Pharmacotherapy of Comorbidities: Cancer Patients with HIV/AIDS

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NON FDA/EMEA Approved use of drugs or products will be referenced with regards to AIDS Malignancies.

Michelle A. Rudek, Pharm.D., Ph.D.
Overview

• Trends of AIDS malignancies
• Goals of HIV management
• How to manage individual patients and develop clinical trials for HIV patients with cancer
• Discuss current Guidance Documents
Cancers in Patients with HIV/AIDS

AIDS-DEFINING:
- Kaposi’s sarcoma
- Non-Hodgkin’s lymphoma
- Cervical cancer

NON-AIDS-DEFINING:
- Anal cancer
- Colorectal
- Head and neck cancer
- Hepatocellular carcinomas
- Hodgkin’s lymphoma
- Leukemia
- Lung cancer
- Melanoma
- Renal
- Vaginal

Excess Cancer Cases in People Living with HIV (PLWH)
HIV Treatment

• **Goal:** To suppress plasma HIV RNA, preserve or improve immune function while preventing transmission and decreasing HIV-associated morbidity/mortality while improving the duration and quality of survival

• In developed countries, initiate antiretroviral therapy (ART):
  • In all individuals with HIV regardless of CD4 counts with increased urgency in:
    - Pregnancy
    - Lower CD4 counts (<200 cells/mm³)
    - AIDS-defining conditions
    - HIV-associated nephropathy
    - Acute opportunistic infections
    - Acute/early infection
    - HIV/hepatitis B virus coinfection
    - HIV/hepatitis C virus coinfection

• Initial regimens selected for maximal compliance considering:
  • Pretreatment viral load, CD4 count, and HIV genotypic drug resistance testing
  • HLA-B*5701 status
  • Individual preference
  • Anticipated adherence
  • Comorbidities and Coinfections
  • Drug-specific factors
## Drug Interaction Potential: Antiretrovirals

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Route of Elimination</th>
<th>Effect on CYP450/transporter</th>
<th>Drug Interaction Potential As a Perpetrator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nucleoside reverse-transcriptase inhibitor</td>
<td>Renal excretion, ABC and SLC transporter, UGT</td>
<td>No known effect or no clinically relevant effect</td>
<td>Unlikely</td>
</tr>
<tr>
<td>Nucleotide reverse-transcriptase inhibitor</td>
<td>Renal excretion, ABC and SLC transporter</td>
<td>CYP450 and ABC transporter inhibitor</td>
<td>Possible</td>
</tr>
<tr>
<td>Non-nucleoside reverse-transcriptase inhibitor</td>
<td>CYP450, UGT, ABC transporter</td>
<td>CYP450 and transporter inhibitor and inducer</td>
<td>Critical or Significant</td>
</tr>
<tr>
<td>HIV-1 protease inhibitor</td>
<td>CYP450, UGT, ABC transporter</td>
<td>CYP450 and transporter inhibitor and inducer</td>
<td>Critical or Significant</td>
</tr>
<tr>
<td>Integrase strand-transfer inhibitor</td>
<td>UGT, ABC and SLC transporter</td>
<td>CYP450 and transporter inhibitor and inducer</td>
<td>Critical or Significant</td>
</tr>
<tr>
<td>Fusion inhibitor</td>
<td>Catabolism</td>
<td>No known effect or no clinically relevant effect</td>
<td>Possible or Unlikely</td>
</tr>
<tr>
<td>Entry inhibitor (chemokine receptor antagonists)</td>
<td>CYP450, ABC and SLC transporter</td>
<td>No known effect or no clinically relevant effect</td>
<td>Possible or Unlikely</td>
</tr>
<tr>
<td>Ritonavir- or cobicistat-boosted regimens</td>
<td>CYP450, ABC transporter</td>
<td>CYP450 and transporter inhibitor</td>
<td>Contraindicated or Critical</td>
</tr>
</tbody>
</table>

DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. October 2017; 1-298
Lancet Oncol. 2011;12(9):905-12. Micromedex; UpToDate Online v. 18.1
General Considerations in Treating PLWH with Cancer

• What is the treatment goal for the stage of cancer?
• How advanced is the HIV infection? Are there multiple complications (opportunistic infections)?
• When does cancer diagnosis occur relative to HIV-infection diagnosis?
• Management complicated by:
  • Lymphadenopathy complicates staging
  • Perceived significant comorbidities
  • Perceived to be poor surgical candidates
  • Combination of ART with chemotherapy
    • Drug-drug interactions
    • Overlapping toxicity
    • Prophylaxis for opportunistic infections
    • Hematopoietic growth factor support
Determinants of Dosing Regimen Selection

**State of Patient**
- Age
- Weight
- Other disease states

**Other Factors**
- Cost
- Route of administration
- Dosage form
- Tolerance-dependence
- Drug interactions

**Management of Therapy**
- Convenience of regimen
- Compliance of patient

**Pharmacokinetics**
- Absorption
- Distribution
- Metabolism
- Excretion

**Pharmacodynamics**
- Therapeutic window
- Side effects
- Exposure-response relationships

**Pharmacogenetics**
- Target genes
- Drug metabolizing enzymes
- Drug transporter

Adapted from *Cancer: Principles & Practice of Oncology*, 10th edition. 2014 DeVita, Lawrence, Rosenberg, eds.
Toxicity-Related Concerns

<table>
<thead>
<tr>
<th>AIDS</th>
<th>Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td>Zidovudine</td>
</tr>
<tr>
<td></td>
<td>Ritonavir-boosted ART</td>
</tr>
<tr>
<td></td>
<td>Cytotoxic Agents</td>
</tr>
</tbody>
</table>

*Due to toxicity concerns, these agents are not first-line in developed countries.*
In mice, the CYP3A4 inhibitors ritonavir and ketoconazole resulted in a 6.9- and 3.1-fold increase in AUC, respectively.
Special Populations

- Organ dysfunction
- Pregnant/breastfeeding women
- Elderly
- Pediatric
- Obese
- Cancer patients with HIV/AIDS
Drug Development Paradigm in Oncology

Phase 0
- First-in-Human
- Microdose Study
- Lack of Therapeutic Intent
- First-in-Human
- All-comers
- Dose escalation
- Tolerability (MTD)
- PK
- n=20-100

Phase 1
- Specific tumor types
- One dose level
- Efficacy
- Tolerability
- n=100s

Phase 2
- Specific tumor types
- Efficacy vs. standard of care
- Tolerability
- Tolerability vs. standard of care
- n=1000s

Phase 3
- Specific tumor types
- Efficacy vs. standard of care
- Tolerability vs. standard of care
- n=1000s

Phase 4 (Post-Marketing)
- MedWatch by FDA
- Long-term risks/benefits/use

Special Populations
HIV Patients with Cancer
Typical Clinical Trial Population

• Relapsed/refractory disease
  • all-comers vs. select tumors

• Good performance status

• Adequate marrow and organ function

• Exclude co-morbidities

• Exclude potentially interacting drugs
Clinical Trial Design Considerations

Consider the overall objective of the trial.
- Proof-of-concept vs. Therapeutic Intent vs. Maximum Tolerate Dose

Further considerations based on anticancer agent:
- Is there a probable cause for interaction (PK or PD)?
- What is the likely magnitude of the interaction?
- What should a reasonable starting dose of anticancer drug X be in patients on ART?
- Is there a potential for overlapping toxicity?
Clinical Trial Design

Unable to utilize traditional drug-drug interaction designs:
- Randomized crossover
- One-sequence crossover
- Parallel

If ART drug-drug interactions likely, utilize a stratum design:
- ART regimens containing enzyme/transporter inducers
- ART regimens containing enzyme/transporter inhibitors
- Neutral ART regimens

Other considerations:
- Exclude other concomitant medications with potential drug-drug interactions
- Monitor ART adherence, viral load, and CD4+ count
Clinical Trial Design Without Stratification

RAPAMYCIN
AMC-051 Rapamycin Pilot Study

- Rapamycin is an mTOR inhibitor and a sensitive CYP3A4 substrate.
- The *a priori* trough level of 5-10 ng/mL was more readily achieved in the NNRTI setting.

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Baseline Weight (kg)</th>
<th>PI or NNRTI Received</th>
<th>Initial Rapamycin Regimen</th>
<th>Maintenance Rapamycin Regimen at Target Trough</th>
<th>Maximum Rapamycin Trough Level (ng/mL) by LCMS/MS</th>
<th>Best Response of KS to Rapamycin</th>
</tr>
</thead>
<tbody>
<tr>
<td>001</td>
<td>78.5</td>
<td>Lopinavir/r</td>
<td>2 mg daily</td>
<td>0.2 mg twice a week</td>
<td>172</td>
<td>Partial</td>
</tr>
<tr>
<td>002</td>
<td>64.9</td>
<td>Atazanavir/r</td>
<td>0.3 mg twice a week</td>
<td>0.2 mg twice a week</td>
<td>64.4</td>
<td>Partial</td>
</tr>
<tr>
<td>003</td>
<td>74.5</td>
<td>Atazanavir/r</td>
<td>0.3 mg twice a week</td>
<td>0.3 mg three times a week</td>
<td>16.8</td>
<td>Stable</td>
</tr>
<tr>
<td>005</td>
<td>83.9</td>
<td>Lopinavir/r</td>
<td>0.4 mg twice a week</td>
<td>0.1 mg twice a week</td>
<td>19.2</td>
<td>Partial</td>
</tr>
<tr>
<td>004</td>
<td>97.0</td>
<td>Nevirapine</td>
<td>4.9 mg daily</td>
<td>2.8 mg daily</td>
<td>13.1</td>
<td>Progression</td>
</tr>
<tr>
<td>006</td>
<td>90.3</td>
<td>Efavirenz</td>
<td>4.5 mg daily</td>
<td>6.7 mg daily</td>
<td>7.4</td>
<td>Stable</td>
</tr>
<tr>
<td>007</td>
<td>71.6</td>
<td>Efavirenz</td>
<td>3.7 mg daily</td>
<td>2.3 mg daily</td>
<td>11.9</td>
<td>Stable</td>
</tr>
</tbody>
</table>

/r, ritonavir-boosted protease inhibitor; LCMS/MS, liquid chromatography tandem mass spectrometry.

- In patients with Kaposi’s sarcoma, rapamycin induced tumor regression and affected its molecular targets.
Clinical Trial Design with Stratification

SUNITINIB
Sunitinib in Combination with ART in PLWH

Primary Endpoint:
- Determine the safety of sunitinib in patients receiving ART therapy

Secondary Endpoints:
- Determine the PK of sunitinib in patients receiving ART
- Detect alterations in immune parameters during sunitinib therapy
- Efficacy

<table>
<thead>
<tr>
<th>Treatment Arm/Dose Level</th>
<th>Sunitinib Dose, mg</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm 1: NNRTI/non-ritonavir PI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-ritonavir PI</td>
<td>50</td>
<td>1</td>
</tr>
<tr>
<td>NNRTI</td>
<td>50</td>
<td>3</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>50</td>
<td>6</td>
</tr>
<tr>
<td>Arm 2: ritonavir PI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level 1</td>
<td>25</td>
<td>3</td>
</tr>
<tr>
<td>Level 2</td>
<td>37.5</td>
<td>6</td>
</tr>
<tr>
<td>Level 3</td>
<td>50</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: NA, not applicable; NNRTI, nonnucleoside reverse transcriptase inhibitors; PI, protease inhibitor.

QD for 4 weeks with 2 week rest.
ART Significantly Alters Sunitinib Metabolite

**ART**

Sunitinib $\Rightarrow$ Ritonavir

Sunitinib $\Rightarrow$ Efavirenz

Sunitinib $\Rightarrow$ NNRTI

\[ \text{Cancer}. \text{2014;120}(8):1194-202. \]

**Sunitinib $C_{\text{max}}$ (ng/mL)**

- Ritonavir: 25 mg
- Ritonavir: 37.5 mg
- Efavirenz: 50 mg
- NNRTI: 50 mg

**N-desethyl sunitinib $C_{\text{max}}$ (ng/mL)**

- Ritonavir: 25 mg
- Ritonavir: 37.5 mg
- Efavirenz: 50 mg
- NNRTI: 50 mg

**Sunitinib $C_{\text{min,ss}}$ (ng/mL)**

- Ritonavir: 25 mg
- Ritonavir: 37.5 mg
- Efavirenz: 50 mg
- NNRTI: 50 mg

**N-desethyl sunitinib $C_{\text{min,ss}}$ (ng/mL)**

- Ritonavir: 25 mg
- Ritonavir: 37.5 mg
- Efavirenz: 50 mg
- NNRTI: 50 mg

**Effect on Metabolite**

\[ P=0.0008^{*} \]

**Effect on Neutropenia**

\[ P>0.05 \]

**Effect on Steady-State**

\[ P=0.006^{*} \]

**Single Dose**

\[ Sunitinib P=0.08 \]

\[ Metabolite P=0.008^{**} \]

\[ 5\% \downarrow \]

\[ 41\% \downarrow^{**} \]

\[ 48\% \downarrow^{**} \]

**Steady-State**

\[ Sunitinib P=0.07 \]

\[ Metabolite P=0.006^{**} \]

\[ 3\% \downarrow \]

\[ 234\% \uparrow \]

\[ 12\% \downarrow \]

**Efavirenz > Ritonavir but neither different than NNRTI.**

Sunitinib sold symbols; metabolite open symbols.

AMC-061 Clinical Trial Conclusion

• Patients on non-ritonavir based ART regimens tolerated standard dosing of sunitinib.

• Patients receiving ritonavir-based ART regimens who were treated with a dose of 37.5 mg/day experienced higher toxicities and dose reductions may be warranted.
Modernizing Clinical Trial Eligibility Criteria: Recommendations of the American Society of Clinical Oncology–Friends of Cancer Research HIV Working Group

Thomas S. Ulrick, Gwynn Ison, Michelle A. Rudek, Ariela Noy, Karl Schwartz, Suanna Bruinooe, Caroline Schenkel, Barry Miller, Kieron Dunleavy, Judy Wang, Jerome Zeldis, and Richard F. Little

Abstract

Purpose
People with HIV are living longer as a result of effective antiretroviral therapy. Cancer has become a leading cause of morbidity and mortality in this patient population. However, studies of novel cancer therapeutics have historically excluded patients with HIV. Critical review of eligibility criteria related to HIV is required to accelerate development of and access to effective therapeutics for HIV-infected patients with cancer and make studies more generalizable to this patient population.

Methods
From January through April 2016, the HIV Working Group conducted a series of teleconferences; a review of 46 New Drug Applications from registration studies of unique agents studied in adults with cancer that led to the initial US Food and Drug Administration approval of that agent from 2011 to 2015; and a review of HIV-related eligibility criteria from National Cancer Institute–sponsored studies. Results were discussed and refined at a multistakeholder workshop held May 12, 2016. The HIV Working Group developed recommendations for eligibility criteria that focus on pharmacologic and immunologic considerations in this patient population and that balance patient safety, access to appropriate investigational agents, and study integrity.

Results
Exclusion of patients with HIV remains common in most studies of novel cancer agents. Models for HIV-related eligibility criteria in National Cancer Institute–sponsored studies are instructive. HIV infection itself should not be an exclusion criterion for most studies. Eligibility criteria related to HIV infection that address concurrent antiretroviral therapy and immune status should be designed in a manner that is appropriate for a given cancer.

Conclusion
Expanding clinical trial eligibility to be more inclusive of patients with HIV is justified in most cases and may accelerate the development of effective therapies in this area of unmet clinical need.
HIV Eligibility Criteria in Select NCI-supported Trials (2011-2015)

<table>
<thead>
<tr>
<th>Disease, Lead Organization, and ClinicalTrials.gov Identifier</th>
<th>Study Drug(s)</th>
<th>Study Phase</th>
<th>CD4+ Count (cells/μL)</th>
<th>ART</th>
<th>HIV Viral Load</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Open to HIV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Advanced Kaposi sarcoma, CCR, NCT02559630</td>
<td>Pomalidomide + liposomal doxorubicin</td>
<td>I</td>
<td>None</td>
<td>Effective ART required</td>
<td>None</td>
<td>Allows for treatment-naive or uncontrolled HIV in patients with progressive or life-threatening disease</td>
</tr>
<tr>
<td>Myeloid malignancies, Princess Margaret Cancer Center, NCT02381548</td>
<td>Belinostat + AZD1775</td>
<td>I</td>
<td>Preleukemia ≥ 250</td>
<td>Willing to adhere to ART with minimal overlapping toxicity and PK interactions; AZT, ritonavir, and cobicistat contraindicated</td>
<td>None</td>
<td>No history of AIDS-defining condition other than CD4+ count &lt; 200 cells/μL</td>
</tr>
<tr>
<td>Burkitt lymphoma, Intergroup CTSU 01-17T/AMC 366, NCT01902162</td>
<td>EPOCH-R</td>
<td>II</td>
<td>None</td>
<td>Suspended ART (with exceptions)</td>
<td>None</td>
<td>Exclude patients with advanced immunosuppression and evidence of HIV resistance to all ART considered at high risk of non-lymphoma-related death within 12 months as a result of AIDS</td>
</tr>
<tr>
<td>Relapsed oral cancer, The University of Texas MD Anderson Cancer Center-P2C, NCT02314169</td>
<td>Nivolumab</td>
<td>II</td>
<td>≥ 300</td>
<td>Required</td>
<td>Undetectable</td>
<td>HIV case by infectious disease specialist required; HIV-related laboratory studies sent to study team</td>
</tr>
<tr>
<td>Relapsed refractory cancer, ECOG-ACRIN, NCT02446006</td>
<td>Genetic testing-directed therapy (12 agents*, some FDA approved)</td>
<td>II</td>
<td>≥ 250</td>
<td>Not required; if used, minimal interactions or overlapping toxicities</td>
<td>None</td>
<td>Exclude history of AIDS-defining conditions other than low CD4+ counts; probably long-term survival if cancer not present</td>
</tr>
<tr>
<td>Operable hormone receptor-positive HER2-positive breast cancer, NSABP-B-52, NCT02002309</td>
<td>Diocetaxel, carboplatin, trastuzumab, and pertuzumab with or without estrogen deprivation</td>
<td>III</td>
<td>≥ 250</td>
<td>ART with potential overlapping toxicities excluded</td>
<td>None</td>
<td>No prior AIDS-defining conditions</td>
</tr>
<tr>
<td>Previously untreated CLL in patients ≥ 65 years old, Alliance 041202, NCT01896972</td>
<td>Rituximab and bendamustine or rituximab and ibritinib</td>
<td>III</td>
<td>≥ 350</td>
<td>ART with cyclophosphamide P-interacting medications prohibited</td>
<td>None</td>
<td>NA</td>
</tr>
<tr>
<td>Lymphoblastic leukemia before and after stem-cell transplantation in DLBCL, Alliance 051301, NCT02443077</td>
<td>Ibrutinib, autologous stem-cell transplantation</td>
<td>III</td>
<td>None</td>
<td>AZT, protease inhibitors, and colchicin prohibited</td>
<td>Patients with multidrug-resistant HIV excluded</td>
<td>No history of AIDS-defining conditions other than low CD4 count; HIV expert opinion of long-term survival from HIV perspective</td>
</tr>
<tr>
<td>HIV-specific studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relapsed refractory cancer, C1TN12-C2R, NCT03985666</td>
<td>Pentostatin</td>
<td>I</td>
<td>Stratified 100-199, 200-350, &lt; 350</td>
<td>ART ≥ 4 weeks</td>
<td>&lt; 400 copies/mL</td>
<td>opportunistic infection requiring systemic therapy in past 6 months</td>
</tr>
<tr>
<td>Relapsed refractory solid tumors, ECOG-ACRIN, NCT02408881</td>
<td>Mepolizumab + nivolumab</td>
<td>I</td>
<td>Stratified 100-200 and &gt; 200</td>
<td>ART &gt; 4 weeks</td>
<td>Undetectable (&lt; 75 copies/mL)</td>
<td>ART strata for PK studies; under care of physician with experience in HIV management; exclude patients with active infections requiring systemic therapy in past 28 days</td>
</tr>
<tr>
<td>Relapsed refractory solid tumors, ECOG-ACRIN, NCT01812322</td>
<td>Cabotegravir</td>
<td>I</td>
<td>&gt; 50</td>
<td>ART if clinically indicated</td>
<td>None</td>
<td>Opportunistic infection requiring systemic therapy in past 6 months</td>
</tr>
<tr>
<td>HIV-associated advanced Hodgkin lymphoma, ECOG-ACRIN, NCT01771107</td>
<td>AHD + brentuximab</td>
<td>III</td>
<td>≥ 50</td>
<td>Required ART according to guidelines; prohibited AZT, ddi, ritonavir, colchicin</td>
<td>None</td>
<td>Opportunistic infection requiring systemic therapy in past 6 months</td>
</tr>
<tr>
<td>HIV-associated aggressive B-cell lymphomas, ECOG-ACRIN, NCT01193642</td>
<td>Vincristine + EPOCH-R</td>
<td>II</td>
<td>≥ 50</td>
<td>Concurrent ART, if not on ART, start after first cycle; AZT excluded</td>
<td>None</td>
<td>Opportunistic infection requiring systemic therapy in past 6 months</td>
</tr>
</tbody>
</table>

**Table 1. HIV Eligibility Criteria in Select NCI-Supported Studies From 2011 to 2016**

Abbreviations: AMC, AIDS Malignancy Consortium; ART, antiretroviral therapy; AHD, doxorubicin, vincristine, and dacarbazine; AZT, zidovudine; CCR, Center for Cancer Research, National Cancer Institute; C1TN, Cancer Immunotherapy Trials Network; CLL, chronic lymphocytic leukemia; CTSU, Clinical Trials Support Unit; ddi, didanosine; DLBCL, diffuse large B-cell lymphoma; ECOG-ACRIN, Eastern Cooperative Oncology Group; American College of Radiology Imaging Network; EPOCH-R, etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab; Fda, US Food and Drug Administration; HCR2, human epidermal growth factor receptor 2; NCI, National Cancer Institute; NSABP, National Surgical Adjuvant Breast and Bowel Project; P2C, Phase II Consortium; PK, pharmacokinetics.

*Number of agents listed on ClinicalTrials.gov as of May 1, 2016.
Eligibility Criteria Principals

1. Criteria to define a population with HIV that is sufficiently healthy from this comorbid perspective to participate in almost any oncology study are recommended.
2. Criteria should select patients with probable long-term survival in the absence of cancer.
3. The later the phase of the trial, the more information is known about a particular therapeutic agent for the treatment of a particular condition. The level of experience with a given agent may inform eligibility criteria.
4. Criteria should not be more stringent than for HIV uninfected patients with the same disease or treatment history.
Eligibility Criteria Recommendations: Immune Criteria

1. Patients with CD4+ T-cell counts ≥350 cells/mL
   • Lower CD4+ count eligibility is often appropriate
2. Patients with no active history of AIDS-defining opportunistic infections
3. Exclusion of AIDS-defining opportunistic infections:
   • No opportunistic infections within past 12 months
   • For studies of AIDS-defining cancers with curative potential, exclusion limited to uncontrolled opportunistic infections may be appropriate
   • Patients on prophylactic antimicrobials need not be excluded due to DDI or toxicity-related concerns
Eligibility Criteria Recommendations: HIV Therapy

1. Concurrent treatment with ART according to DHHS treatment guidelines
2. Recommend criteria specifying timing of ART initiation that are appropriate for study goals and considerations for recently diagnosed PLWH or those not on effective ART.
3. Recommend exclusion of specific ART agents, when indicated, based on predicted drug-drug interactions or potential overlapping toxicities.
4. Although effective ART is generally recommended, exceptions should be considered:
   • Treatment interruption or deferred initiation is appropriate in curable malignancies when ART may compromise intended full-dose oncology therapy with investigational agent(s).
   • Treatment interruptions for toxicity management
   • Treatment interruptions to meet scientific objective of study
NCCN Guideline Recommendations

• Most PLWH who develop cancer should be offered the same cancer therapies as HIV-negative individuals, and modifications to cancer treatment should not be made solely on the basis of HIV status.

• Care for patients diagnosed with HIV should be co-managed with an oncologist and an HIV specialist.

• Oncologists and HIV clinicians, along with HIV and oncology pharmacists, if available, should review proposed cancer therapy and ART for possible drug-drug interactions and overlapping toxicity concerns prior to initiation of therapy.
Conclusions

• Patients with HIV should not be excluded from cancer clinical trials nor from standard of care