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Research Article

Malignancies Trends in a Hispanic Cohort of HIV Persons in Puerto Rico before and after cART

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Abstract

Background: The study describes the cancer trends in a Puerto Rican Hispanic HIV/AIDS cohort for three different time periods as defined by the availability of combination antiretroviral therapy (cART) in the Island: Pre (1992-1995), early (1996-2002) and recent (2003-2009). **Methodology:** AIDS and non-AIDS related malignancies risk, standardized incidence rate and 1 year mortality were evaluated in the cohort before and after cART. **Results:** Of the 281 malignancies found in 265 persons; 72% in men, 38% in injecting drug users and 42.3% in AIDS related cancers. The AIDS related cancer standardized incidence rates decreased significantly in the cART eras; however, Kaposi's sarcoma and invasive cervical carcinoma incidence remained significantly higher in the cohort when compare to the general population. On the contrary, non-AIDS related cancer standardized incidence rates increased significantly in the cART eras, specifically those of the oral/cavity/pharynx, liver, anus, vaginal and Hodgkin's and non-Hodgkin's Lymphomas. Around 50% of the persons with cancers were reported dead within the 1st year of their diagnoses without a significant variation during the cART eras. **Conclusion:** The higher incidence of Kaposi's sarcoma, invasive cervical carcinoma, non-AIDS related malignancies and their high mortality in the cART eras is suggestive of the role of oncogenic viruses, environmental agents, risky lifestyle behaviors and inadequate cancer prevention efforts that contribute and accelerate the risk of malignant transformation in these subjects. Aggressive intervention in the form of vaccines, risky practice reduction, early screening, early treatment and adequate risk reduction education needs to be incremented in this vulnerable population.

Key words: Cancer trends, HIV, AIDS/non-AIDS defining malignancies, cART, SIR, Hispanics, mortality risk

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Individuals infected with the Human Immunodeficiency Virus (HIV) have an elevated risk for developing malignancies¹⁻⁸. Some of the cancers are intrinsic due to the immunological impact of the HIV infection; others are more often related to the risk scenarios associated with the virus^{2,8-10}. The presence of HIV infection, particularly in the context of a deteriorated immune system is associated to an increased risk for the development of AIDS defining cancers including Kaposi's sarcoma (KS), high-grade non-Hodgkin's Lymphomas (NHL), Central Nervous System (CNS) Lymphoma and invasive uterine cervical carcinoma (ICC). The spectrum of HIV associated malignant disorders also comprise of non-AIDS defining cancers, including Hodgkin's Lymphomas (HL), non-AIDS-NHL, non-small cell lung cancer, head and neck cancer, ano-genital cancer and hepatic cancer^{1,4-9}. The introduction of multiple spectrum antiretroviral therapy (ART) and the availability of combination antiretroviral therapy (cART) have led to a dramatic improvement in the immunological function of infected subjects with an associated increment in the overall survival of these patients^{7,11}. The HIV infection has now become a chronic condition associated with longer patient's lifespan but can lead to additional co-morbid conditions, including cancer. Under this scenario, understanding the trends on cancer development in different HIV/AIDS populations is of marked importance, since they represent the next boundary that is limiting the survival of the HIV infected patient. The present study describes almost two decades of changing trends of malignant disorders in a Puerto Rican HIV infected Hispanic cohort and their relation with the availability of cART in the Island. Since the beginning of the epidemic, Puerto Rico has been one of the United States and Territories with the highest HIV/AIDS incidence and prevalence with the 7th position in HIV diagnosis (Rate of 19.4 per 100,000) and the 5th position in AIDS cases¹² (Rate of 11.4 per 100,000 cases) by 2014.

MATERIALS AND METHODS

In order to explore the association of neoplasm with HIV infection in a Hispanic adults setting, the study matched data of the Retrovirus Research Center (RCC) HIV cohort with the Puerto Rico Central Cancer Registry (PRCCR) data and the Puerto Rican Morality Registry (PRMR) of the Island's Health Department. These registries matches allowed the study to determine the incidence rate trends of AIDS and non-AIDS defining cancers in the HIV infected cohort and compared

them with the cancer incidence in the matched general population in the Island. In addition, the matched data allowed for the evaluation of mortality risk in the HIV cohort. The RRC study was an IRB approved study that includes over 4,500 adult (21 years and older) HIV infected persons who are followed every 6 months in the immunological clinic and the university hospital located in the health region of Bayamon¹³, Puerto Rico, since 1992. The PRCCR is part of the Center for Disease Control and Prevention (CDC) National Program of Cancer Registries designed for the compilation, handling and analysis of data of people with a diagnosis of cancer or neoplasm in Puerto Rico. Its basic source of information is the clinical file of the patients and the US cancer registries¹⁴. The probabilistic algorithm Link Plus, developed by the CDC's Division of Cancer in support with the National Program of Cancer Registry was used to match the databases. First and subsequent malignant neoplasms were included in the study analysis. Cancer incidence embraces only neoplasm diagnosis made at least 2 months after the first HIV positive reported test or after the RRC enrollment, whichever comes first. On the other hand, the RRC cohort's mortality was determined yearly by a match with the PRMR. Death was confirmed with available medical records data. The follow ups of the study subjects ended with the last RRC contact visit or the participant's death. Follow up was terminated by December 31, 2010.

Demographic factors, clinical manifestations, laboratory findings and ART prescriptions at or within 12 months prior to study entry were tabulated and compared across three different time periods that were defined on the basis of the availability of cART in the Island: 1992-1995 (pre-cART), 1996-2002 (early-cART) and 2003-2009 (recent-cART). Prescriptions of ART, including nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors and protease inhibitors were collected and tabulated. The cART was defined as the use of three or more antiretroviral drugs of two or more different classes. Laboratory findings included CD4⁺ T cell count and HIV viral load. The CD4⁺ T cell level was grouped according to cell counts: Less than 200, 200-400, 401-800 and greater than 800 cells per microliter. The AIDS clinical manifestation included the diagnosis of at least one of the AIDS defining condition other than AIDS defining neoplasm. The overall cancer incidence rates, expressed per 100,000 prospective person years of observation were calculated for each of the study periods. Incidence of specific AIDS defining cancers including KS, high-grade NHL, CNS Lymphoma and ICC were explored and evaluated. Non-AIDS defining cancer incidence includes: Oral/pharynx, colon/rectal, anus, liver/biliary ducts,

lung, eye, breast, ovary, vagina, prostate, testis, kidney, bladder, CNS, non AIDS-NHL, HL, leukemia and multiple myelomas were also evaluated. Malignant neoplasm diagnoses were classified according to the International Classification of Diseases 9th and 10th revision of the World Health Organization and/or the International Classification of Diseases for Oncology 3rd edition¹⁵⁻¹⁷. The present study was approved by the Universidad Central del Caribe Institutional Review Board.

Statistical analysis: The Statistical Package of Social Sciences (SPSS) program was used to perform univariate, bivariate and proportional hazard analysis. Chi-square, Fisher exact test and the student t test were used to evaluate differences between cART groups in relation to cancer incidence, one year mortality and patient's enrollment characteristics that included: Risky behaviors, clinical manifestations, laboratory findings and therapies. Cox proportional hazard analysis with relevant covariates, including variables with $p \leq 0.05$ in the bivariate analysis were used to evaluate 5 years cancer risk after study enrollment. Data were presented as percentage, median with inter quartile range and Hazard Ratios (HR) with their 95% Confidence Interval (CI). The p value used to determine statistical significance was <0.05 .

General and specific malignancies incidences and the standardized incidence ratios (SIRs) by cART time periods were also calculated and evaluated. The RRC's AIDS and non-AIDS defining cancer incidences were compared to the general Puerto Rican population cancer incidence for the same time periods with the help of the SIR statistical approaches. The SIR was defined as the ratio of the RRC observed vs. expected number of malignant neoplasms, as a risk relative to the general population. Expected counts were estimated by applying gender, age group (20-40, 41-60 and >60) and calendar years PRCCR's specific cancer incidence rates of the general population to the studied cohort. A two sided exact poisson distribution 95% confidence intervals (CIs) was estimated for each SIR¹⁸.

RESULTS

Cohort characteristics: A total of 4,213 HIV infected persons were enrolled in the RRC from January, 1992 through December, 2009. Among them, 71.1% were male, 50.4% reported Injecting Drug Use (IDU) and around 29% of the male cases reported male to male sexual (MSM) contact behavior as the mode of HIV exposure. When comparing the cohort's subjects by cART treatment period,

those patients enrolled in the pre-cART era consists of fewer MSM cases, reported more frequent IDU practices and entered the cohort at a younger age (Table 1).

Characteristics of malignancies by study periods: A total of 310 cancers were diagnosed in the cohort during the study period. Of them, 281 neoplasms were diagnosed in 265 participants after HIV infection and 42.3% were AIDS related cancers. Eighty cancers were diagnosed in the pre-cART era and the remaining 201 (113 early and 88 last) in the cART era. General cancer incidence rates fell from 1,227 per 100,000 in the pre cART era to 603 per 100,000 in the late cART period. About 72% of the 281 cancers were in men and 38% in IDUs. Table 1 shows a significant reduction in AIDS related neoplasm cases, especially with KS after the availability cART in the Island. However, the trend of ICC cases was not significantly affected in the cART era. A significant increment in the number of non-AIDS related cancers were observed for the same period, especially with malignancies of the oral-pharyngeal cavity, liver, anus and lung. Similarly, HL and non AIDS NHL showed an increase in the number of cases diagnosed in the cART era.

Cox proportional hazard analysis confirmed that patients who entered the cohort in the cART periods (HR = 0.71, 95% CI 0.56-0.90), who reported IDUs (HR = 0.52, 95% CI 0.35-0.76) and with a higher CD4⁺ T cell count at study enrollment (HR = 0.57, 95% CI 0.15-0.72) had a lower risk of developing a malignancy during the first 5 years of follow up, after controlling for age, sex and AIDS diagnosis (Table 2). On the contrary, co-existence of clinical AIDS (HR = 1.83, 95% CI 1.24-2.67) and an older age at enrollment (HR = 1.04, 95% CI 1.02-1.05) were associated with a higher cancer risk (Table 2).

Overall malignancies incidence: Table 1 and Fig. 1 show the SIRs sorted by AIDS/non-AIDS relation, site or neoplasm type and cART study time periods. The overall cancers SIRs in the three study periods were significantly higher in the HIV-infected cohort when compared to the general Puerto Rican population. Even though the cohort's cancers SIR decreased significantly after the availability of cART, the cancer's incidence remained significantly higher in the HIV cohort when compared to the general population.

Specific malignancies incidences: When sorted by AIDS defining malignancies, the overall incidence of these cancers declined after the availability of cART in Puerto Rico. The

Table 1: Cohort characteristic's, neoplasm incidence and SIRs and (95% CI) by study periods

	Retrovirus research center (n = 4.213)		
	Pre cART 1992-1995	Early cART 1996-2002	Late cART 2003-2009
Number of subjects	2,067	1,320	826
Sex (%) Male	75.7	69.5	62.1*
Female	24.3	30.5	37.9
Mean age enrollment (years)	36.6	40.1	41.5*
IDU percentage (%)	65.9	52.9	42.6*
Man sex with man (%)	28.8	29.0	32.0
Clinical AIDS enrollment (%)	27.3	19.7	6.2*
CD4 <200 at enrollment (%)	49.0	49.5	43.6
cART at enrollment (%)	0	40.6	59.2*
Cancer incidence × 10 ⁵ person per year	1,227	929	603*
Tumor types	Cancer N-SIR (95%CI)	Cancer N-SIR (95%CI)	Cancer N-SIR (95%CI)
All types	80-10.4 (8-13)	113-5.5 (5-7)	88-2.1 (1.7-3)
AIDS cancers*	54-90 (67-118)	48-54 (40-72)	17-17 (10-26)
Kaposi's sarcoma	40-111 (79-151)	36-150 (105-207)	10-50 (24-92)
Burkitt's NHL	3-75 (15-219)	2-29 (6-103)	0-n/d
High-grade NHL	1-n/d	1-n/d	0-n/d
Brain Lymphoma	2-n/d	1-n/d	0-n/d
Invasive cervix carcinoma	8-47 (20-93)	8-15 (6-29)	7-9 (4-19)
Non-AIDS cancers	26-3.7 (2-5)	65-3.3 (3-4)	71-1.8 (1.4-2)
Oral cavity/pharynx	2-3.8 (0.4-14)	6-4.9 (2-11)	6-3.4 (1.2-7)
Esophagus	0-n/d	1-n/d	1-n/d
Stomach	2-n/d	1-n/d	1-n/d
Colon and rectum	2-2.7 (0.3-10)	4-1.6 (0.4-4)	4-0.8 (0.2-2)
Anus	0-n/d	0-n/d	3-18 (4-52)
Liver/hepatic ducts	0-n/d	4-9 (2-22)	6-6 (2-13)
Lung and bronchus	3-6.7 (1.4-20)	6-5.4 (2-12)	5-2.6 (0.8-6)
Skin	2-n/d	3-n/d	2-n/d
Eye	1-33 (0.4-185)	3-50 (10-146)	1-11 (0.2-62)
Breast	0-n/d	5-2 (0.6-5)	3-0.6 (0.1-2)
Ovary	1-14.3 (0.2-80)	1-4.4 (0.1-24)	2-5.6 (0.7-20)
Vagina	0-n/d	1-50 (0.7-278)	2-40 (5-144)
Prostate	0-n/d	3-0.9 (0.2-3)	4-0.4 (0.1-1)
Testis	0-n/d	0-n/d	2-5.7 (0.6-21)
Urinary bladder	0-n/d	1-1.8 (0.1-12)	3-3.1 (0.7-10)
Kidney	0-n/d	0-n/d	2-2.1 (0.2-8)
Brain-nervous system	1-4.8 (0.1-27)	1-2.3 (0.1-13)	1-1.5 (0.1-9)
Non-Hodgkin's Lymphoma	7-13 (5-27)	19-17 (10-20)	11-6 (3-11)
Hodgkin's Lymphoma	2-10 (1.1-34)	2-6 (0.7-23)	3-8 (2-23)
Leukemia	0-n/d	1-1.8 (0.1-10)	2-2.6 (0.3-9)
Multiple myeloma	1-11 (0.2-62)	0-n/d	2-4 (0.5-16)
Other cancers	2-n/d	3-n/d	5-n/d

*p<0.05, *Included KS, Burkitt's NHL and Invasive cervical carcinoma, IDU: Injecting drug use, cART: Combination antiretroviral therapy, n/d: No data

Table 2: Five years cancer risk after enrollment by cox proportional hazard

	Cancer hazard ratio	95% CI	p
Female	0.89	0.61-1.32	0.587
Age at study entry	1.04	1.02-1.05	0.000
IDU antecedent	0.52	0.35-0.76	0.001
CD4+ T _H ≥ 200 cells	0.57	0.15-0.72	0.000
Clinical AIDS	1.83	1.24-2.67	0.002
cART period groups	0.71	0.56-0.90	0.005

CI: Confidence interval, IDU: Injecting drug use, cART: Combination antiretroviral therapy

AIDS related cancers SIRs decreased significantly over the time, from 90 (95% CI: 67-118) in pre cART to 17 (95% CI: 10-26) in late cART era. However, the incidence of AIDS cancers remained 17 times higher in the HIV cohort when

compared to the general population even in the late cART era. Similar trends were observed separately in each AIDS defining neoplasms, however only KS and ICC incidence remained significantly higher among the HIV cohort [SIRs = 50 (95% CI: 24-92) vs. SIR = 9 (95% CI: 4-19), respectively] in the late cART era (Fig. 1).

On the other hand, the non-AIDS defining malignancies SIRs also decrease over the study periods from 3.7 (95% CI: 2-5) in the pre cART era to 1.8 (95% CI: 1.4-2) in the late cART era. Despite this reduction, the non-AIDS malignancies incidence remained almost two times higher in the HIV cohort than the general population at the late cART period. Most of the specific neoplasms SIRs that were significantly higher in

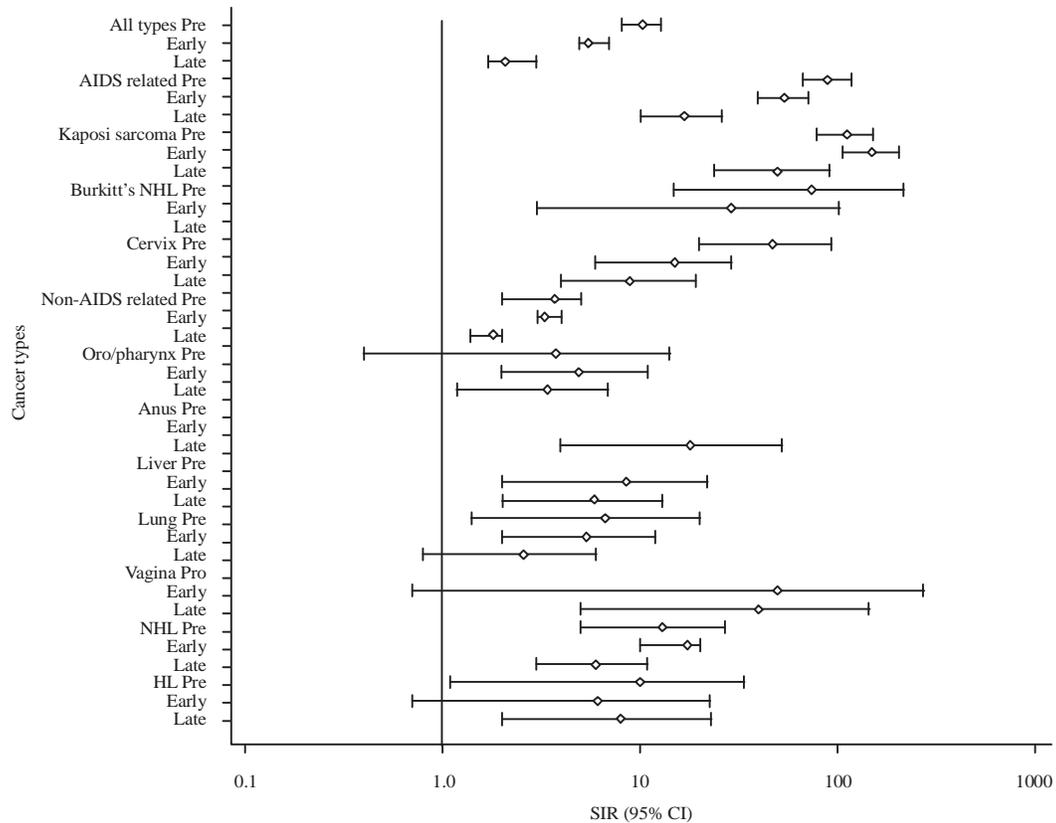


Fig. 1: Neoplasms SIRs and (95% CI) by study periods

the HIV cohort by the pre cART era remained higher afterwards. They include the non-AIDS NHL and HL with a SIR of 6.0 (95% CI: 3-11) and 8.0 (95% CI: 2-23) in the later cART era, respectively. On the contrary, oral cavity and pharynx cancers SIRs that showed higher incidence in the cohort reached statistical significance in cART period, with a SIR of 3.4 (95% CI: 1.2-7) in the late era. The lung neoplasm before cART was significantly higher in the HIV cohort (SIR 6.7 [95% CI: 1.4-20]), but decreased moderately in the later study period and became not statistical significant (2.6 [95% CI: 0.8-6]). Conversely, the incidence of anus, liver and vaginal neoplasms that were not reported in the HIV cohort during the pre-cART period had an incremental improvement afterwards, 18.0 (95% CI: 4-52), 5.9 (95% CI: 2-13) and 40 (95% CI: 5-144), respectively (Fig. 1).

Figure 2 shows the SIRs for specific neoplasms besides ICC, breast and genital target organs cancers and was sorted by gender in the study time periods. When compared with the general population the cancers incidence trends in the cohorts were as follows: KS incidence that was extremely high in both genders of the cohort during the pre and early cART eras remained higher in men but was not diagnosed in

women in the late cART period. Oral cavity and pharynx neoplasms incidence that was not significantly higher in the cohort during the pre-cART era reached statistical significance only in women during the early and late cART periods. Liver and lung cancer incidences were significantly higher only in men of the cohort during the late cART era. On the other hand, NHL incidence in the pre-cART era from being only significantly higher for men became significantly higher also in women during the cART eras. Finally, HL incidence that was only significantly higher for men in the pre-cART era lost its significance in the cART era.

One year mortality after neoplasm diagnosis: Table 3 shows the mortality trends of the cohort within 12 months after the cancer diagnosis by cART periods. Death occurred in about 50% of the cases within the first 12 months of neoplasm diagnosis, without any changes in mortality after the availability of cART in the Island. Lung cancer was the only neoplasm that had a significant increment in the 1 year mortality during the cART era. The ICC, NHL and HL had a similar 1 year mortality trend and their increment in the late cART era was not statistically significant. None of the anal cancers cases died within the one year after their diagnoses.

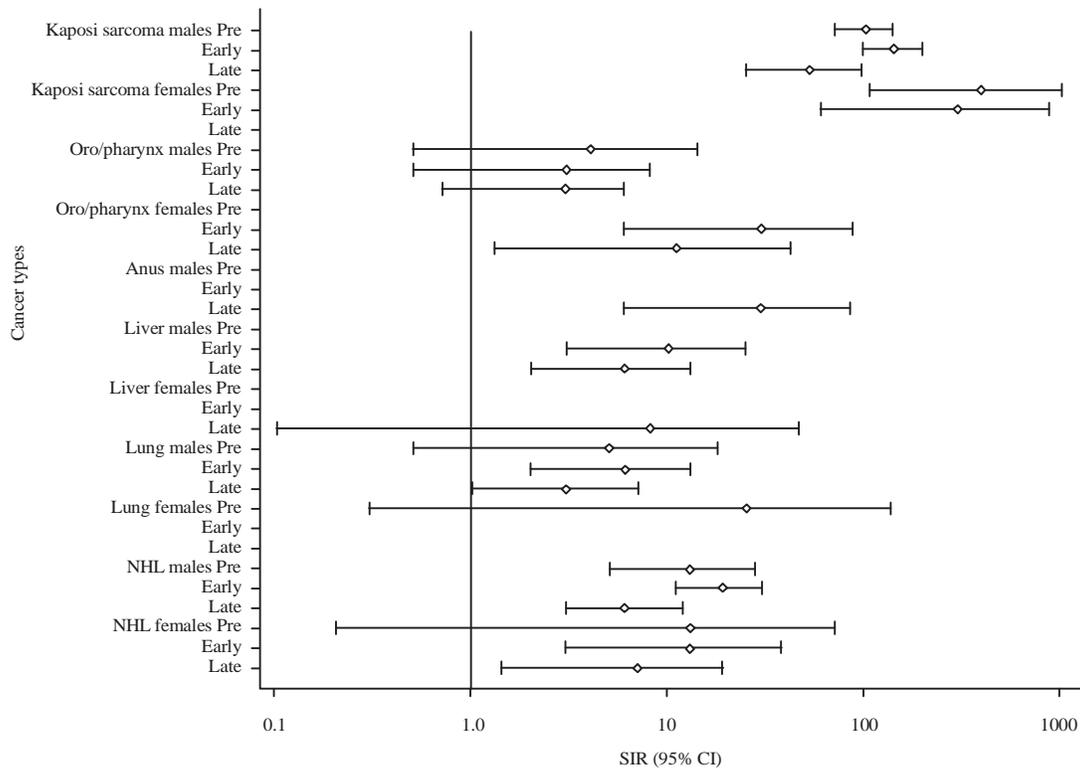


Fig. 2: Neoplasms SIRs and (95% CI) by gender and study periods

Table 3: One year mortality percentage after neoplasm diagnose by study periods and by tumor types

Tumor types	One year mortality (%)			p-value
	Pre cART (1992-1995)	Early cART (1996-2002)	Late cART (2003-2009)	
AIDS-cancers				
Kaposi's sarcoma	57.5	58.3	50	0.846
Burkitt's NHL	100	50	N/A	0.4
High-grade NHL	100	0	N/A	1
Brain Lymphoma	50	100	N/A	1
Invasive cervix carcinoma	37.5	37.5	42.9	0.971
Non AIDS-cancers				
Oral cavity/pharynx	50	16.7	66.7	0.211
Colon and rectum	0	50	50	0.435
Anus	N/A	N/A	0	N/A
Liver	N/A	75	50	0.571
Lung	33.3	100	100	0.010*
Non-Hodgkin's Lymphoma	57.1	68.4	81.8	0.519
Hodgkin's Lymphoma	50	50	66.7	0.907
All cancers	55.7	56.7	50	0.631

*p<0.05

DISCUSSION

The availability of multiple spectrum of ART and their combination has been resulted in dramatic immunological function improvement, reduction in opportunistic infections, morbidity and the overall survival of HIV infected persons. This

study represents one of the largest and most complete cancer risk follow-up studies performed in a HIV/AIDS cohort in Puerto Rico for a 17 years period, before and after the introduction of cART. As expected, the present study demonstrated a substantial reduction in the five years cancer risk among a Hispanic cohort of HIV-infected patients after the availability of cART (HR = 0.71) and a beneficial trend in those with a higher CD4+ T cell count (HR = 0.57) at the time of study enrollment. In addition, the overall cancer SIR of the study cohort declined in the cART era; however, neoplasm incidence remained significantly higher in HIV infected individuals when compared to the general population, after the availability of cART in the Island (SIR = 2; 95% CI = 1.7-3). Previous studies in and outside the US have also reported a higher malignancies' incidence in persons living with HIV/AIDS when compare to the general population, even with the availability of various treatment regimens^{2-4,6-9,11,19}. A poor adherence to combined therapies, an Immune Reconstitution Inflammatory Syndrome (IRIS) and the effects of non-HIV related cancer risk factors could be involved in the neoplasm disparity among this vulnerable population. Furthermore, the persisting high mortality within the first year after the cancer diagnosis despite cART availability is an interesting finding that needs further evaluation. Primary, secondary and also tertiary cancer

prevention gaps could be closely related to these findings. Consequently, an extensive evaluation and adaptation of cancer preventive strategies for persons living with HIV needs to be conducted to reduce the cancer risk in this vulnerable population.

Among the cohort most of the AIDS defining tumor incidences decreased significantly in the cART era, particularly KS, NHL and ICC. This is mainly due to the effects of cART in reducing immunosuppression induced by HIV. However, even almost 15 years after the cART regimen implementation, KS and ICC incidence remained significantly higher when compared to the general population. Similar trends of AIDS defining neoplasms incidence were reported in previous US studies^{3,4,6-8,11}. Because of the multi factorial nature of neoplasms, other oncogenic factors beyond the HIV infection could be having an important role in this cancer disparity. These factors include oncogenic viruses and other life style and behavioral factors.

For KS and ICC they are known to associate to specific oncogenic viruses, Human Herpes Virus-8 (HHV-8) and the Human Papilloma Virus (HPV), respectively and a persistent co-infection with these viruses, partial restoration of the immunity plus prolonged life expectancy could be related to the lasting higher incidence of these cancers in the cART era^{1,2,4-8}. It is interesting that the anal intra epithelial neoplasm, closely related to the HPV was exclusively detected among men during the late cART era and predominantly in men who had sex with men (data not shown). As suggested, the cART availability in the HIV study cohort could prolong the oncogenic virus exposure time allowing the anal cancer manifestation^{1,4,6}. Previous studies have extensively described the relation of persistent oncogenic viral exposure with the higher ICC and non-AIDS cancer incidence during cART era^{1,2,4-8}. Regarding behavioral and life style factors, survival improvement in the HIV infected persons in the cART era will elongate their exposure to tobacco and alcohol and increases the lung, oral cavity-pharynx and liver malignancies risk^{4,8,9}.

With regards to the non-AIDS defining neoplasm incidences in the cART era, an excess risk in the oral cavity-pharynx, vagina, anus and liver neoplasm, HL and NHLs were observed more frequently among this Hispanic cohort when compared to the general population. These findings were similar to the ones reported in previous HIV/AIDS studies^{1,2,4-8}. However, it is remarkable that SIRs neoplasms of the oral cavity-pharynx (3.4 vs. 1.8 and 2.1), vagina (40.0 vs. 6.7 and 4.4) and liver (5.9 vs. 4.4 and 3.3) were higher in the Puerto Rican cohort than in two other US cohorts^{4,8}. On the

contrary, SIRs of the anus neoplasm (18.0 vs. 32.0 and 19.6) and HL (8.0 vs. 11.0 and 13.6) were lower in the Hispanic cohort, but remained significantly higher when compared to the general population of the Island^{4,8}. As in the AIDS defining cancers, other oncogenic factors beside the HIV infection, may solely or synergistically predispose the development of these non-AIDS defining neoplasms. Certain oncogenic viruses including Epstein-Barr, HPV, Hepatitis C Virus (HCV) and Hepatitis B Virus (HBV), environmental agents, genetic mutations and risky lifestyle or behavioral factors are often present in the HIV infected patients scenario. Smoking, alcohol, use of illegal drugs and sexual promiscuity may contribute and accelerate the risk of malignant transformation in these subjects even in the cART era^{2,6,9}. This scenario that AIDS and non-AIDS defining cancers are still higher in the HIV infected population as compared to the general population in the cART era, together with the persisting higher mortality in the first year of cancer diagnosis in the cART era, highlights possible prevention gaps and the need for evaluating and enhancing the existing cancer prevention strategies, especially for the HIV infected population. However, there are no specific prevention guidelines for HIV infected individuals, other than an early and adequate diagnose and treatment for many types of tumors. For example, the HPV immunization in Puerto Rico was implemented in the young general adolescent population few years ago and its efficacy in the HIV persons is not well known^{8,20}. Thus, studies need to be carried out to evaluate the HPV vaccine acceptability; its use and effectiveness in HIV infected individuals in the Island. Education, prophylaxis, adequate screening, early detection, adequate management and opportune treatment of neoplasms and their related oncogenic factors need to be evaluated and develop plans which can be reinforced them in this Hispanic cohort^{8,9,11,21}.

This study has several limitations. First, the study subjects were from a passive surveillance cohort, in which patients had come to the hospital or outpatients facilities to have the data collected. This could have increased the probability of lost to follow/up and missing data, especially for cases in which treatments and follow ups were done outside the study's health facilities. Second, the study obtained the cancer data from secondary databases or registries in which the reported dates are not necessarily the first neoplasm diagnosis dates. Third, the study could not evaluate the cancer treatment pattern in the HIV cohort, because of the lack of this information in the data sources. Fourth, the study is not a population based survey that could be generalized to all HIV/AIDS patients on the Island. Fifth, the study used death from all cause to evaluate mortality and did not analyze causes of death.

CONCLUSION

In summary, neoplasm remains an important comorbidity for hispanic HIV-infected individuals in the cART era, particularly for the non-AIDS defining cancers. Improvement of the HIV treatment have resulted in a decline of the neoplasm incidence overtime but new cases are likely to arise in the hispanic cohort as a result of a mounting burden of other oncogenic factors beside the HIV infection. More aggressive prevention strategies targeting oncogenic viruses, environmental agents, risky lifestyle behaviors and more opportune-adequate cancer diagnosis and treatments among HIV infected individuals are highly recommended in order to reduce their cancer burden.

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SIGNIFICANT STATEMENTS

Because of the availability of new antiretroviral therapy (cART), HIV infection has become a chronic condition that can lead to higher cancer incidence in this vulnerable population. By evaluating the cancers trends among a cohort of Puerto Rican hispanic HIV infected individuals before and after cART and comparing them with the general cancers incidence in the Island, the study found that the AIDS and non-AIDS defining cancers are still higher in the HIV infected population as compared to the general population in the cART era, together with a persisting higher mortality in the first year of cancer diagnosis, highlights possible prevention gaps and the need for evaluating and enhancing the existing cancer prevention strategies, especially for the HIV infected population.

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