HIV, Hepatitis C, Aging and Cancer

*Virus and Other Infection-associated Cancers (VOIC) 2019 Retreat*

Amy C. Justice, MD, PhD
HIV in 2019
More People Are Living With HIV in the United States than Ever Before

www.aids2012.org
Percentage of Adults Living with HIV Aged 50+ By Year and World Region

Source: UNAIDS 2012 estimates.
Age and HIV in the United States: 2014-15

50+ Year of Age:
- 18% of new diagnoses
- 45% of those living with HIV
- 65% of those dying with HIV

Baby Boomers

Center for Disease Control: New Diagnoses 2015, Living 2015, Deaths in 2014
AIDS Events Rare After HIV-1 Suppression

### Period After Starting HAART

- **0-3 mo**
- **4-6 mo**
- **7-12 mo**

#### 13-24 mo

#### 25-36 mo

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<td><strong>Incidence per 1000 Person-Years</strong></td>
<td>25</td>
<td>20</td>
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1. Mycobacterium avium Disease
2. Kaposi Sarcoma
3. Cytomegalovirus Disease
4. Pneumocystis carinii Pneumonia
5. Tuberculosis
6. Esophageal Candidiasis
7. HIV-Related Encephalopathy
8. Toxoplasmosis of the Brain
9. Non-Hodgkin Lymphoma
10. Herpes Simplex Virus Disease
11. Wasting Syndrome
12. Progressive Multifocal Leuкоencephalopathy
13. Cryptococcosis
14. Cryptosporidiosis
15. Bacterial Pneumonia
>50% of Deaths Attributed to “Non-AIDS”
But, Aging with HIV is Not Just Like Aging without HIV

HIV is Associated with Increased Risk of Non AIDS Defining, Aging Associated Conditions Including Cancer
Strategies for Management of Antiretroviral Therapy (SMART):
Continuous Vs. Episodic ART if CD4 350+
N=5472

HIV, not ART toxicity, drives non AIDS disease.

*N Engl J Med 2006;355:2283-2296*
Return to Health? After HIV-1 RNA Suppression Differential Cancer Risk Continues

• Damage to GI lymphatics remains
• Ongoing microbial translocation and inflammation
• CD4 expansion monoclonal, counts good but diversity limited
• Health behaviors
  – Alcohol
  – Smoking
  – Patients gain weight
    • Fatty liver and steatohepatitis
    • Diabetes incidence differentially increases with weight gain
Weight Change Over 12 Months by Baseline Weight Status

**Uninfected**

**HIV Infected After ART Initiation**

- Weight change over 12 months following start date
- Lost > 5 lbs
- Remained within ± 5 lbs
- Gained > 5 lbs

Tate J et al. CROI [Poster] Atlanta, Georgia, March 3-6, 2013
Weight Gain and Incident Diabetes Among HIV-Infected Veterans Initiating Antiretroviral Therapy Compared With Uninfected Individuals

**FIGURE 3.** Relative risk of diabetes in HIV+ (N = 6845) and uninfected (N = 24,345) veterans, by weight change in a 1-year interval compared with those without weight change, adjusted for age, race, sex, baseline BMI, smoking, HCV infection, and calendar year at baseline (excludes those with baseline BMI <18.5 kg/m²). Black circles, HIV+; white circles, uninfected.
Co-infections, Aging, and Sociodemographics Are Important
75% of Hepatitis C Infections Among Those Born in 1945-65
Cancer Incidence by Age: Cancer Research UK
Mortality Disparities by HIV, Race/Ethnicity and Age

Death Rates by Age and Race/Ethnicity

- Black Non-HIV-related
- Black HIV-related
- Hispanic Non-HIV-related
- Hispanic HIV-related
- White Non-HIV-related
- White HIV-related
- NYC all-cause
Cumulative Cancer Risk

Continued alcohol, tobacco, and drug use.

Born 1945-65
Reached adulthood before HCV and HIV testing available

Risk Behaviors
Injection drug use and multiple sexual partners, overlapping HIV/HCV risks

HIV/ HCV Interactions
Immune dysfunction, inflammation

Aging
Birth cohort living well past age of increased cancer incidence
Cancer incidence trends (1997-2012)

With aging of the population, absolute rates of cancer increasing for HIV+ and uninfected. Accounting for demographics, rates are decreasing for those with HIV, but excess risk of cancer persists.

Fig. 1. All cancer crude and standardized incidence rates by HIV status and calendar period and P values for incidence rate period trend. HIV+, HIV-infected; IR, incidence rate.

HIV and Cancer: Risk

Shiels et al. JAIDS. 2009.

Standardized Incidence Ratio for Cancer in HIV+
Why study cancer in the context of HIV infection?
Potential Mechanistic Insights For Cancer

• By comparing uninfected, HIV+ suppressed, and HIV+ unsuppressed, can demonstrate “dose-response”

• Weight gain occurs after HIV-1 suppression, may be an opportunity to study short vs. long term effects of obesity in adulthood

• ART may offer opportunity to study role of medication toxicity

• Not all cancers increased, an opportunity to understand differential role of HIV associated:
  – Immune dysfunction
  – Chronic inflammation/microbial translocation
  – Direct viral effects

• Differential tumor subtypes may also offer insights
NCI Provocative Questions in Cancer with an Underlying HIV Infection RFA-CA-15-012 & 013

1. Are there unique features of HIV-associated inflammation and do these contribute to cancer incidence or outcome?

*Other than immune dysfunction/inflammation:*

2. What are the HIV-mediated mechanisms that underlie differential cancer risk in HIV?

3. What are the mechanisms that underlie differential cancer risk in well-treated HIV?

4. How do the biology of aging and HIV interact in the development of various cancers?

5. What are the differences between analogous tumors in HIV+/- and can these inform prognosis or treatment decisions?

6. Why are only certain cancer types increased whereas others are unchanged or even decreased in HIV infection?

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