HIV Cancer Care Program: Establishing a Regional Center for Multidisciplinary Care

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University Medical Center – New Orleans
Louisiana Cancer Research Center
New Orleans, LA
Overview

The intersection of HIV and cancer

HIV cancer outcome disparities in Louisiana

Establishing a multidisciplinary approach to care for patients in Louisiana

Patient Navigation

Clinical Trials
Attributable Causes of Death in Patients with HIV infection

- Cancer: 23.5%
- Infection: 16.3%
- Heart Disease: 15.4%
- Liver Disease: 14.1%
- Violence/Sub Abuse: 15.4%
- Other: 9.0%
- Kidney Disease: 3.0%
- Lung Disease: 3.1%
- Other: 9.0%

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Oncogenic Virus</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kaposi sarcoma (KS)</td>
<td>KSHV (HHV-8)</td>
<td>1000-2000</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma (NHL)</td>
<td>EBV and KSHV</td>
<td>7-15</td>
</tr>
<tr>
<td>Invasive cervical carcinoma</td>
<td>HPV</td>
<td>3-40</td>
</tr>
<tr>
<td>Anal cancer</td>
<td>HPV</td>
<td>40-80</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>EBV</td>
<td>6-18</td>
</tr>
<tr>
<td>Hepatocellular carcinoma (HCC)</td>
<td>HCV and HBV</td>
<td>3-10</td>
</tr>
<tr>
<td>SCC/penile/vaginal cancers</td>
<td>HPV</td>
<td>2-25</td>
</tr>
<tr>
<td>Brain/head and neck cancers</td>
<td>Polyomaviruses (JC and MCV)</td>
<td>2</td>
</tr>
</tbody>
</table>
Factors Associated with Cancer-related Mortality in Patients with HIV

- 8 US sites (1996-2009), N=20,677, 650 invasive cancers, 305 deaths

- Cancers associated with highest mortality
  - non-Hodgkin lymphoma (NHL)
  - Hepatocellular CA (HCC)
  - lung cancer

<table>
<thead>
<tr>
<th></th>
<th>Adjusted HR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, per decade</td>
<td>1.44 (1.25-1.66)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>CD4 count at cancer, per 100 cells/mm³</td>
<td>0.90 (0.83-0.98)</td>
<td>.01</td>
</tr>
<tr>
<td>HIV-1 RNA suppression to ≤400 copies/mL</td>
<td>0.32 (0.23-0.44)</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

Challenges for HIV and cancer in modern era

Not just AIDS-related:
• Cancers seen increasingly in patients with good CD4# and low HIV VL

Need for improved treatment efficacy and morbidity:
• cytotoxic chemotherapy still the standard
• interactions with ART
  ❖ Additive toxicities (myelosuppression, neuropathy)
  ❖ Drug-drug interactions
• resistance to chemotx (KS and NHL)

What to do with ART?

HAART classes and cancer risk: existing data

Non-nucleoside reverse transcriptase inhibitor effects:
one large study (>71,000 pt-years of f/u) reported an increased RR of Hodgkin’s lymphoma with NNRTI vs other HAART classes

Protease inhibitor effects:
• induce apoptosis and cell cycle arrest
  (inhibits proteasome and Akt activity)

• intrinsic anti-angiogenic effects

• induce surface expression of drug transporters
  (increase doxorubicin resistance for KSHV-infected SLK cells)

• increased risk for anorectal cancer with prolonged PI exposure

General Approach: use INSTIs, minimize nephrotoxicity, VL < 20 c/ml

Racial Disparities for HIV/AIDS Cancers

HIV patients of African decent:

- More often infected by oncogenic HPV subtypes not covered by the HPV vaccine within high-grade cervical intraepithelial lesions

- In Louisiana: increased risk for invasive cervical cancer relative to non-AA women (not seen for rest of U.S.)

- reduced survival for Hodgkin’s lymphoma and NHL

- reduced survival for KS in one recent large study

***Approximately 70% of our patients at the UMCNO ID Center are of African decent

*J Infect Dis.* 2012 Dec 15;206(12):1878-86
*Cancer Causes Control.* 2008 Oct;19(8):841-58
*Cancer Epidemiol Biomarkers Prev.* 2010 Nov;19(11):2718-26
HIV+ DLBCL Outcome Disparities

Anticipated outcomes:
- 5-year survival of $\approx70\%$ (HIV+ or HIV-)
- 50% of untreated patients survive $<1$ year

Urban, minority-predominant HIV+ cohorts:
- $<50\%$ at 2-4 years
- Reduced CD4#
- Detectable HIV viral load
- IVDU

References:

*J Clin Oncol.* 2004; 22(8): 1491-1500

*Blood.* 2006; 107(10): 3832–3840

*JAIDS.* 2010; 54(1): 78-84

*AIDS.* 2011; 25(5): 691-700


*AIDS.* 2009; 23(15): 2029–37

*Blood.* 2014; 123 (23): 3553-62

SEER Cancer Stats Review 1975 – 2009. NCI/NIH

SEER Review. 1969 – 2010. NCI/NIH
DLBCL Outcome Disparities

Greater proportion of HIV+ individuals do not receive treatment for DLBCL

Among HIV+, factors independently associated with lack of cancer treatment:

• low CD4 count
• injection drug use as mode of HIV exposure
• age 45 to 64 years
• AA race

*J Clin Onc.* 2014; 32: 2344-2350
HIV+ cancer outcome disparities

National Cancer Data Base 2003 – 2011

- 10,265 HIV+
- 2,219,232 HIV-

HIV+ more likely to lack cancer treatment:
- Head and neck 1.09 – 2.01
- Upper GI 2.04 – 3.37
- Colon 1.17 – 2.48
- Lung 2.19 – 2.76
- Breast 1.16 – 3.98
- Cervix 1.77 – 4.45
- Prostate 1.69 – 2.76
- HL 1.66 – 2.22
- DLBCL 1.65 – 2.00

Predictors:
- AA race
- lack of private insurance

Cancer. 2016 May 17. doi: 10.1002/cncr.30052
HIV+ cancer outcome disparities: provider bias?

- 300 Medical/Radiation Oncologists
- self-reported delivery of standard cancer treatment
- 45% - rarely/never discussed treatment plan with HIV provider
- 70% - insufficient guidelines for AIDS-associated cancers
- 20-23% - reported not routinely recommending standard treatment for HIV+ patients

- 21% of respondents reported treating HIV+ cancer patients differently:
  - uncomfortable with treatment discussion with patients
  - lack of understanding of HIV-associated factors
  - perception of increased toxicity
  - perception of lack of efficacy

*J Oncol Pract.* 2015; 11(3):e380-7
LA HIV-Cancer Data Linkage

- Cancer Registry – HIV/STD Registry

- Linkage performed using Link-Plus. Match based on name, date of birth, social security number, race, sex, and address.

Table 2. 5-Year Relative Survival Rate of HIV with Cancer by Race, Age, and Stage in Louisiana, 1995-2012

<table>
<thead>
<tr>
<th></th>
<th>Count</th>
<th>%</th>
<th>Survival Rate (%)</th>
<th>Count</th>
<th>%</th>
<th>Survival Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>2,074</td>
<td>100.00</td>
<td>37.2</td>
<td>320,145</td>
<td>100.0</td>
<td>58.5</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whites</td>
<td>820</td>
<td>39.54</td>
<td>41.4</td>
<td>229,734</td>
<td>71.8</td>
<td>60.7</td>
</tr>
<tr>
<td>Blacks</td>
<td>1,244</td>
<td>59.98</td>
<td>34.3</td>
<td>87,604</td>
<td>27.4</td>
<td>52.8</td>
</tr>
<tr>
<td><strong>Age at diagnosis cancer</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;=20</td>
<td>15</td>
<td>0.72</td>
<td>86.4</td>
<td>3,365</td>
<td>1.1</td>
<td>77.0</td>
</tr>
<tr>
<td>21-30</td>
<td>125</td>
<td>6.03</td>
<td>45.5</td>
<td>4,309</td>
<td>1.3</td>
<td>79.2</td>
</tr>
<tr>
<td>31-40</td>
<td>520</td>
<td>25.07</td>
<td>35.8</td>
<td>10,780</td>
<td>3.4</td>
<td>75.6</td>
</tr>
<tr>
<td>41-50</td>
<td>695</td>
<td>33.51</td>
<td>34.6</td>
<td>30,841</td>
<td>9.6</td>
<td>66.2</td>
</tr>
<tr>
<td>51-60</td>
<td>493</td>
<td>23.77</td>
<td>39.3</td>
<td>64,505</td>
<td>20.1</td>
<td>62.3</td>
</tr>
<tr>
<td>61-70</td>
<td>186</td>
<td>8.97</td>
<td>35.7</td>
<td>86,975</td>
<td>27.2</td>
<td>60.4</td>
</tr>
<tr>
<td>71+</td>
<td>40</td>
<td>1.93</td>
<td>40.2</td>
<td>119,370</td>
<td>37.3</td>
<td>50.1</td>
</tr>
</tbody>
</table>

*LSUHSC SPH Cancer Registry; HIV/STD Registry – LA Office of Public Health; NAACR, 2016, St. Louis, MO*
$N = 331$ patient referrals

**Age Distribution**

- <=20: 4
- 21-30: 60
- 31-40: 73
- 41-50: 84
- 51-60: 88
- 61-70: 18
- >71: 3
- Unknown: 1

**Ethnicity Distribution**

- White: 32%
- Black: 60%
- Asian: 1%
- Other: 2%
- Unknown: 1%
- Hispanic: 5%

**Cancer Care Program**
Table 1. Proportion of Cancer with HIV vs. Cancer by Region in Louisiana, 1995-2013

<table>
<thead>
<tr>
<th>OPH Region</th>
<th>Cancer with HIV</th>
<th>Cancer</th>
<th>% of HIV in cancer patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Count</td>
<td>Count</td>
<td></td>
</tr>
<tr>
<td>Region 1_New Orleans</td>
<td>1089</td>
<td>92,570</td>
<td>1.18</td>
</tr>
<tr>
<td>Region 2_Baton Rouge</td>
<td>594</td>
<td>58,216</td>
<td>1.02</td>
</tr>
<tr>
<td>Region 3_Southeast</td>
<td>126</td>
<td>35,301</td>
<td>0.36</td>
</tr>
<tr>
<td>Region 4_Acadiaana</td>
<td>172</td>
<td>55,188</td>
<td>0.31</td>
</tr>
<tr>
<td>Region 5_Southwest</td>
<td>97</td>
<td>29,234</td>
<td>0.33</td>
</tr>
<tr>
<td>Region 6_Central</td>
<td>94</td>
<td>30,001</td>
<td>0.31</td>
</tr>
<tr>
<td>Region 7_Northwest</td>
<td>181</td>
<td>58,487</td>
<td>0.31</td>
</tr>
<tr>
<td>Region 8_Northeast</td>
<td>121</td>
<td>36,362</td>
<td>0.33</td>
</tr>
<tr>
<td>Region 9_Northlake</td>
<td>168</td>
<td>48,529</td>
<td>0.35</td>
</tr>
<tr>
<td>Louisiana</td>
<td>2642</td>
<td>443,888</td>
<td>0.60</td>
</tr>
</tbody>
</table>

LSUHSC SPH Cancer Registry; HIV/STD Registry – LA Office of Public Health; NAACR, 2016, St. Louis, MO
### Non-Viral etiology Versus Viral etiology

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Count</th>
<th>%</th>
<th>Survival Rate (%)</th>
<th>Count</th>
<th>%</th>
<th>Survival Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-viral etiology cancer</td>
<td>1,145</td>
<td>55.21</td>
<td>39.1</td>
<td>289,091</td>
<td>90.3</td>
<td>59.2</td>
</tr>
<tr>
<td>Viral etiology cancer</td>
<td>929</td>
<td>44.79</td>
<td>35.1</td>
<td>31,054</td>
<td>9.7</td>
<td>52.5</td>
</tr>
<tr>
<td>Kaposi sarcoma and primary effusion lymphoma¹</td>
<td>347</td>
<td>16.73</td>
<td>39.5</td>
<td>176</td>
<td>0.1</td>
<td>80.8</td>
</tr>
<tr>
<td>Diffuse large B-cell lymphoma (DLBCL)²</td>
<td>246</td>
<td>11.86</td>
<td>22.9</td>
<td>4,003</td>
<td>1.3</td>
<td>53.8</td>
</tr>
<tr>
<td>Cervical cancer, anorectum, oral squamous cell cancer ³</td>
<td>287</td>
<td>13.84</td>
<td>44.3</td>
<td>22,891</td>
<td>7.2</td>
<td>58.9</td>
</tr>
<tr>
<td>Hepatocellular cancer (HCV)⁴</td>
<td>49</td>
<td>2.36</td>
<td>12.4</td>
<td>3,984</td>
<td>1.2</td>
<td>12.1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>2,074</td>
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</tr>
</tbody>
</table>

¹ KSHV etiology: Kaposi sarcoma and primary effusion lymphoma
² EBV etiology: diffuse large B-cell lymphoma
³ HPV etiology: cervical cancer, anorectum, oral squamous cell cancer.
⁴ HCV etiology: liver
Management of Cancer in HIV-infected patients:

Need for dual-disease management (HIV and Oncology): “Having dedicated and experienced HIV doctors and oncologists in the same space who communicate with one another and make decisions jointly together—that’s the best approach”

Patient “Navigation”

Clinical trials screening – adopt as standard care

AACR, Sept. 2016
AIDS Malignancies Consortium, NCI/NIH, 10/2015
LSUHSC ID Oncology Clinic
Identification and enrollment

Cancer Diagnosis

Navigation
- Social service assessment
- Med-Onc Team
- Clinical trials screening

Navigation/Outreach
Medical Oncology
HIV/subspecialty care
Clinical Trials
Biorepository

Research Themes
- Clinical trials
- Navigation/case management: impact on care/retention/outcomes
- Translational studies
- Health disparities

Treatment

Standard of Care
Clinical Trial
HIV Cancer Care Program Staff

**Patient Navigation and Outreach:**
Sam Euraque, MA  
Keri Watson, GSW  
Natalie Dietz, MSW

**Clinical Trials Management:**
Jim Outland, RN, BSN, CCRC, CIP  
Sharon Weiser, RN

**Medical Oncology:**
Tom Reske, MD/PhD  
Suki Subbiah, MD  
Michelle Loch, MD  
Brian Boulmay, MD

**HIV/Virology:**
Michael Hagensee, MD/PhD  
Chris Parsons, MD

**Radiology:**
Bradley Spieler, MD

**Pharmacy:**
Katie Nguyen, PharmD

**Clinical Trials Unit (CTRC):**
Mary Meyaski-Schluter, RN  
Virginia Garrison, RN  
Erin Plaia, RN

**LSUHSC SPH Cancer Registry**
XC Wu  
X Li  
Patricia Andrews  
Billy Robinson

**Surgery:**
Guy Orangio, MD  
Jeff Barton, MD
Patient Navigation Services: August 2016
N=1495
August 2016
Medical Service Referrals
N=665
August 2016 - Others Referrals
N=209
Hope Lodge-
New Orleans

- Private rooms

- ACS volunteers help visitors access NIH/NCI information about cancer

- Assistance with ADLs

- Located minutes from downtown New Orleans
HIV Clinics

- LSUHSC HIV Outpatient (HOP) Clinic
- HIV Early Intervention Clinic (Baton Rouge)
- North (ID) Clinic/Acadiana Cares (Lafayette, LA)
- HIV Go Care (Monroe, LA)
- HIV Caring Clinic (Hammond, LA)
- Philadelphia Center (Shreveport, LA)
- Crescent Care (formerly No-AIDS Task Force Clinic, New Orleans, LA)

Hospitals

- Feist-Weiller Cancer Center (Shreveport, LA)
- Mary Bird Perkins Hospital (Baton Rouge, LA)
- Lafayette General/University Hospital and Clinics
- Tulane Medical Center
- Ochsner Medical Center
- University of Mississippi Medical Center (Jackson, LA)

HIV-Based Community Organizations

- New Orleans Regional AIDS Planning Council (New Orleans)
- Connect to Protect (HIV community-based organization, New Orleans)
- Excelth (HIV community-based organization, New Orleans)
- Family Services of Greater Baton Rouge
August 2013 - August 2016
Referral Sources

Priority Health
Belle Reve
Drop In Clinic
American Cancer Society
LSU Shreveport
Caring Clinic
Ochsner
SLAC
Self-Referral
Acadiana Cares
Private Physician
Crescent Care
Go Care
Unknown
Tulane
University of Medical Center
NO AIDS Task Force
Infectious Disease Center
North Clinic

Referral Sources
Cancer Referrals

1. Kaposi sarcoma 48
2. Non-Hodgkin Lymphoma 34
3. Anal 18
4. Hodgkin Lymphoma 8
5. Prostate 7
6. Lung-Non-Small Cell 5
7. Cervical 5
8. Breast 5
9. Oral Cavity and Oropharyngeal 4
10. Liver 4
11. Burkitt Lymphoma 3
12. Adenocarcinoma 3
13. Lung-Small Cell 3
14. Colorectal 3
15. Bladder 3
16. Unknown 2
17. Skin-Basal & Squamous Cell 2
18. Renal Cell Carcinoma 2
19. Penile 2
20. Esophagus 2
21. Viral Infection 1
22. Merkel Cell 1
23. Vulvar 1
24. Vaginal 1
25. Testicular 1
26. Sarcoma Soft Tissue 1
27. Pancreatic 1
28. Castleman's Disease 1
29. Appendix 1
**Clinical Trials:**

ALDOX-P2-KS-01
2R42-CA183708  CytRx Corp.; KS
Apogee Biotech.; DLBCL, KS

CITN-12  NCI/Fred Hutch.; KS, Heme, HCC, lung, melan.

2U01-CA121947  AIDS Malignancies Consortium: HPV studies
Anchor Study
AMC-088
AMC-092

GS-US-311-1717  cART switch: ABC/3TC to F/TAF backbone
GS-US-380-1489  ART naïve - F/TAF/9883
GS-US-380-1844  cART switch: ABC/3TC/DTG to F/TAF/9883
GS-US-380-1878  cART switch: ATZ/r + TDF/FTC to F/TAF/9883
Challenges for Kaposi’s sarcoma (KS)

- Still around 2% lifetime incidence for HIV patients
- No way to predict or prevent KS (other than HIV medication)
- Median survival of 1.5 years with low CD4 and visceral disease
- Risk factors
  - Reduced CD4#
  - Reduced ART adherence
  - MSM
- The single cancer with the highest racial incidence disparity in the United States!!
  - Improvement in survival over time with better HIV treatment has been more limited for AA (*Cancer Epidemiol Biomarkers Prev.* 2010; 19(11); 2718–26)
  - The greatest difference in race-based cancer incidence (new cases per capita) in the United States  (*American Cancer Society*, 2014)
Liposomal Doxorubicin (*Cancer*. 2010, 116(16): 3969-3977)

*Urban, minority-predominant KS cohort with moderate to severe disease*

- **CR +PR response rates:** 47%
- **Median PFS:** 12.2 months
- **Grade 3+ adverse events:**
  - CD4: 29%
  - Neutropenia: 37%
  - Overall: 66%

---

Aldoxorubicin (*ASCO*. 2016)

*Urban, minority-predominant KS cohort with moderate to severe disease*

- **CR +PR response rates:** 85%
- **Median PFS:** 26 months
- **Grade 3+ adverse events:**
  - CD4: 0%
  - Neutropenia: 22%
  - Overall: 44%
An Early-Phase Clinical Trial Evaluating ABC294640 in Patients with Refractory/Relapsed DLBCL or Kaposi sarcoma (2R42-CA183708; NCT02229981)

- Phase I/IIa
- ABC294640 = inhibitor of Sphingosine Kinase-2 (SK2)
- HIV+ or HIV-negative
- Projected MTD: 500mg BID capsules
- Endpoints:
  - Safety
  - PK
  - Preliminary efficacy
Phase I Study of MK-3475 (Pembrolizumab) in Patients with Human Immunodeficiency Virus (HIV) and Relapsed/Refractory or Disseminated Malignant Neoplasm (NCT02595866)

- Phase I
- Pembrolizumab = humanized a-PD1 mAb
- Sites: NYU, Roswell Park, Yale, UCSF, U Wash, Mt Sinai, Moffitt, LSUHSC, NCI
- Inclusion: KS, NHL, HL, BL, NSCLC, HCC, Melanoma
- Endpoints:
  - AEs
  - cART/immune ECI
  - PFS, OS, duration of response, ORR
HIV Biorepository

Accomplishments
• >29,500 specimens banked (plasma, PBMC, saliva, KS/lymphoma tissue)
• Samples distributed to > 20 investigators from 6 institutions

Translational Research Awards
R01-CA121979   EBV-HPV cervical dysplasia
R01-CA142362   HIV Cancer Prevention; oxidative stress
P60-AA009803   EtOH/KSHV pathogenesis
F31-CA180449   viral lymphoma genomics
U54-GM104940   EBV/lymphoma pathogenesis
U54-GM104940   HIV cancer prevention, cognitive impairment
P20-RR021970   KSHV regulation of emmprin
UL1-TR000165   hyaluronic acid and cancer risk

Infrastructure/program awards
UG1-CA189854 (NCORP)
U54-GM104940 (LaCATS)
P20-GM103501 (COBRE)
NIH/NCI AIDS Cancer Specimen Resource (ACSR)
CANCER CARE PROGRAM

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cpars1@lsuhsc.edu

www.hivcancercare.com