%. Furthermore, similar programs are operational at public and private institutions in Houston, together performing about 6000 tests per month[11] Cancer centers and oncology clinics may be able to replicate these successful opt-out testing programs.

Support for opt-out HIV testing of cancer patients

Prevalences of HIV infection Among Specific Cancers

Although HIV-infected individuals are at increased risk for many malignancies, including both AIDS-defining cancers (Kaposi sarcoma, non-Hodgkin lymphoma, and cervical cancer), as well as non-AIDS defining malignancies (e.g. lung cancer, Hodgkin lymphoma, anal cancer, among others),[12, 13] there are only limited data on the rate of HIV infection among patients with cancer. A recent retrospective study, for example, found that 15% of all anal cancers in the national Veteran's Affairs (VA) database were HIV-associated.[14] However, because this study used ICD-9 codes and not HIV laboratory test results to determine HIV infection status, the authors were unable to determine the rate of HIV testing – and hence the true HIV infection rate – in their anal cancer cases. In addition, Hakimian et al[15] evaluated 2,042 lung cancer patients who were seen at the University of Maryland from

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1996–2003 and found that 29 or 1.4% of them were HIV infected. Finally, a study performed in the pre-HAART era (from 1990–1998) by the California Cancer Registry (CCR) estimated that out of 10,126 non-Hodgkin lymphoma cases reported to the CCR, 1,900 or approximately 19% were associated with HIV infection.[16] Although these numbers provide a general idea of the prevalence of HIV in certain cancer population, it is important to note that these estimates may change with time. For example, the percent of non-Hodgkin lymphoma associated with HIV may be lower in the HAART era. Also, these HIV prevalence data provide no information regarding the prevalence of *undiagnosed* HIV infection. Indeed, there are no published data evaluating the prevalence of undiagnosed HIV infection among individuals diagnosed with any type of cancer.

Current HIV testing Practices for Individuals with New Cancer Diagnoses

We were only able to identify one study that documented the rate of HIV testing among cancer patients. That study, conducted in the United Kingdom, found that of 113 patients diagnosed with Hodgkin and non-Hodgkin lymphoma, 41% had no HIV test, and of those diagnosed with aggressive non-Hodgkin lymphoma (an AIDS-defining condition), 37% had no HIV test.[17] This study highlights that even when patients present with malignancies known to be associated with high HIV prevalence, HIV testing is not routinely performed.

Although an opt-out approach does not guarantee universal screening,[18] preliminary studies in different outpatient settings (e.g. prenatal clinics) have shown that opt-out testing does increase HIV testing rates.[19] Of note, one study from Alberta, Canada showed that prior to opt-out HIV testing, the testing rate among patients with tuberculosis was approximately 45%, but increased to 82% after opt-out testing was implemented.[20] Thus, opt-out testing appears to be particularly successful when instituted for patients who have an additional medical incentive, such as the health of their unborn child, or to improve a secondary disease process outcome such as tuberculosis, and could very well apply to other diseases including cancer.

The Changing Epidemiology of HIV Disease and HIV-Related Cancers

One reason that HIV testing may not routinely be offered to all cancer patients is because cancer is often a disease associated with older age, whereas the HIV epidemic has been primarily associated with younger persons. However, incident HIV infection is substantial among older individuals. A recent estimate of the U.S. HIV incidence in 2006 by Hall et al[21] showed that the rate of new HIV infections in 2006 (per 100,000 population) were 30.7 (95% CI, 25.8–35.6), 42.6, and 26.6 (95% CI, 22.8–31.0) for those aged 40–49, 30–39, and 13–29 years, respectively. In addition, they reported that 35% of all newly diagnosed HIV infections were in individuals over the age of 40 years. Although cancer risk is usually thought to substantially increase among individuals over the age of 50 years rather than those in their 40's, HIV-infected individuals often present with malignancies at younger ages than HIV-uninfected individuals, with the median age at presentation commonly reported between 40 and 50 years of age.[14] This observation is likely due in part to the younger age distribution of individuals infected with HIV, but may change as the HIV-infected population ages. Of note, a recent anonymous study evaluating the prevalence of HIV in both inpatient and outpatient settings in the VA healthcare systems found that the prevalence of HIV among individuals aged 55–64 years was 3.5%, and that patients with previously undocumented HIV-infection were significantly more likely to be over the age of 55 compared to those who were previously known to be HIV-infected.[22]

Multiple recent cohort studies and linked AIDS-cancer registry studies have calculated the elevated risk of cancer for HIV-infected individuals. These non-AIDS defining cancers include anal cancer, Hodgkin lymphoma, lung cancer, head and neck cancers, testicular

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cancer, skin carcinomas, and melanoma.[23, 24] Since the advent of HAART, individuals infected with HIV have had significantly improved survival and decreased mortality from AIDS-related infections. The increased incidence of non-AIDS defining malignancies has been thought to be partly due to the prolonged survival experienced among those with HIV disease. In addition, as awareness of the association with certain non-AIDS defining malignancies and HIV has grown, increased HIV testing among individuals newly diagnosed with non-AIDS defining malignancies may lead to fewer missed diagnoses of HIV infection. For example, since 2004, there have been seven new diagnoses of HIV infection during lung cancer treatment as a result of increased HIV testing among lung cancer patients at the Johns Hopkins Hospital in inner-city Baltimore.[25] This is compared to only a total of three individuals who were newly diagnosed with HIV receiving lung cancer treatment during the previous 18 years (from 1986–2004).[26]

Two recent meta-analyses have evaluated the Standardized Incidence Ratios (SIR) of AIDS-defining and non-AIDS defining cancers among HIV infected individuals[12], as well as patients with other causes of immunsuppression[13], compared to the general population (see Table 1). Grulich et al[13] conducted a meta-analysis analyzing the risks of these malignancies in seven cohorts and AIDS cancer linkage studies of individuals with HIV/AIDS, as well as five cohorts and linkage studies of kidney transplant recipients. They found that the pattern of risk was similar in both populations, and hypothesized that immune deficiency is the likely explanation for increased cancer risk. Subsequently, Shiels et al[12] compared the risk of non-AIDS malignancies utilizing 13 cohort studies, and AIDS cancer linkage studies including 4,797 non-AIDS cancers among 625,716 HIV infected individuals.

With decreasing rates of AIDS-defining malignancies in the HAART era, and the corresponding increasing proportion of non-AIDS defining malignancies,[24] routine HIV testing to facilitate appropriate early treatment of underlying HIV disease in all cancer patients is now of paramount importance. This is especially true in the growing number of patients with non-AIDS defining malignancies who may present with rapidly progressing or late-stage disease and who may manifest with unusual presentations.[27, 28] With regard to lung cancer, for example, several studies have consistently shown that over 80% of HIV-infected patients initially presented to their physicians with advanced or metastatic disease[26, 29, 30]. For other non-AIDS defining malignancies which do not appear to be associated with an increased risk of HIV (such as prostate and breast cancer) routine opt-out HIV testing will still be important because of its potential public health benefits, as well as the benefit to the patient through appropriate opportunistic infection prophylaxis, HIV treatment, and coordination of HIV and oncology care

Finally, the pathogenesis of AIDS-defining malignancies is thought to be multifactorial with immunosuppression, viral co-factors (e.g. Epstein-Barr virus (EBV), human papilloma virus (HPV), Kaposi sarcoma herpesvirus (KSHV)), and HIV itself playing key roles in the development of these cancers. Of note, the increased risk of developing lung cancer in the HIV-infected population is only partly accounted for by smoking status.[31] HIV infection could directly or indirectly lead to the more rapid evolution of genetic events integral to the development of lung cancer. A better understanding of the presence of HIV infection in the cancer population may enhance our overall understanding of some types of cancer and influence our prevention and treatment strategies.

Outcomes of AIDS-defining and Non-AIDS defining malignancies in HAART era compared to pre-HAART era

Perhaps the strongest argument for standard opt-out HIV testing for all patients presenting for oncologic care is the increased risk of morbidity and mortality associated with surgery,

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radiation therapy and cytotoxic chemotherapy in patients with moderate to severe HIV-related immunosuppression.[32] For these patients, preventing further immunosuppression with immediate HAART initiation, and commencement of appropriate prophylaxis appears to improve survival.[33–35] Even patients who have preserved immune function and high CD4 cell counts will need careful monitoring because cytotoxic chemotherapy often suppresses CD4 cell counts. Coordination of HIV and oncology care will still be of utmost importance for these patients. Because HIV-infected patients are often excluded from therapeutic cancer clinical trials, the impact of HAART on oncologic drug metabolism is not currently well understood. Thus, the decision to start HAART immediately versus deferring HAART for those patients with preserved CD4 counts (CD4 counts greater than 350 cells/μl) will need to be weighed carefully. Despite the potential interactions between HAART and cytotoxic chemotherapy, the overall evidence presented in the sections below suggest that early HAART initiation, even in individuals with relatively preserved immune function, may improve HIV-related cancer survival.

Prior to widespread HAART utilization, the outcomes of HIV-related malignancies were extremely poor, with median survivals for both AIDS-defining and non-AIDS defining malignancy often less than 6 months.[36, 37] However, since the widespread access to HAART, survival and outcomes of individuals with AIDS-related malignancies have greatly improved[34, 38], and for certain cancers are now comparable to those of HIV uninfected cancer patients.[14, 39, 40] Table 2 shows different studies by cancer type and the effect of HAART on their outcome. Most of the studies in Table 2 have shown that HIV-infected patients on HAART tolerate standard treatment options for common HIV-related cancers, highlighting the importance of HAART mediated immune reconstitution on cancer treatment outcomes.

AIDS-Defining Cancers

HAART has dramatically decreased the rate of KS and non-Hodgkin lymphoma in developed countries, but has had less of an effect on cervical neoplasia.[4142] In a large meta-analysis of 20 international cohort studies that compared the incidence rate ratios of AIDS malignancies in the post HAART time-period from 1992–1996 to the pre-HAART time period from 1997–1999, the rate ratio for KS was 0.32 ($p<0.0001$), compared to 0.58 ($p<0.0001$) for lymphomas.[42], and 1.87 for cervical cancer ($p=0.07$).[42] In addition, HAART has been shown to often be an effective treatment for KS confined to skin and/or minimal oral diasease.[43] HAART has also been shown to improve greatly the prognosis of individuals with HIV and non-Hodgkin lymphoma.[44] Besson et al[35] reported a median survival of over 21 months in patients treated in the HAART era, compared to 6.3 months in the pre-HAART era. Finally, there is little data regarding the effect of HAART on invasive cervical cancer, and these studies, which mainly describe small case series, have shown mixed results.[45]

Common Non-AIDS Defining Cancers

Although the incidence of non-AIDS defining cancers has increased since the advent of HAART,[24] HAART has been shown to improve survival in three of the most common non-AIDS defining malignancies: Hodgkin lymphoma, lung cancer, and anal cancer. In Hodgkin lymphoma, for example, Berenguer, et al[34] compared treatment and outcomes between HIV-infected Hodgkin lymphoma patients who received HAART and those who did not. The 5-year survival was 44% in the group that did not receive HAART and 72% in the HAART group. Furthermore, there have been three studies that specifically compared survival among HIV-infected patients with anal cancer in the pre-HAART versus HAART eras. In all three studies, there was a non-significant trend toward improved survival, better tolerance of chemoradiotherapy, and improved local tumor control in the HAART era.[33, 46–48] Other

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studies have also shown an equivalent median survival among HIV-infected and HIV-uninfected patients with anal cancer.[14, 49, 50]

For lung cancer, there are few published data that directly compare the survival between the pre-HAART era and the HAART era. Lavole et al.[29] found that the use of HAART was a favorable, independent prognostic factor for survival along with stage of presentation and patient performance status. In addition, pooled data from the pre-HAART era [51, 52] compared to the post-HAART era[40] showed that survival in the HAART era is improved. Furthermore, Powles et al[40] found that median survival did not differ between HIV-infected patients and HIV-uninfected patients in the HAART era. Finally, for hepatocellular carcinoma, a recent study conducted mainly in the HAART era compared the presentation and outcomes of HIV-infected individuals to HIV-uninfected individuals. In a multivariable survival analysis, these authors reported that HIV infection did not influence survival, and that the median survival in both groups was similar.[53] Thus, in the pre-HAART era, cytotoxic chemotherapies administered in the setting of underlying HIV infection were associated with possibly higher morbidity and mortality among individuals infected with HIV.[32] In contrast, in the HAART era, early treatment with antiretroviral medication and careful coordination between cancer care and HIV care has led to improvement in the cancer survival of HIV-infected patients, which is now nearly comparable to that of HIV-uninfected patients.

Conclusion

Although the CDC issued recommendations for universal opt-out HIV testing for all patients in 2006, widespread HIV testing has yet to be achieved. The recommendation for opt-out HIV testing has been shown to be extremely effective in certain clinical settings, including pregnant women and Emergency Departments. Oncology clinics and cancer centers represent another setting where opt-out HIV testing could greatly benefit patients, given the higher risk for malignancies among HIV-infected individuals. Increased use of prophylaxis against opportunist infections and earlier HAART initiation in HIV-infected individuals with cancer may lessen the risk of opportunistic and other infectious complication during treatment, as well as strengthen host immunity, and thereby improve therapeutic outcomes. Even among HIV-infected patients with relatively preserved immune function as evidenced by high CD4 counts, there are potential benefits from early HIV detection because these individuals may be eligible for AIDS-related malignancy clinical trials that incorporate assessments of pharmacologic interactions between chemotherapy and antiretroviral drugs and would benefit from coordinated HIV and oncology care. Not testing cancer patients for HIV represents a missed opportunity. Systematically implementing routine opt-out HIV testing of cancer patients will help to expand current improvements in therapeutic outcomes in the HIV-infected cancer population.

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Table 1

Standardized Incidence Ratios (SIR)s and 95% Cl from Meta-Analyses for Non-AIDS Defining Cancers and AIDS Defining Cancers (in bold) among HIV-Infected Individuals Compared with the General Population (Derived from Grulich et al[11] and Shiels et al[12])

Cancer Risk Significantly Increased			**Cancer Risk Non-Significantly Increased**			**Cancer Risk Significantly Decreased**		
Type of Cancer	**Number of cases**	**SIR, 95% CI**	**Type of Cancer**	**Number of cases**	**SIR, 95% CI**	**Type of Cancer**	**Number of cases**	**SIR, 95% CI**
Lung	847	2.6 (2.1, 3.1)	Colorectal	174	1.1 (0.69, 1.7)	Prostate	159	0.69 (0.55, 0.86)
Hodgkin's Lymphoma	643	11 (8.8, 15)	Melanoma	161	1.2 (0.88, 1.6)	Female Breast	142	0.74 (0.56, 0.97)
Anus	253	28 (21, 35)	Lip, Oral, Pharynx	84	2.2 (1.0, 4.7)			
Liver	171	5.6 (4.0, 7.7)	Esophagus	51	1.5 (0.99, 2.3)			
Skin Cancer	160	3.5 (1.8, 6.8)	Bladder	48	1.1 (0.72, 1.7)			
Kidney	109	1.7 (1.3, 2.2)	Pancreas	39	1.0 (0.74, 1.4)			
Oropharynx	108	1.9 (1.4, 2.6)	Colon	26	0.81 (0.48, 1.4)			
Leukemia	102	2.6 (1.9, 3.5)	Thyroid	24	1.1 (0.56, 2.3)			
Stomach	96	1.7 (1.2, 2.5)	Ovary	14	1.4 (0.78, 2.4)			
Testis	96	1.4 (1.1, 1.9)	Uterus	14	1.5 (0.68, 3.4)			
Brain	75	1.8 (1.2, 2.7)						
Multiple Myeloma	72	2.6 (1.5, 4.5)						
Larynx	62	1.5 (1.1, 2.0)						
Vagina	25	9.4 (4.9, 18)						
Penis	16	6.8 (4.2, 11)						
Small intestine	10	2.2 (1.4, 3.3)						
Bone	7	2.6 (1.3, 5.0)						
Eye	7	3.1 (1.6, 5.9)						
Nasopharynx	7	4.1 (2.1, 7.9)						
Gall Bladder	3	2.6 (1.1, 6.4)						
KS	**494**	**364.0 (3326, 3976)**						
Non-Hodgkin's Lymphoma	**5295**	**76.67 (39.4, 149)**						
Cervical Cancer	**104**	**5.8 (2.98, 11.3)**						

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Table 2

Studies Describing HIV Outcomes associated with HAART Utilization

Cancer	Type of Study	Year of Publication	Number	Findings	References
AIDS Defining Cancers					
Non-Hodgkin's Lymphoma	HAART vs pre-HAART eras	2001	145	HAART era median survival over 21 months compared to 6.3 months in pre-HAART era. (p=0.004)	35
Non-AIDS Defining Cancers					
Hodgkin's Lymphoma	HAART vs no HAART	2003	203	Overall Survival (OS) at 5 years 60% with HAART compared to 5% among those who did not receive HAART. In multivariable analysis, HR for death with HAART was 0.36 (p=0.014)	39
	HAART vs no HAART	2008	104	The complete response rates in the HAART treated group was 71 (91%) vs. 14 (70%) in the no HAART group p=0.023 in the. OS was also longer (p=0.009).*	34
Anal Cancer	HAART vs pre-HAART eras	2004	14	24 month OS was 67% in the "HAART" group and 17% in the "pre-HAART" group (P=0.052)	36
	HAART vs pre-HAART eras	2004	26	2- year OS was 57% in HAART vs 37% in pre-HAART eras (p=0.19)	47
	HIV-infected vs HIV-uninfected patients*	2008	175 HIV-infected, 1,109 HIV-uninfected	OS 77% among HIV-infected individuals and 75% among HIV-uninfected individuals (p=0.16)	14
	HIV-infected vs HIV uninfected*	2008	40 HIV-infected and 81 matched HIV-uninfected	5-year OS 61% HIV-infected individuals and 65% among HIV-uninfected controls (p=0.23)	55
	HIV-infected vs HIV-uninfected*	2009	44-HIVinfected, 107 HIV-uninfected	3- year OS 85% HIV-infected individuals and 84% HIV-uninfected (p=0.92)	51
	HIV-infected vs. HIV-uninfected*	2009	21 HIV-infected, 66 HIV-uninfected	Mean OS was 39.6 months in the HIV-infected group and 50 months in the HIV-uninfected group (p=0.56)	56
Lung Cancer	HAART vs. no HAART	2009	36 with HAART, 13 without HAART	Median survival of patient receiving HAART was 9 months compared to 4.5 months for those without HAART (p=0.04) †	30
	HAART vs. no HAART	2007	17 with HAART, 12 without	Median survival of patients receiving HAART was 6.7 months compared to 2.8 months for those without HAART (p=0.55)	15

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Cancer	Type of Study	Year of Publication	Number	Findings	References
	HIV-infected vs HIV-uninfected*	2003	9 HIV-infected, 27 HIV-uninfected	Median Survival was 4 months for both groups (p=0.55)	41
Liver Cancer	HIV-infected vs HIV-uninfected*	2007	63 HIV-infected, 226 HIV-uninfected	Median Survival was 6.9 month for HIV-infected and 7.5 months for HIV-uninfected (P=0.44)	54

*All "HIV-infected vs HIV-uninfected" studies were done in the HAART era

†Of note, Median nadir CD4 count and CD4 count at diagnosis between no HAART and HAART groups were not significantly different.