HIV/AIDS-Related Cancer

Shabnam Tehrani M.D.

Associate Professor of Infectious Diseases

Shahid Beheshti University of Medical Sciences

Clinical HIV/AIDS Fellowship

Introduction

- People living with human immunodeficiency virus (PLWH) are at increased risk of several cancer types, including those considered to be AIDS-defining events (ie, Kaposi sarcoma, certain non-Hodgkin lymphomas, and invasive cervical cancer), as well other types of cancer, particularly anal, lung, and liver cancers, and Hodgkin lymphoma.

AIDS-defining malignancies

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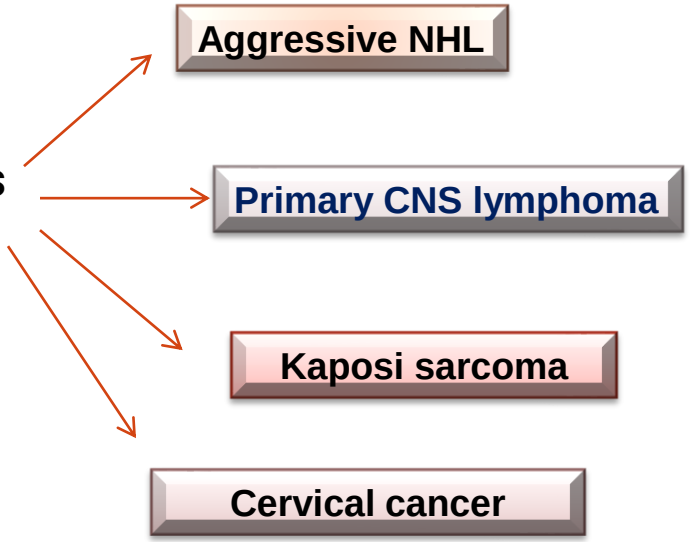


Introduction

- **Effective antiretroviral therapy (ART) has decreased AIDS-defining cancer rates and increased survival of PLWH.**

- **cancer is now the leading cause of non-AIDS death in the US population with HIV**. In addition to a higher morbidity of cancer, PLWH also have a higher mortality from cancer than the general population in part due to inadequate cancer treatment.

NHL in PWH

- **NHL is an AIDS-defining cancer, and the risk of NHL is elevated 7- to 23-fold in PWH, with the risk being even higher for certain subtypes such as primary CNS lymphoma.**

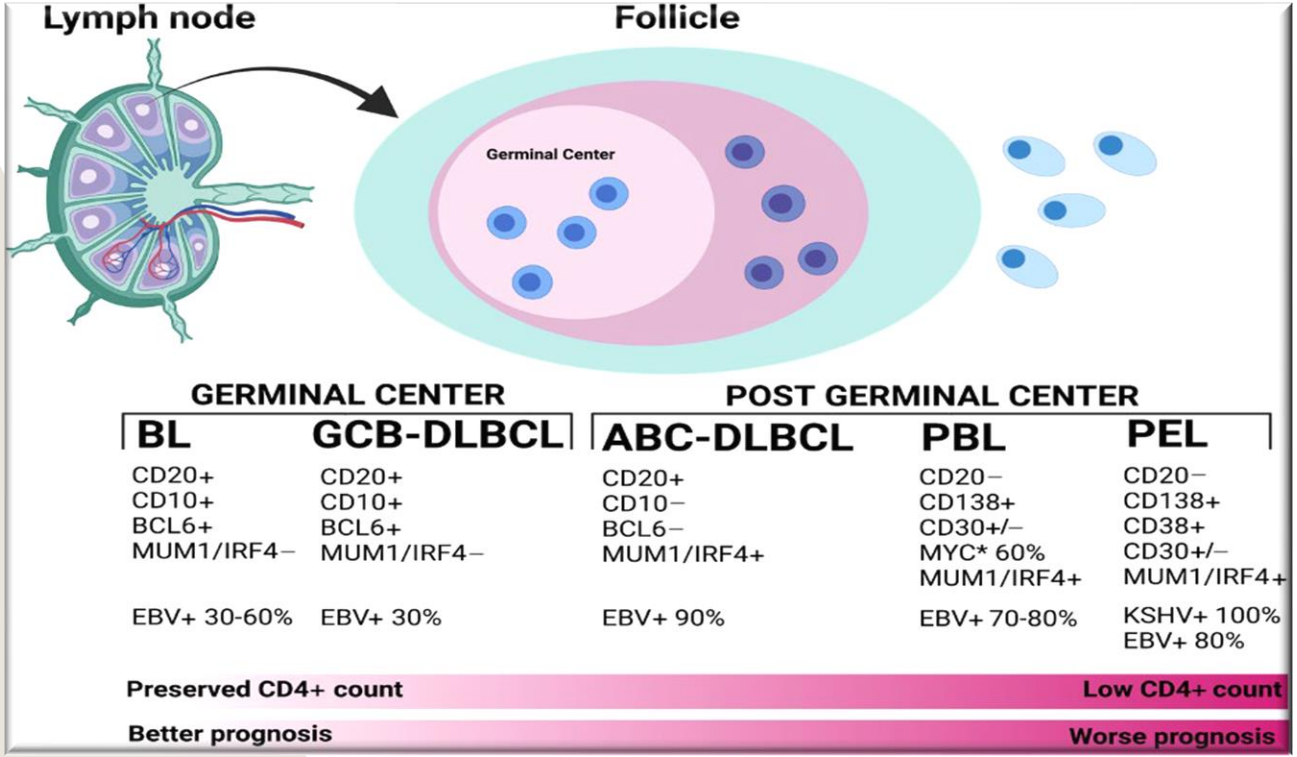
- **In the ART era, the incidence of NHL has declined. Despite the introduction of cART, the incidence of lymphoma in PLWH is increasing compared to the general population.**

NHL in PWH

- Lymphomas occurring in PLWH are characterized by advanced stage, extranodal involvement at presentation, an aggressive clinical course, and are usually associated with Epstein Barr virus (EBV) and/or Kaposi-sarcoma-associated herpesvirus (KSHV) .

- They include those KSHV- and EBV-related entities that are particularly concentrated in this population at high risk of infection-related cancers, i.e., primary effusion lymphoma (PEL), large B-cell lymphoma arising in multicentric Castleman disease (MCD), and plasmablastic lymphoma (PBL).

Pathologic, immune, and viral characteristics of HIV-associated NHL

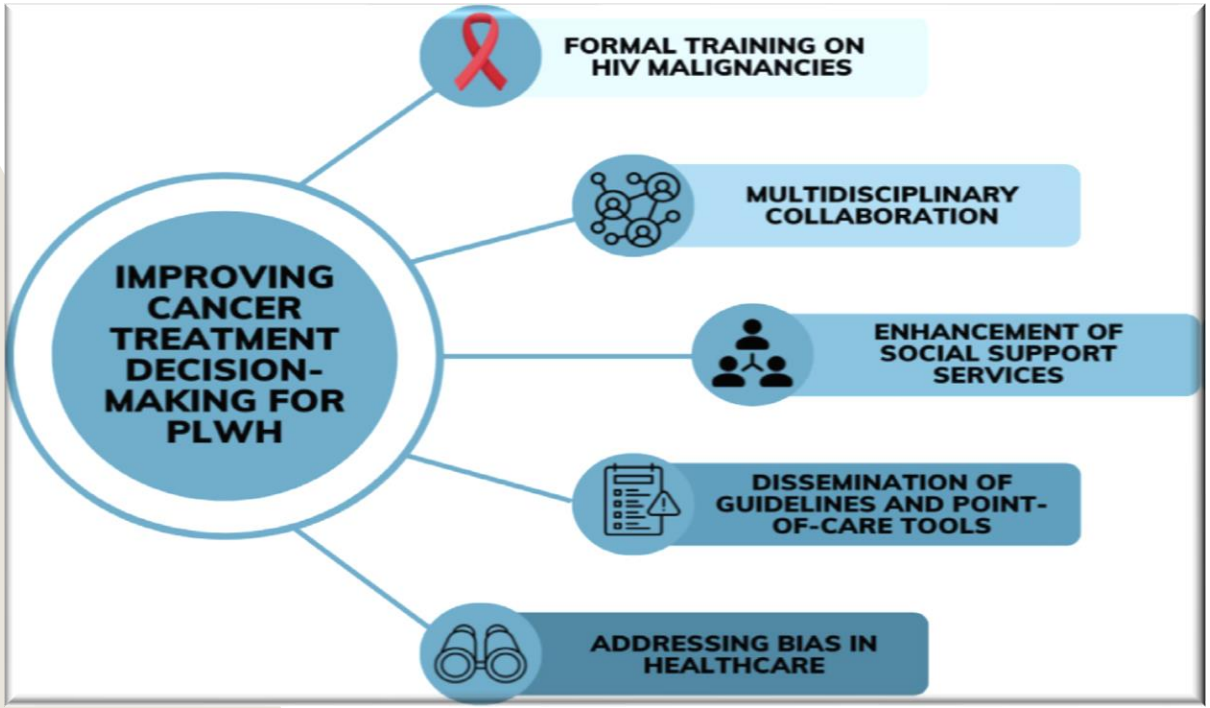


Major clinical features and laboratory findings in lymphomas occurring in individuals infected by HIV

Histotype	Common presentation	CD4/μL at diagnosis	Clinical features
BL	Nodal, extranodal, bone marrow	>200*	Increasing prevalence in cART era Improved outcomes in cART era Only in EBV+, immunoblastic plasmacytoid morphology
DLBCL†	Nodal and extranodal	<200	The most common lymphoma Late manifestation of HIV infection May have CNS involvement Improved outcome in cART era
PEL	Effusions; nodal and extranodal presentations are found (solid PEL)	<100	Concurrent Kaposi sarcoma common Aggressive behavior Poor prognosis
PBL	Extranodal, oral cavity or other extranodal or nodal sites	<200	Aggressive behavior Poor prognosis
MCD-associated large cell lymphoma	Extranodal and nodal	>200	Aggressive behavior Poor prognosis
MCD	Nodal	>200	Severe B symptoms Increased KSHV viral load and elevated levels of circulating vIL6, h-IL6, and IL10
HL	Nodal and extranodal	≈200	Increased incidence over time (SIR 22) Good prognosis

Treatment Strategies

Recommendations for improving cancer treatment



PRINCIPLES OF HIV MANAGEMENT WHILE UNDERGOING CANCER THERAPY

- All patients should be offered HIV screening at least once during their lifetime. **Consider HIV testing in patients with a new cancer diagnosis who have not been recently screened**.

- **HIV therapy should be initiated or continued during cancer therapy.**

- **ART interruptions should be avoided because of the risk of immunologic compromise, opportunistic infection, and death. Continuation of ART might result in better tolerance of cancer treatment, higher response rates, and improved survival.**

Treatment Strategies

- **The combination of cART with chemoimmunotherapy significantly improved the outcomes of the lymphomas in PLWH, with 5-year survival increasing from 13% in the pre-cART era (1986–1995) to 70–80% in the late cART era (2005–2015)**

- **Side effects due to drug–drug interactions may occur with CYP3A4 inhibitors such as ritonavir and cobicistat-based antiretroviral regimens.**

- **Integrase strand-transfer inhibitors (INSTIs) without cobicistat (raltegravir, dolutegravir, and bictegravir)** have advantages in drug–drug interactions and result in a more rapid decline in HIV viremia.

PRINCIPLES OF HIV MANAGEMENT WHILE UNDERGOING CANCER THERAPY

- If there are potential interactions between ART and cancer-related or other supportive care therapies leading to decreased effectiveness of ART, more frequent HIV viral load testing (eg, once a month for the first 3 months and then every 3 months6) may be needed.

- Consider measuring the CD4+ T-cell count more frequently in patients receiving cancer treatments anticipated to cause lymphopenia.

- Additional risk beyond that predicted by CD4+ T-cell counts may occur due to effects of cancer-related therapy on immune function.

PRINCIPLES OF SUPPORTIVE CARE

- **Required/Strongly Recommended:**

- **Myeloid growth factor support** : Myeloid growth factor support is required in regimens that are high risk for febrile neutropenia,
  - **Pre-existing neutropenia and/or low CD4+ T-cell counts (<200 cells/µL)** increase risk of chemotherapy-associated neutropenic fever; myeloid growth factor support is strongly recommended with these risk factors.

- **PJP prophylaxis and toxoplasmosis prophylaxis** : Continue until CD4+ T-cell counts recovered to **≥200 cells/µL for ≥3 months** duration post completion of cancer therapy

Should rituximab be included within the regimen in CD20+ HIV-NHL?

- **The combination of rituximab and chemotherapy results in significant clinical benefit for all CD20+ HIV-NHL patients compared with chemotherapy alone ,as in the general population.**

- **There is need to maximize opportunistic infection prophylaxis in patients with CD4 count ≤50/mL, according to current guidelines on HIV management.**

What is the best chemotherapy regimen

- **In the cART era, the standard treatments of HIV-associated lymphomas mirror that of HIV negative patients, but controversy remains regarding the optimal chemotherapy regimen.**

Should antiretroviral therapy be suspended during chemotherapy?

- All HIV-infected patients with cancer must be mainteined on cART during antineoplastic treatment.
- Ritonavir or cobicistat-based antiretroviral regimens must be avoided because of drug-drug interactions.
- Moreover, many new antiretrovirals with fewer drug interactions are now available, such as integrase strand-transfer inhibitor without cobicistat (raltegravir, dolutegravir, and bictegravir).

Is the approach with intensive chemotherapy and peripheral stem cell rescue feasible?

- **HIV infection should not preclude lymphoma patients from undergoing HDC-ASCT, according to the same eligibility criteria adopted for the general population.**

Primary CNS Lymphomas

PCNSL

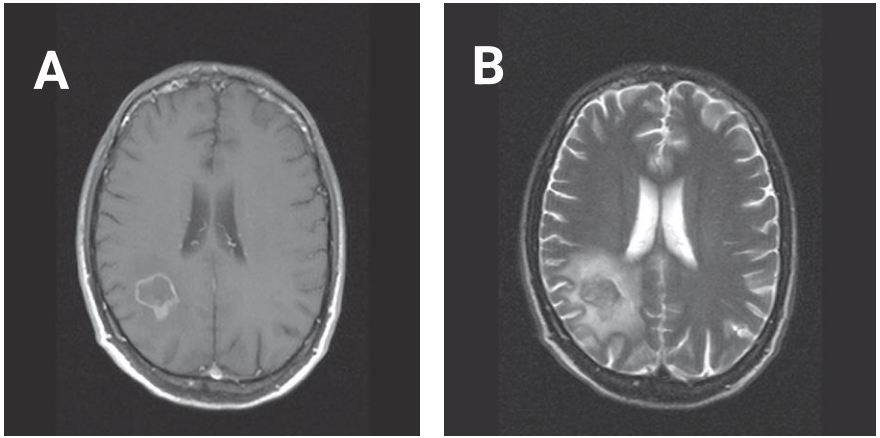
- This condition, which affected 2% of patients with AIDS at the beginning of the epidemic, has seen its incidence decrease considerably in the ART era.
- It is an aggressive form of non-Hodgkin lymphoma that develops within the brain, spinal cord, eye, or leptomeninges without evidence of systemic involvement.
- The tumor is infiltrative and typically extends beyond the primary lesion, as shown by CT or MRI scans, into regions of the brain with an intact BBB.

PCNSL

- **Clinical presentation:**
- The onset of symptoms is generally **subacute.**
- Confusion, lethargy, and memory loss → (disease progresses) → hemiparesis, aphasia, seizures.
- Craniospinal involvement only, **no systemic involvement.**

PCNSL

- **Imaging studies:**
- **Solitary mass lesions are as frequent as multiple lesions**. Most lesions display some degree of enhancement, which is usually nodular or patchy.
- **Ring enhancement, identical to that commonly seen in TE, can occur and correlate with central tumor necrosis.**
- Lesions are frequently located in the corpus callosum, the **periventricular white matter.**



(A) A 2-cm ringenhancing lesion is present in the right parietal lobe, surrounded by edema.
(B) The T2-weighted image shows low signal intensity centrally, which is more consistent with cellular proliferation than with an infectious process

PCNSL

Diagnosis

- **Confirm histologically by brain biopsy**
- **CSF EBV DNA PCR** :sensitivity of 80% to 90% & specificity of 87% to 98% for the diagnosis of PCNSL
- **cytologic analysis of the CSF**

Treatment

- **INDUCTION THERAPY**
- **High-dose methotrexate-based regimen**
- **Whole brain RT (WBRT) if patient is not acandidate for systemic therapy**

Kaposi Sarcoma in PWH

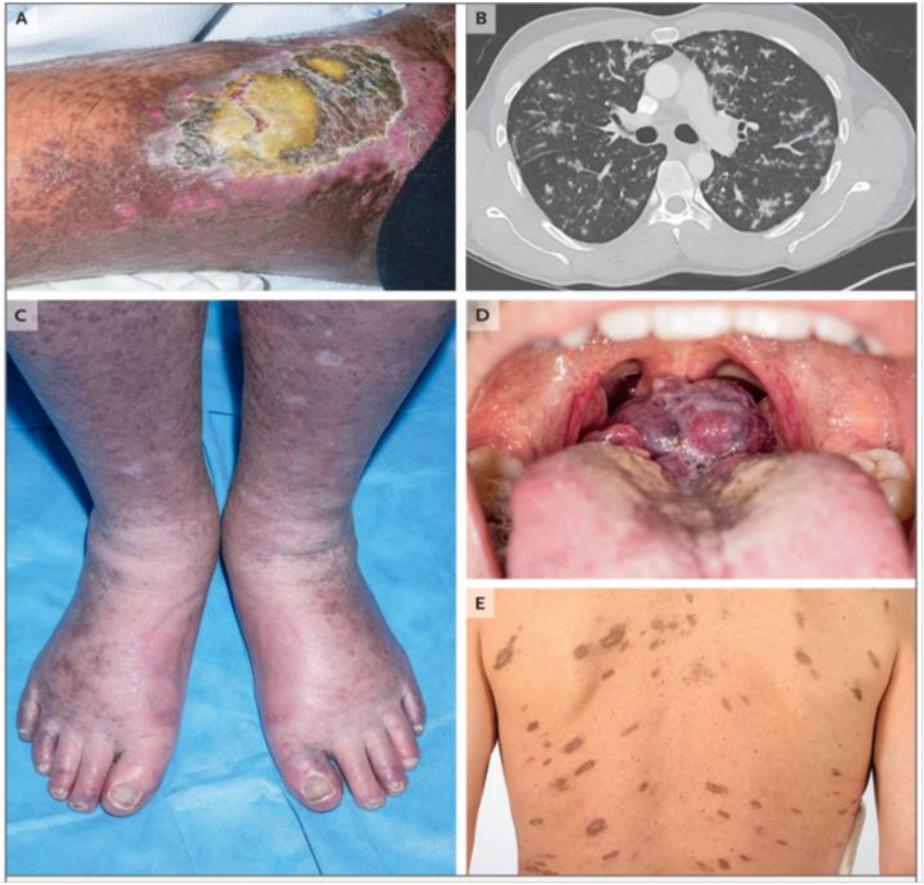
Kaposi Sarcoma

- AIDS-related Kaposi sarcoma is also an AIDS-defining cancer. The risk for Kaposi sarcoma in the setting of HIV has been as high as 3640-fold increased over the general population but this risk has declined in the ART era.

- **Kaposi's sarcoma is a multicentric tumor characterized by lesions ranging from a few indolent skin lesions to multiple lesions involving one or more organs, especially the oral mucosa, gastrointestinal tract, lymph nodes, lungs, and bones**

- Kaposi's sarcoma lesions are characterized by proliferation of spindle cells of endothelial origin, with varying degrees of abnormal vascularity, inflammatory infiltrates, and fibrosis. Red cells and hemosiderin deposits give lesions their characteristic purplish color.

- In Panel A, advanced Kaposi's sarcoma with tumor-associated edema and ulceration are shown on the thigh of a patient .
- Panel B, the CT scan shows diffuse, infiltrative pulmonary Kaposi's sarcoma.
- Panel C, Kaposi's sarcoma of both legs and both feet, with associated "woody" edema,
- Panel D shows Kaposi's sarcoma of the oral cavity
- Panel E shows characteristic Kaposi's sarcoma lesions on the skin of the back.



Kaposi Sarcoma

- When immunosuppression is advanced, AIDS-related Kaposi sarcoma is more common, more aggressive, and more likely to involve viscera and/or lymph nodes than when immunosuppression is minimal.
- In fact, CD4+T-cell counts and HIV viral load correlate with the risk of Kaposi sarcoma development in PWH, and effective ART lowers that risk.

- KS Stage:
  - Limited cutaneous disease
  - Advanced cutaneous ,oral,visceral, or nodal disease

FIRST-LINE THERAPY (Limited cutaneous)

- **Symptomatic and/or cosmetically bothersome:**
  - **ART with or without another first-line therapy.
  - **Topicals**
  - **Intralesional chemotherapy**
  - **RT**
  - **Local excision**
  - **Cryotherapy**
  - **Systemic therapy**

- **Asymptomatic and cosmetically acceptable:**
  - **Observe and Start or continue Antiretroviral therapy**
  - **(Patients who are only on ART should be reassessed within 4 weeks, particularly to monitor for KS-IRIS.)**

- ***FIRST-LINE THERAPY***
  (Advanced cutaneous, oral, visceral):

- ***Systemic therapy and Continue or initiate ART***
- ***Liposomal doxorubicin***
- ***Paclitaxel***

Cervical Cancer in PWH

Cervical Cancer in PWH

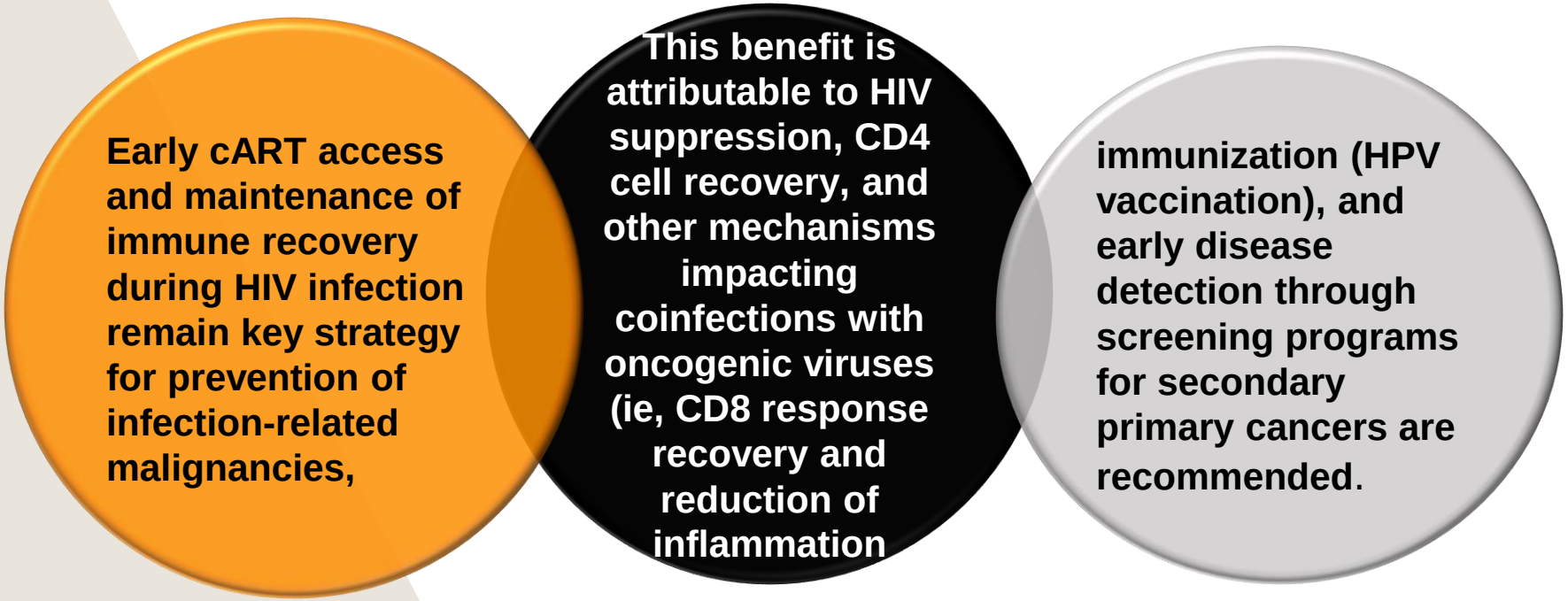
- The risk of cervical cancer is elevated approximately 3- to 5-fold in PWH.
- Persistent infection with high-risk human papillomavirus (HPV) leads to the development of cervical cancer.
- Premalignant cervical lesions are common in PWH. Treatment of these lesions is generally safe and effective regardless of HIV status.
- However, endocervical extension is more frequent among PWH. Therefore, loop excision is less effective, with higher recurrence rates in PWH than in patients without HIV.

Cervical Cancer in PWH

- PWH who have cervical cancer should be referred to an HIV specialist to ensure they are on an effective ART regimen.
- PWH should be treated for cervical cancer, including use of concurrent chemotherapy for patients receiving definitive radiation treatment. Modifications to cancer treatment are not recommended based solely on HIV status.
- HPV vaccination: 3-dose HPV vaccine should be offered to patients of both sexes up to 26 years of age and may be considered in patients up to 45 years of age.

Preventive measures

Preventive measures



Thank You

Any questions?