AIDS Associated Malignancies

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Objectives

• List and describe the mechanisms of AIDS associated malignancies
• Identify and describe oncoviruses seen in the setting of HIV infection
• Describe the 3 AIDS defining malignancies
• Develop a basic cancer therapy plan for patients with AIDS defining malignancies
A. Pathogenesis of malignancy in the setting of HIV and Viral Oncogenesis

B. AIDS associated malignancies
   1. Non-Hodgkin’s Lymphoma
   2. Kaposi’s Sarcoma
   3. Cervical Cancer

C. Impact of HAART

D. Chemotherapy Considerations in HIV positive patients

E. Screening guidelines
Types of HIV Associated Malignancies

AIDS defining cancers
- Kaposi’s Sarcoma (1000x)
- Non-Hodgkin’s Lymphoma (70x)
- Invasive Cervical Cancer (5x)

Non-AIDS defining cancers
- Anal Cancer (25x)
- Liver Cancer (5x)
- Lung Cancer (3x)
- Hodgkin’s Lymphoma (10x)

Pathogenesis of Malignancy in HIV

- Decreased tumor surveillance from immunosuppression
- Chronic Antigenic Stimulation
- Immune Dysregulation
- Co-infection with oncoviruses
Chronic stimulation of B cells by HIV can lead to B cell mistakes. Tumor suppressor genes such as P53 and Retinoblastoma are compromised in this process. Co-infection with HHV8, HPV, and EBV leads to an amplified risk.
## Decreased Immune Surveillance

<table>
<thead>
<tr>
<th>Cancer</th>
<th>SIR* in HIV/AIDS patients</th>
<th>SIR* in Transplant Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non Hodgkin’s Lymphoma</td>
<td>22.6-353.5</td>
<td>5.5-9.9</td>
</tr>
<tr>
<td>Hodgkin’s Lymphoma</td>
<td>3.6-18</td>
<td>2.2-8.0</td>
</tr>
<tr>
<td>Kaposi’s Sarcoma</td>
<td>3640</td>
<td>208</td>
</tr>
<tr>
<td>Cervical Cancer</td>
<td>22</td>
<td>1.5-2.5</td>
</tr>
<tr>
<td>Anal</td>
<td>19.6-50</td>
<td>2.8-10.3</td>
</tr>
<tr>
<td>Breast</td>
<td>0.7-1.4</td>
<td>1.0-1.5</td>
</tr>
<tr>
<td>Colorectal</td>
<td>0.9-1.4</td>
<td>1.4-2.1</td>
</tr>
<tr>
<td>Lung</td>
<td>1.4-4.5</td>
<td>1.7-2.1</td>
</tr>
<tr>
<td>Liver</td>
<td>1.9-22.2</td>
<td>1.1-3.2</td>
</tr>
</tbody>
</table>

*Standard Incidence Ratio

HIV Infection

• HIV does not infect the neoplastic cells
• Chronic antigenic stimulation of B cells leads to polyclonal B cell expansion and leads to emergence of monoclonal B cell populations which lead to B cell malignancies
HIV Infection

- Tat protein of HIV is taken up by B lymphocytes

Concentration of phosphorylated Rb

- DeFalco et al. oncogene. 2003;22:6214
Immune Dysregulation

- Pelvic lymph nodes were collected from HIV positive and normal healthy patients.
- Dissected and evaluated by immunohistochemistry, flow cytometry, and cytokine production.

**Biancorro. Blood. 2007; 109:4272**

Marker of activated T Cell

Marker of cell death
• causes T cell activation
• IL-2 levels >10 fold higher

• enhances B cell survival

• Produces INF-γ and mediates toxicity of cytotoxic NK cells

Co-infection with Oncogenic Viruses

- HHV-8 (human herpes virus 8 or Kaposi’s sarcoma-associated virus)
- EBV (Epstein Barr virus): lymphoma
- HPV (human papilloma virus): cervical cancer, anal cancer, penile cancer, vaginal cancer, vulvar cancer, head and neck cancer
Co-infection with HHV8

- 1872: Mortiz Kaposi described blood vessel tumor (idiopathic multiple pigmented sarcoma of the skin)
- Mid 1900’s: epidemiological data suggested increased risk in the Jewish, Mediterranean, and Sub-Saharan African populations
- 1980’s: increased incidence of KS in AIDS patients
- 1994: novel gamma herpesvirus identified from biopsies of KS

Pathogenesis

Mesri. Blood. 1999; 93 (12)
HHV8 associated malignancies

Co-infection with HPV

- HPV infection is a result of the same lifestyle risks as HIV infection
- HIV infected patients are unable to clear oncogeneic HPV strains due to poor T cell response
Pathogenesis

p53 Mechanisms

DNA damage

p53 induction

p53

Cell cycle arrest

Apoptosis (cell death)

DNA repair
Pathogenesis

Papillomavirus Infection

E7 Action on Rb
Co-Infection with EBV

- Patients with AIDS lack T cell immunity needed to clear EBV infected B cells
- Most AIDS related lymphomas demonstrate direct infection of the malignant cells with EBV
- Risk of lymphoma in patients with AIDS is inversely proportional to the number of EBV specific cytotoxic T cells
- Risk of lymphoma is not associated with EBV viral load (unlike post-transplant lymphoproliferative disorders)
EBV Viral Genome

EBV Genome, 172 kb
Targeted by EBV specific cytotoxic T cells.
EBV Induced Oncogenesis

Blood. 2013;122(3):328
AIDS Defining Malignancies
Types of HIV Associated Malignancies

AIDS defining cancers (ADC)
- Kaposi’s Sarcoma (1000x)
- Non-Hodgkin’s Lymphoma (70x)
- Invasive Cervical Cancer (5x)

Non-AIDS defining cancers (NADC)
- Anal Cancer (25x)
- Liver Cancer (5x)
- Lung Cancer (3x)
- Hodgkin’s Lymphoma (10x)

**CD4 and VL Correlate to Risk of ADCs**

<table>
<thead>
<tr>
<th>Kaposi's sarcoma (n=565)</th>
<th>Non-Hodgkin lymphoma (n=511)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 count (cells per µL)</td>
<td>RR (95% CI)</td>
</tr>
<tr>
<td>≥500</td>
<td>1.0 (1.0–1.0)</td>
</tr>
<tr>
<td>350–499</td>
<td>1.9 (1.3–2.7)</td>
</tr>
<tr>
<td>200–349</td>
<td>3.3 (2.3–4.6)</td>
</tr>
<tr>
<td>100–199</td>
<td>6.2 (4.2–9.0)</td>
</tr>
<tr>
<td>50–99</td>
<td>14.1 (9.4–21.3)</td>
</tr>
<tr>
<td>0–49</td>
<td>25.2 (17.1–37.0)</td>
</tr>
<tr>
<td>Viral load (copies per mL)</td>
<td>RR (95% CI)</td>
</tr>
<tr>
<td>&lt;500</td>
<td>1.0 (1.0–1.0)</td>
</tr>
<tr>
<td>≥500–10 000</td>
<td>1.0 (0.7–1.4)</td>
</tr>
<tr>
<td>&gt;10 000–100 000</td>
<td>1.4 (1.1–1.9)</td>
</tr>
<tr>
<td>&gt;100 000</td>
<td>3.1 (2.3–4.2)</td>
</tr>
</tbody>
</table>

Guiguet et al. Lancel Onocol. 2009; 10:1152
NHL

- **Systemic NHL**
  - Diffuse Large B cell Lymphoma
    - 80% EBV related
    - Usually occurs with CD4 of <100
  - Burkitt’s Lymphoma
    - 40% EBV related
    - Occurs at any CD4 count
  - Plasmablastic Lymphoma
    - 74% EBV associated

- **Primary Effusion Lymphoma (PEL)**
  - EBV or HHV 8 related

- **Primary CNS Lymphoma (PCNSL)**
  - 100% EBV related

Tend to occur in immunocompromised hosts
Diffuse Large B Cell Lymphoma

- **Path**
  - Large lymphocytes with nuclei greater than twice the size of normal, prominent nucleoli, basophilic cytoplasm

- **Flow Cytometry**
  - CD19, CD 20, CD22, CD79a
Burkitt’s Lymphoma

- Morphology:
  - Medium size cells
  - Basophilic cytoplasm
  - Lipid vacuole
  - Starry sky appearance: due to macrophages ingesting apoptotic tumor cells
FISH for c-myc

Chromosomal translocations in Burkitt’s lymphomas

normal chromosomes

Burkitt’s lymphoma t(8;14)

8q- 14q+

q24.13 myc q32.33 IgH

der(14) 3’MYC+

der(8) 5’MYC+
Primary Effusion Lymphoma (PEL) and Plasmablastic Lymphoma (PBL)

PBL: Presents in oral cavity
PEL: Presents in body cavities (pleural, pericardial, peritoneal spaces)
Both associated with HHV8
Both have a poor prognosis
Table 1. DLBCL patient characteristics by HIV infection status

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HIV-infected (N = 80)</th>
<th>HIV-uninfected (N = 80)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, mean (SD)</td>
<td>47.9 (9.2)</td>
<td>50.6 (15.9)</td>
<td>0.97</td>
</tr>
<tr>
<td>Male gender</td>
<td>74 (92.5%)</td>
<td>70 (87.5%)</td>
<td>0.29</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>47 (58.8%)</td>
<td>47 (58.8%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Non-white</td>
<td>33 (41.2%)</td>
<td>33 (41.2%)</td>
<td></td>
</tr>
<tr>
<td>Known duration of HIV infection, year, mean (SD)</td>
<td>5.2 (5.80)</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Prior AIDS diagnosis</td>
<td>34 (42.5%)</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Prior use of ART</td>
<td>52 (65.0%)</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>CD4 cell count at DLBCL diagnosis, cells/mm³, mean (SD)</td>
<td>206.2 (166.9)</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Lowest CD4 cell count recorded in KP before DLBCL diagnosis, cells/mm³, mean (SD)</td>
<td>712 (66.7)</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>SEER summary stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I (localized)</td>
<td>20 (25%)</td>
<td>38 (47.5%)</td>
<td>0.01</td>
</tr>
<tr>
<td>II (regional)</td>
<td>14 (17.5%)</td>
<td>15 (18.8%)</td>
<td></td>
</tr>
<tr>
<td>III (advanced)</td>
<td>38 (47.5%)</td>
<td>23 (28.8%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>8 (10.0%)</td>
<td>4 (5%)</td>
<td></td>
</tr>
<tr>
<td>Extranodal involvement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>33 (41.3%)</td>
<td>9 (11.3%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Unknown</td>
<td>0 (0%)</td>
<td>19 (23.8%)</td>
<td></td>
</tr>
<tr>
<td>Cell-of-origin phenotype</td>
<td></td>
<td></td>
<td>0.01</td>
</tr>
<tr>
<td>Germinal center (GC)</td>
<td>31 (38.8%)</td>
<td>21 (26.3%)</td>
<td></td>
</tr>
<tr>
<td>Non-GC</td>
<td>41 (51.3%)</td>
<td>58 (72.5%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>8 (10.0%)</td>
<td>1 (1.3%)</td>
<td></td>
</tr>
<tr>
<td>DLBCL subtype</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Centroblastic</td>
<td>56 (70.0%)</td>
<td>72 (90%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Immunoblastic</td>
<td>18 (22.5%)</td>
<td>5 (6.3%)</td>
<td></td>
</tr>
<tr>
<td>Plasmablastic</td>
<td>6 (7.5%)</td>
<td>1 (1.3%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>0 (0%)</td>
<td>2 (2.5%)</td>
<td></td>
</tr>
</tbody>
</table>
Evaluation

- PET scan
- Excisional biopsy to examine architecture of the LN
- Bone Marrow Biopsy
  - Helpful when biopsy is non-diagnostic or demonstrates HIV-related hyperplasia or if lymph node is not accessible
Extranodal involvement

- GI tract 14%
  - GI evaluation if scans show solitary lesions, wall thickening, or cavitation
- Lung/Pleural Effusions
  - Diagnostic tap of fluid for staging
- Liver
- Bone Marrow 25-55%
- Lymphomatous meningitis 5-20%
Lymphomatous meningitis

- Occur in 5-20% of HIV + NHL
- Tends to occur in patients with:
  - Burkitt histology
  - Bone marrow involvement
  - More than one extranodal site with elevated lactate dehydrogenase, paranasal or paraspinal involvement, CD4<100, EBV + tumor

- Diagnosis:
  - Lumbar puncture with flow cytometry, cytology, cell count /differential, total protein, glucose on all patients
    - Total protein usually elevated
    - Lymphocytosis on differential
  - Brain and spine MRI if symptomatic or focal neuro sign

- All patients need prophylactic intrathecal chemotherapy
Kaposi’s Sarcoma

Can also occur in
1. Oral cavity
2. GI tract
3. Lungs
Differential Diagnosis: Bacillary Angiomatosis

![Bacillary Angiomatosis Image]

**Bacillary Angiomatosis**

The Warthin-Starry stain demonstrates numerous bacilli, corresponding to the deep-staining eosinophilic or amphiphilic interstitial material.
Biopsy of KS

- **Hallmarks:**
  - Inflammation
  - Proliferation
  - Angiogenesis

- Vessels are friable/leaky because they lack a basement membrane, appear purple

- **two major abnormalities:**
  - Whorls of spindle-shaped cells
  - Neovascularization
Staging

<table>
<thead>
<tr>
<th></th>
<th>Good Risk (all of the following)</th>
<th>Poor Risk (any of the following)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor</td>
<td>T0: Confined to skin, lymph nodes, or minimal oral disease</td>
<td>T1: tumor associated edema or ulceration Extensive oral KS GI KS (scope if FOBT +) KS in viscera (scope if CXR abnormal)</td>
</tr>
<tr>
<td>Immune System</td>
<td>I0: CD4 &gt;200</td>
<td>I1: CD4 &lt;200</td>
</tr>
<tr>
<td>Systemic Illness</td>
<td>S0: No history of OI No B symptoms Performance status of &gt;70</td>
<td>S1: History of OI B symptoms presents Performance status of &lt;70 Presence of HIV associated illnesses</td>
</tr>
</tbody>
</table>

Prognosis: Swiss HIV Cohort Study

<table>
<thead>
<tr>
<th></th>
<th>Number of patients</th>
<th>Coefficient B</th>
<th>Hazard ratio (95%CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staging</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>113</td>
<td>1 (referent)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>31</td>
<td>1.65</td>
<td>5.22 (2.97–9.18)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CD4 level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At least 200</td>
<td>50</td>
<td>1 (referent)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Below 200</td>
<td>94</td>
<td>0.85</td>
<td>2.33 (1.22–4.45)</td>
<td>0.01</td>
</tr>
<tr>
<td>HHV8 DNA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>106</td>
<td>1 (referent)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>38</td>
<td>0.76</td>
<td>2.14 (1.79–2.85)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

95% CI, 95% confidence interval; HHV8, human herpesvirus 8.

El Amari et al. AIDS. 2008; 22(9): 1019.
Cervical Cancer

Cytology
Histology

LSIL
CIN 1

CIN 2

HSIL
CIN 3

Normal

Very Mild/
Mild Dysplasia

Moderate
Dysplasia

Severe
Dysplasia

In Situ
Carcinoma

Invasive
Carcinoma

HPV Infection,
Virus Production

No Virus
Production

High E6 and E7

Viral DNA
Integration

Microinvasive
Carcinoma

J Am Osteopath Assoc. 2011;111(3 suppl 2):S35-S43
Cervical Cancer Screening: ACOG 2016

- Screen with PAP smear within one year of the onset of sexual activity and the diagnosis of HIV Q6 months x 2
- Screen for the duration of life (unlike for HIV negative population until age 65)
- Age <30
  - Yearly then Q3 years if 3 consecutive cytology tests are normal
  - Colopsopy for:
    - For HPV positive atypical squamous cells of undetermined significance (ASC-US)
    - Low grade squamous epithelial lesion (LSIL), HSIL, ASC-high grade,
- Age >30
  - Can co-test (test cytology and HPV)
  - Co-test negative women can get cytology q 3 years
  - Cytology negative, HPV positive, if HPV 16 or 18 positive → colposcopy
Impact and Implications of HAART on AIDS Associated Malignancies
Introduction of ART in 1996

Concomitant HAART

• Initial trials, HAART was interrupted during chemotherapy
• Intermittent HAART lead to resistance
• Recommendation: concomitant HAART and chemotherapy, ESPECIALLY if cancer therapy is curative
• Exception: dose adjusted R-EPOCH
  o Ensures that maximum dose of chemotherapy is used to treat lymphoma without drug interactions with HAART
  o 74% CR rates
  o After HAART was re-instituted, VL fell and CD4 normalized

Sparano et al. JCO. 2004; 22:1491
# Choice of HAART

- Avoid overlapping toxicities of HAART and chemotherapy

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Chemotherapy/Related Medications</th>
<th>HAART</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurotoxicity</td>
<td>Vincas, Platinum agents, Taxanes, brentuximab</td>
<td>Didanosine, stavudine</td>
</tr>
<tr>
<td>Myelotoxicity</td>
<td>Alkylating agents, Anthracyclines, Topo II inhibitors</td>
<td>Zidovudine, <strong>contraindicated</strong> Ritonanvir</td>
</tr>
<tr>
<td>Cardiotoxicity</td>
<td>Anthracyclines, Ondansetron, Levaquin</td>
<td>QT prolonging agents (dolutegravir, raltegravir, maraviroc)</td>
</tr>
<tr>
<td>Hepatotoxicity</td>
<td>Any chemotherapy metabolized by liver</td>
<td>Didanosine, Stavudine Zidovudine, <strong>avoid in chemo metabolized by liver</strong></td>
</tr>
</tbody>
</table>
Chemotherapy Implications of AIDS Associated Malignancies
Therapy of AIDS Associated Malignancies

- Significant co-morbidities that result in poor performance status
- Increase risk of infection with surgery and myelosuppressive chemotherapy
- HIV associated NHL tend to have increased expression of multidrug resistance gene-1 (MDR-1)

Incorporating HAART in NHL

Rituximab for NHL

Treatment for KS

Local Therapy

• Intralesional chemotherapy with vinblastine (75% partial response lasting median of 4.3 months) (Cancer. 1993:71(5):1722)

• Radiation

• Topical retinoic acid

Systemic Therapy (taxanes or anthracyclines)

• Indications
  o >25 lesions
  o Refractory to local therapy
  o Extensive edema
  o Symptomatic visceral involvement
  o IRIS
IRIS in KS

- Inflammatory response after initiation of HAART
- Results in a paradoxical progression

**Table 1. Clinicopathologic Features of KS Patients and HAART Administration**

<table>
<thead>
<tr>
<th>Features</th>
<th>No IRIS KS</th>
<th>IRIS KS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Patients</td>
<td>%</td>
</tr>
<tr>
<td>Demographic features</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total patients</td>
<td>140</td>
<td>100</td>
</tr>
<tr>
<td>Female</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>38</td>
<td>37</td>
</tr>
<tr>
<td>SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV-related features</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD4 count at KS diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median, cells/mm³</td>
<td>121</td>
<td>335</td>
</tr>
<tr>
<td>IQR</td>
<td>212</td>
<td>195</td>
</tr>
<tr>
<td>HIV viral load at KS diagnosis, copies/mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>309,000</td>
<td>295,000</td>
</tr>
<tr>
<td>IQR</td>
<td>171,000</td>
<td>195</td>
</tr>
<tr>
<td>Prior AIDS-defining illness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>23</td>
<td>0</td>
</tr>
<tr>
<td>KS features</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1 stage</td>
<td>33</td>
<td>24</td>
</tr>
<tr>
<td>T2 stage</td>
<td>87</td>
<td>80</td>
</tr>
<tr>
<td>Tumor-associated edema</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>Extensive oral involvement</td>
<td>17</td>
<td>12</td>
</tr>
<tr>
<td>Pulmonary KS</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Gastrointestinal KS</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>Treatment, first HAART regimen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PI based</td>
<td>63</td>
<td>45</td>
</tr>
<tr>
<td>NNRTI based</td>
<td>70</td>
<td>50</td>
</tr>
<tr>
<td>Triple NRTI based</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Both PI and NNRTI-based</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

Bower et al. JCO. 2005: 23(22):5224
Management of Cervical Neoplasia

Low Grade Lesions
- Regression is common, especially with HAART
- Lesion that persists for one year or progresses should be treated
  - Excision
  - Ablation
  - Adjunctive Topical 5FU
    - Reduces recurrence by 47%
  - HAART

Invasive Cancer
- Surgery for stage I
- Chemoradiation for stage IIA-IIIB
- Chemotherapy used with stage IV disease
Preventing Cancer

• HAART, HAART, HAART
  o Lowers Kaposi and NHL
  o But no change in incidence of cervical cancer

• Smoking cessation

• Viral therapy for hepatitis

• HBV vaccine

• PAP smears and HPV Vaccines

• No recommendation for more aggressive screening guidelines
Conclusions

• Malignancy in the setting of HIV infection is a result of decreased immune surveillance, immune dysregulation, and infection with oncogenic viruses.

• The 3 AIDS defining malignancies are non-Hodgkin’s lymphoma, Kaposi’s sarcoma, and cervical cancer.

• Introduction of HAART has drastically reduced the incidence of AIDS associated malignancies except for cervical cancer.

• HAART should be continued throughout cancer therapy. Individual therapies should be selected based on non-overlapping toxicities.