



Poster # 859: Trends in incidence of AIDS-defining and Non-AIDS-defining cancer among HIV-infected children in the United States, 1984 - 2006

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Abstract

Background: As HIV-infected children live longer, there is concern about chronic illnesses, especially cancer. Recent trends for cancer in HIV-infected adults are well described but data for infected children are limited. We describe cancer trends in two CDC cohorts of HIV-infected children: Pediatric Spectrum of HIV Disease (PSD) and LEGACY. Incidence of pediatric malignancies in the general pediatric population was 0.20 cases/1,000 person years (PY) from 1984-2006, according to the Surveillance Epidemiology and End Results Program.

Methods: PSD was an observational chart abstraction study of HIV-infected children enrolled in 8 U.S. regions from 1988-2004; LEGACY was a similar study conducted at 25 sites from 2005-2006. We evaluated the incidence of all cancers from 1984-2006 based on a person-time analysis (cases/1000 person-years [PY]). Retrospective data on incident cancers among enrollees prior to initiation of PSD in 1988 was also included. We compared characteristics of HIV-infected children with and without cancers; compared the incidence of all cancers, AIDS-defining cancers (ADC), and non-ADCs (NADC) in the pre- (prior to 1997) and post-HAART eras; and calculated cancer incidence rate ratios (IRR) and 95% confidence intervals assuming a Poisson distribution.

Results: There were 112 incident cancers, 71 ADC and 41 NADC, among 5,843 participants contributing 38,587PY of follow-up. Eight of 112 cancers had occurred before 1988. Comparing children with and without cancer, the median age was 7.1 vs 8.8 years (p = 0.21), 46% vs 50% (p=0.38) were female, and 81% vs 85% (p=0.11) were perinatally infected. Non-Hodgkin lymphoma comprised 90% of the ADCs. Kaposi sarcoma (10%) was uncommon and was only diagnosed in the pre-HAART era. The most common NADCs were leukemia (20%) and bone and soft tissue cancers (17%). The overall incidence of cancer was 2.9 cases/1000 PY. The IRR of cancer in the pre-HAART vs. post-HAART eras for all cancers was 1.49 [1.03-2.17]. IRR for ADC was 2.57 [1.53-4.46], and for NADC was 0.66 [0.36-1.22] (Figure 1). The IRR of did not differ between perinatally vs non-perinatally HIV-infected children (IRR 1.38 [0.86, 2.23]).

Conclusions: The overall cancer incidence in two CDC pediatric HIV cohorts was increased as compared to that of the general U.S. pediatric population. As in adults, the incidence of ADC declined significantly following the introduction of HAART and there was no significant increase in NADC among children with HIV infection.

Introduction

•Adults with HIV infection have increased incidence of cancer. While cases of AIDS-defining cancers (ADC) have declined among adults in the post-HAART era, non-AIDS-defining cancers have been increasing in number. [1] Studies have also shown elevated rates of malignancy in children with HIV infection, however, the data are limited. [2, 3, 4]

•The goal of this study was to report incidence of cancer from the PSD and LEGACY cohorts. These two cohorts together provided over 20 years of longitudinal data on HIV-infected children, and this analysis describes one of the largest groups of cancers reported from the pediatric HIV-infected population.

•We also compared incidence of cancers in the pre- and post-HAART eras as well as rates of cancer based on route of infection among children with HIV infection enrolled in these two cohorts.

Methods

• The Pediatric Spectrum of HIV Disease (PSD) study was an observational medical record abstraction of HIV-infected children enrolled in 8 U.S. regions from 1988-2004. Initial data gathered included demographic information, birth history, and exposure history. Every 6 months, each participant's medical records were reviewed, and data were collected regarding new HIV- and non-HIV-associated medical diagnoses and hospitalizations.

•Since the PSD study attempted to capture as many HIV-infected children as possible, the study included 465 HIV-infected individuals who were diagnosed prior to 1988. For these individuals, a retrospective chart review was conducted.

•LEGACY was a similar study conducted at 25 sites from 2005-2006 and includes some children who were initially followed in PSD. This study incorporated the individuals in LEGACY for whom complete retrospective records were available.

•For this analysis, we calculated the incidence (No. Cases/1000PY) of cancer in these two populations based on a person-year analysis.

•We used a chi-square analysis to compare categorical variables and t-tests to compare continuous variables.

Methods

•Statistical analyses also included calculating incidence rate ratios with 95% confidence intervals based on a Poisson distribution. We also compared AIDS-defining cancers (ADC) and non-AIDS-defining cancers (NADC) in the pre- and post-HAART eras based on 95% confidence intervals.

Results

Table 1: PSD vs LEGACY

| | PSD | LEGACY | Total |
|--------------------------------------|-----------|-----------|-----------|
| Total number of enrolled individuals | 5,269 | 574 | 5,843 |
| Number of cancer cases | 105 | 7 | 112 |
| Person time | 33,264 | 5,322 | 38,587 |
| Years included | 1977-2004 | 1986-2007 | 1977-2007 |

•The PSD study included 5,269 individuals contributing 33,264 person-years follow up, while LEGACY enrolled 574 individuals with 5,322 person-years of follow up. There were 112 total cases of cancer, 105 from PSD and 7 from LEGACY.

Figure 2: Demographics of individuals with and without diagnosis of cancer

| Variable | Cancer Diagnosis N=112 (%) | No Cancer Diagnosis N=5731 (%) | Statistical p value (α=0.05) |
|---------------------|-------------------------------|-----------------------------------|---------------------------------|
| Age | | | p= 0.21 |
| 0-12 | 88 (78.6%) | 4192 (73.1%) | |
| 13-18 | 20 (17.8%) | 1209 (21.1%) | |
| 19-24 | 4 (3.6%) | 301 (5.2%) | |
| Median | 7.12 (mean: 8.38) | 8.8 (mean 9.08) | |
| Gender | | | p=0.38 |
| Female | 51 (45.5%) | 2848 (49.7%) | |
| Male | 61 (54.5%) | 2883 (50.3%) | |
| Race | | | |
| White, non-Hispanic | 16 (14.3%) | 675 (11.8%) | |
| Black, non-Hispanic | 46 (41.1%) | 2914 (50.8%) | |
| Hispanic | 47 (42.0%) | 1993 (34.8%) | |
| Asian | 0 | 0 | |
| Other | 5 (4.5%) | 104 (1.8%) | |
| Unknown | 0 | 45 (0.8%) | |
| Treatment era | | | p<0.0001 |
| Pre-HAART | 68 (60.7%) | 2040 (5.6%) | |
| Post-HAART | 44 (39.3%) | 3691 (64.4%) | |
| Transmission | | | |
| Perinatal | 91 (81.25%) | 4872 (85.0%) | |
| Breastfeeding | 1 (0.9%) | 65 (1.1%) | |
| Blood transfusion | 14 (12.5) | 379 (6.6) | |
| Hemophilia | 5 (4.4%) | 152 (2.7%) | |
| Other | 1 (0.9%) | 263 (4.6%) | |

•'Age' in this table refers to the age when an individual was censored, either when their cancer was diagnosed or the date of their last recorded visit for those without a diagnosis of cancer.
•There were significantly more cancers diagnosed in the pre-HAART era than in the post-HAART era.
•There was no significant difference in the age or mode of transmission of HIV-infected children diagnosed with cancers as compared with those without cancers.

Results

Figure 3: Malignancies by type in the PSD and LEGACY cohorts

| | Total (% of total malignancies) | Pre-HAART | Post-HAART |
|--|---------------------------------|-----------|------------|
| AIDS-defining cancers | | | |
| Kaposi sarcoma | 7 (6.3%) | 7 | 0 |
| Non-Hodgkin lymphoma | 64 (57.1%) | 44 | 20 |
| Cervical cancer | 0 | 0 | 0 |
| Total ADC | 71 (63.4%) | 51 (75%) | 20 (43.4%) |
| Non-AIDS defining cancers | | | |
| GI-associated cancer | 3 (2.7%) | 1 | 2 |
| GU-associated cancer | 5 (4.5%) | 2 | 3 |
| Oral cancer | 1 (0.9%) | 0 | 1 |
| Respiratory cancer | 1 (0.9%) | 0 | 1 |
| Malignancy of bone and connective tissue | 7 (6.3%) | 3 | 4 |
| Hodgkin's lymphoma | 5 (4.5%) | 1 | 4 |
| Leukemia | 8 (7.1%) | 7 | 1 |
| Other** | 11 | 3 | 8 |
| Total NADC | 41 (36.6%) | 17 (25%) | 24 (56.5%) |
| Total | 112 | 68 | 44 |

* Other malignancies include: malignant neoplasm of the eye, brain, and unspecified sites, and neoplasm of unspecified nature (of lymph/hematopoietic tissue, bone/soft tissue, GU organs, brain, unspecified sites)

•Of the 112 cancers, 71 (63.4%) were ADC and 41 (36.6%) were NADC. The most common ADC was non-Hodgkin Lymphoma. Kaposi's sarcoma was relatively uncommon, contributing only 7 (6.3%) total cases. The most common NADCs were leukemias and bone and soft tissue cancers.

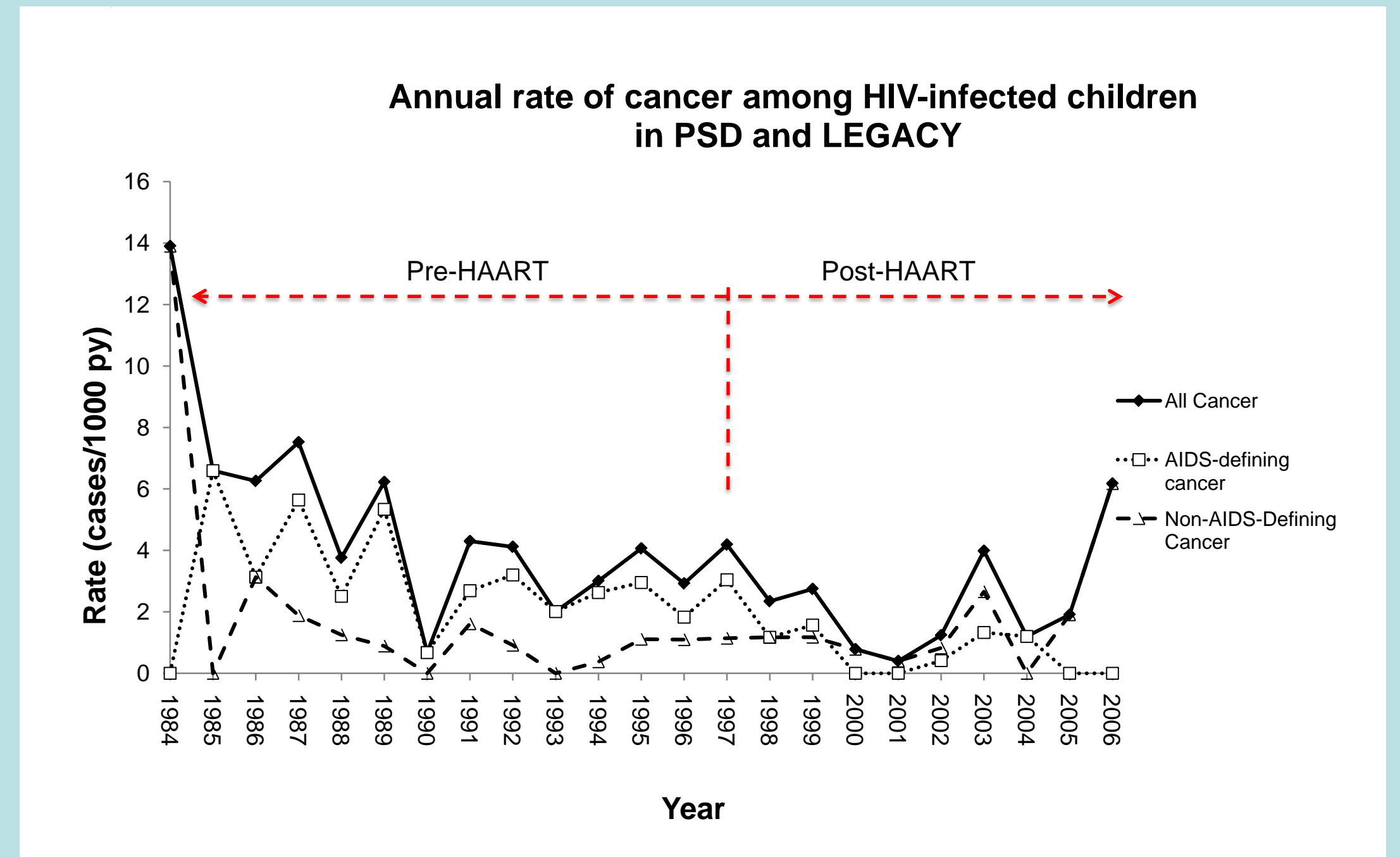
•There were 68 cases of cancer diagnosed in the pre-HAART era and 44 cases diagnosed in the post-HAART era.

Figure 4: Incidence (IR) and Incidence rate ratios (IRR) for major time periods

| | IR (Cases/ 1000PY) | IRR |
|--------------------|--------------------|--------------------|
| Total malignancies | 2.90 | |
| Pre-HAART | 3.54 | 1.49 (1.03-2.17) * |
| Post-HAART | 2.37 | |
| Pre-HAART ADC | 2.66 | 2.57 (1.53-4.46)* |
| Post-HAART ADC | 1.03 | |
| Pre-HAART NADC | 0.88 | 0.66 (0.36-1.22) |
| Post-HAART NADC | 1.34 | |
| ADC | 1.84 | 1.73 (1.17-2.54)* |
| NADC | 1.06 | |

* Statistically significant at α = 0.05

•The overall IR of cancers over all of the years studied was 2.90 cases/1000 PY. The cancer rate in the pre-HAART era was significantly higher than the rate in the post-HAART era
•The rate of ADC was significantly higher than the rate of NADC
•There was a significant decline in the rate of ADC from the pre-HAART to the post HAART era, and a non-significant increase in NADC over the same time period.



•The incidence of cancers declined in the pre-HAART era and continued to fall in the post-HAART era.
•There was a nonsignificant increase in incident rate of NADCs in the most recent years of the HAART era.

Conclusions

•Children with HIV infection had a markedly increased incidence of cancer compared to the general pediatric population in this large group of 5843 individuals with 38,587 PY of follow up.

•The incidence was 2.90 cases/1000 PY, as compared with the incidence in the general pediatric population of 0.20 cases/1,000 P Y[5].

•There was a significant decline in the IRR of all cancers and of ADCs in the post-HAART era that is similar to that seen among adults.

•Unlike the adult population, there were very few cases of Kaposi sarcoma and no cases of cervical cancer found in the PSD and LEGACY cohorts. The lack of cases of cervical cancer may be related to the young age of the individuals in this study. The low rates of Kaposi sarcoma are consistent with other studies of cancer among pediatric HIV-infected individuals [2-4].

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