Going viral: HIV-associated cancers

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NIH NATIONAL CANCER INSTITUTE

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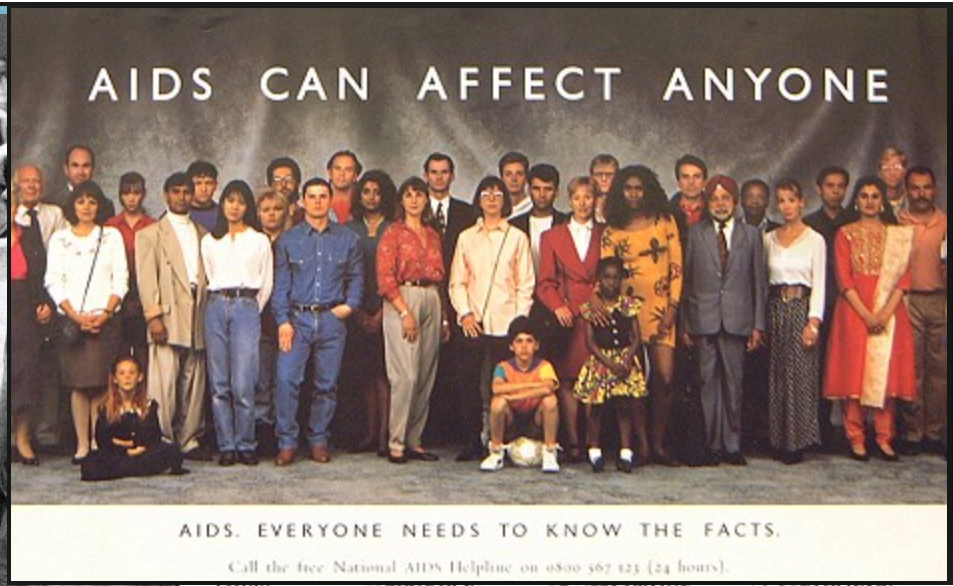
Objectives

- Learn about the types of cancers affecting people living with HIV
- Understand the presentation, diagnosis, and treatment of KSHV-associated cancers
- Understand the unique considerations for the management of cancer in people living with HIV

HIV: From Epidemic to Chronic Disease



infection. Case reports
Patient 1: A previously healthy 33-year-
oral mucosal candidiasis in March 1981 after a 2-month history of
elevated liver enzymes, leukopenia, and CMV viruria. The serum complem
CMV titer in October 1980 was 256; in May 1981 it was 32. The patient's
deteriorated despite courses of treatment with trimethoprim-sulfamethoxa
pentamidine, and acyclovir. He died May 3, and postmortem examinati
pneumonia, but no evidence of neoplasia.
developed *P. carinii* pn
was made.

HIV-associated cancers

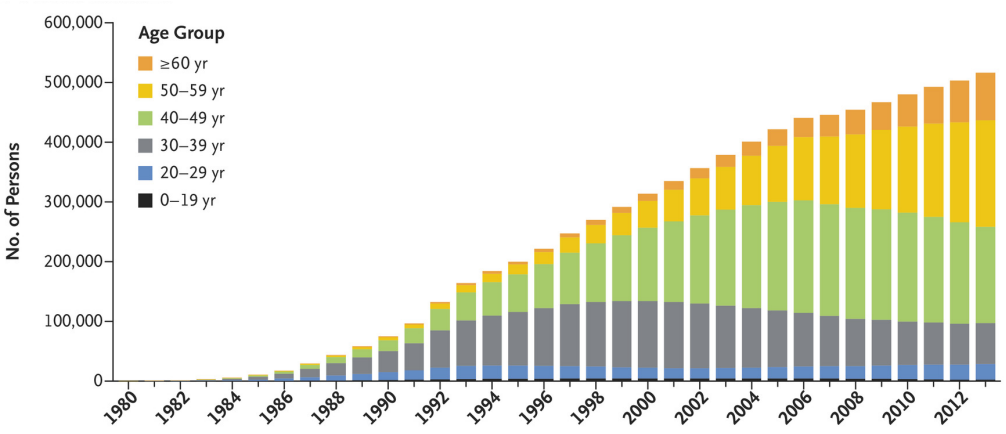
AIDS Defining Malignancies

- Kaposi sarcoma
- Certain aggressive non-Hodgkin lymphomas (AIDS-related lymphoma)
- Primary central nervous system lymphoma
- Cervical cancer

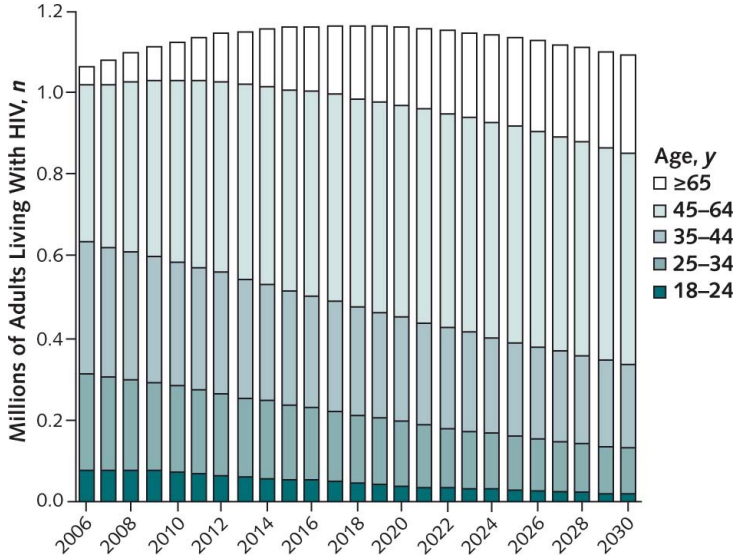
Other Malignancies (Non-AIDS Defining Malignancies)

- Malignancies for which HIV increases risk
- Incidental cancers in patients with HIV
- Non-melanomatous skin cancers

Number of PLWH is increasing because people are aging

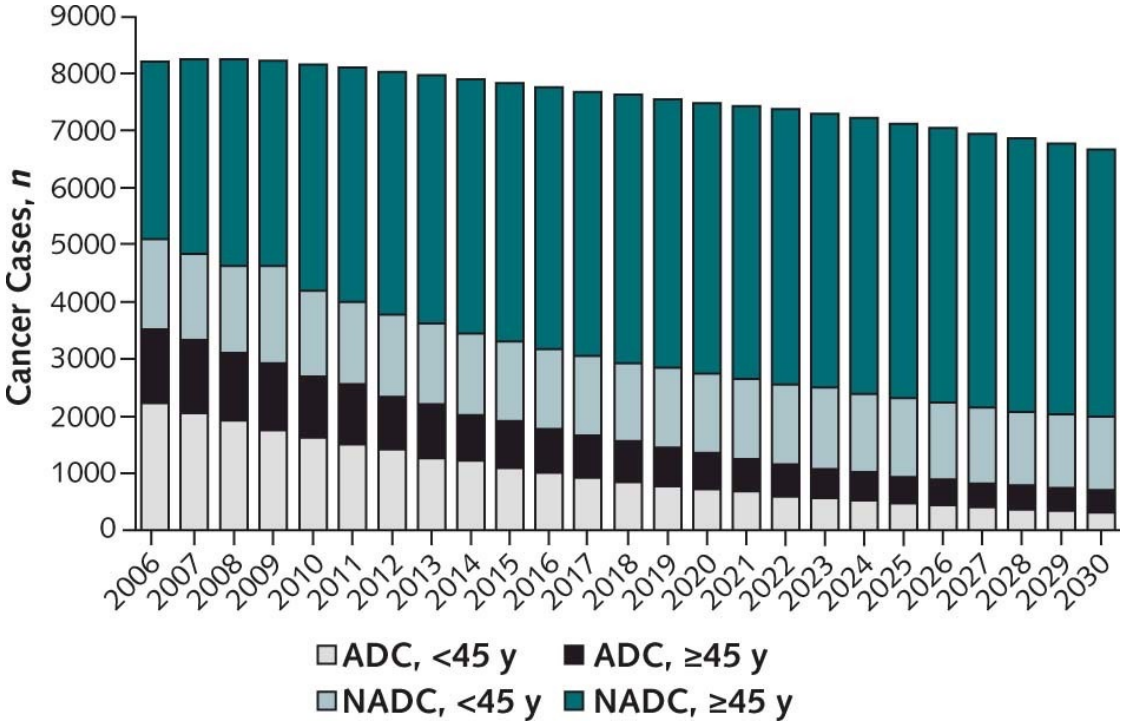


Yarchoan R & Uldrick TS. *NEJM* 2018;378:1029-41.



Shiels et al. *Ann Intern Med*. 2018; 168(12):866-873.

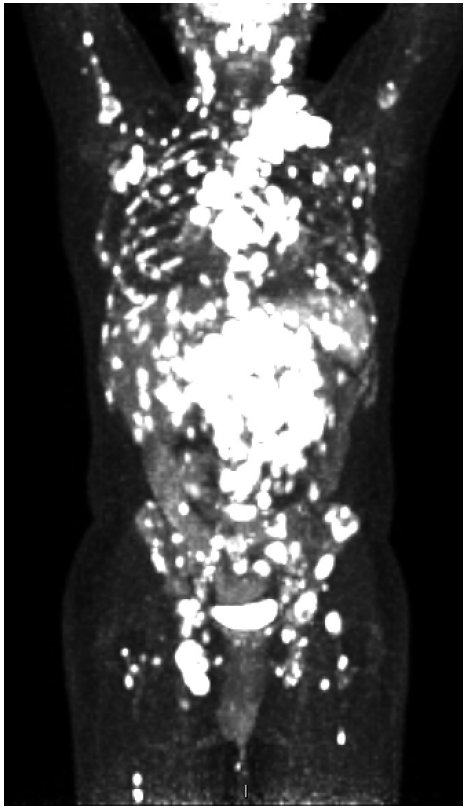
Changing epidemiology of HIV-associated cancers



Shiels et al. *Ann Intern Med.* 2018; 168(12):866-873.

Lymphoma in PLWH

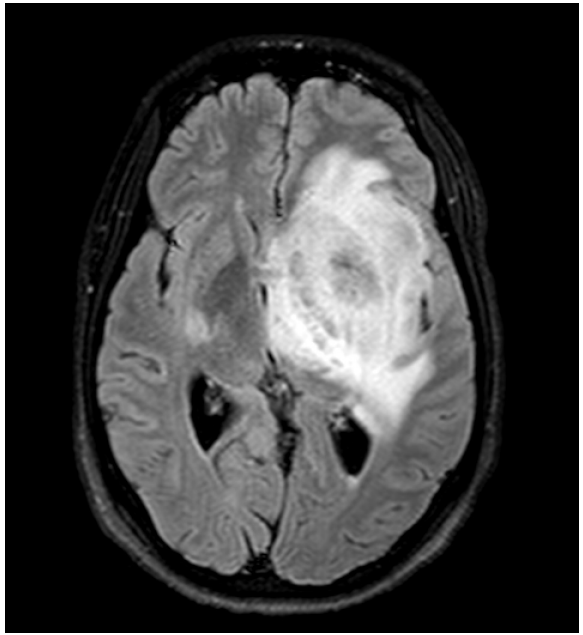
- Most common cancer among PLWH in U.S. and among the most common globally
- Incidence 10-20x more common than general population
- ART has decreased risk of certain subtypes



Patient with newly diagnosed HIV and DLBCL

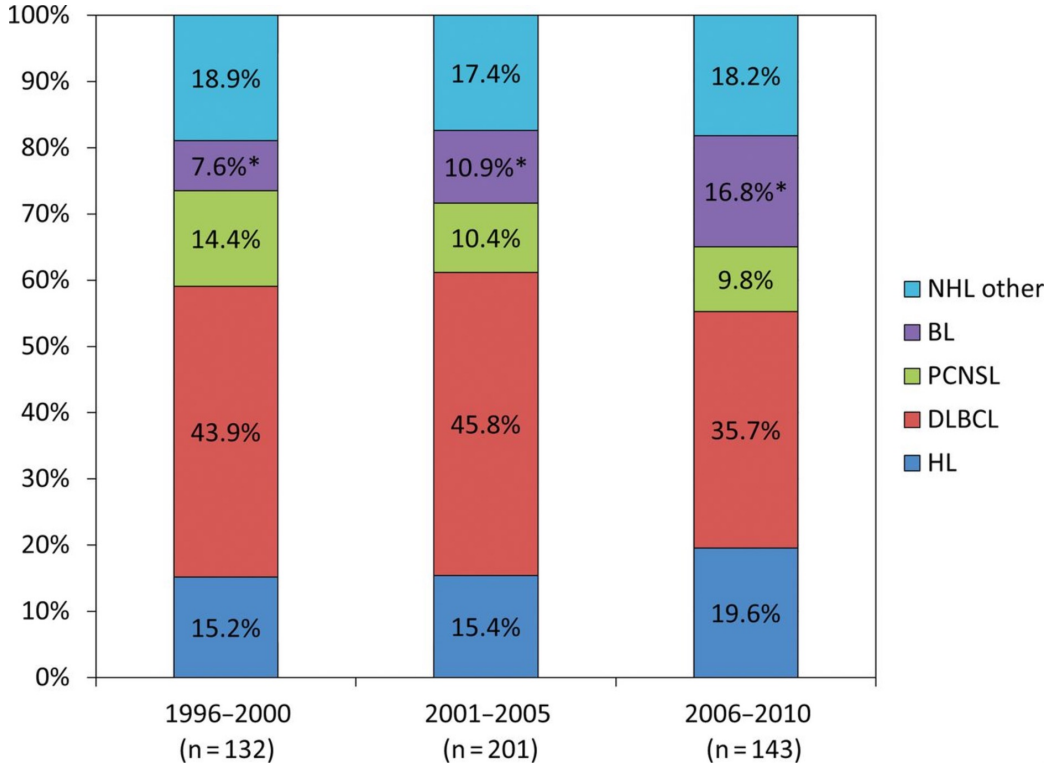
HIV-associated subtypes and features

- Aggressive B cell subtypes:
  - Diffuse large cell lymphoma
  - Burkitt lymphoma
  - Primary effusion lymphoma
  - Plasmablastic lymphoma
  - Primary CNS lymphoma
  - Hodgkin lymphoma
- More frequent high-risk features:
  - CNS involvement or relapse
  - Advanced stage and extranodal disease
  - *MYC* translocation
  - MUM1/IRF4^{+} expression



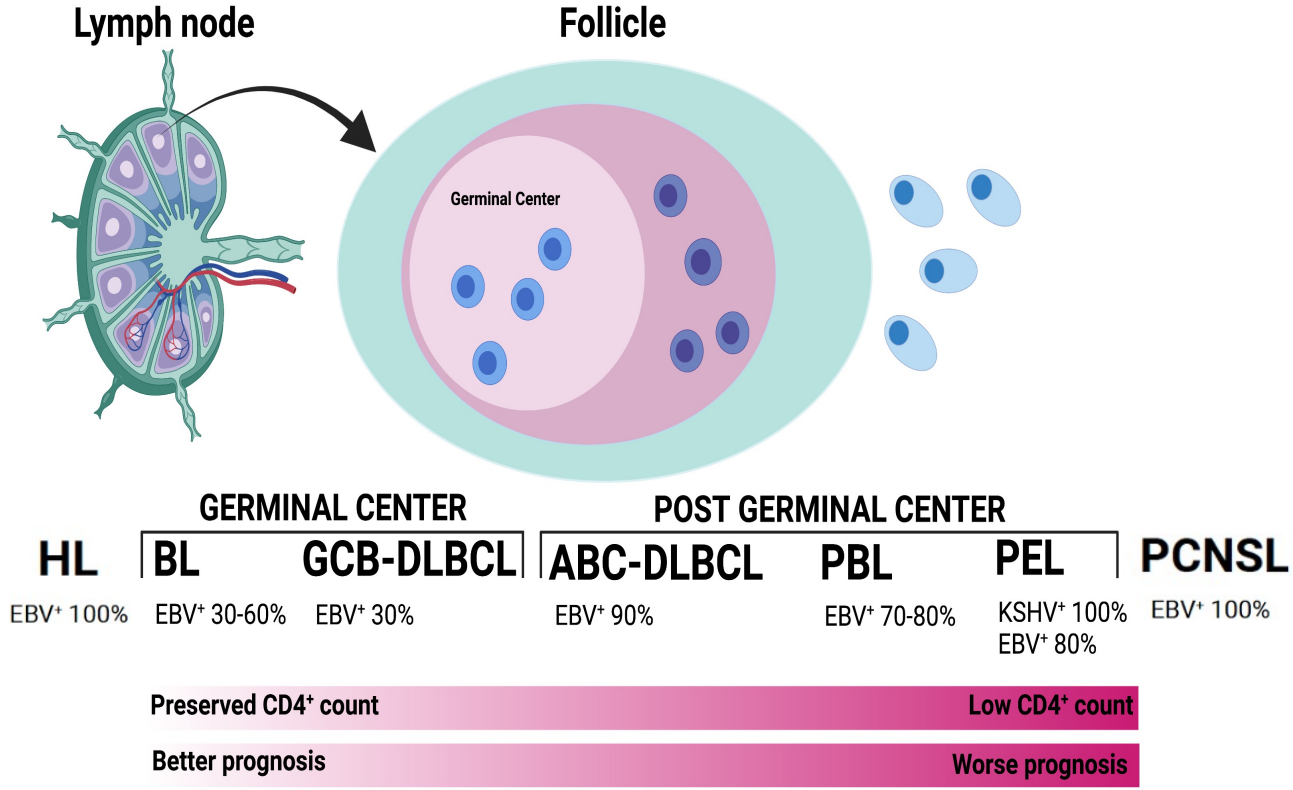
MRI brain in patient with HIV^{+} CNS lymphoma

Changing epidemiology of HIV-associated lymphomas



Gopal S, et al. J Natl Cancer Inst. 2013;105(16):1221-1229.

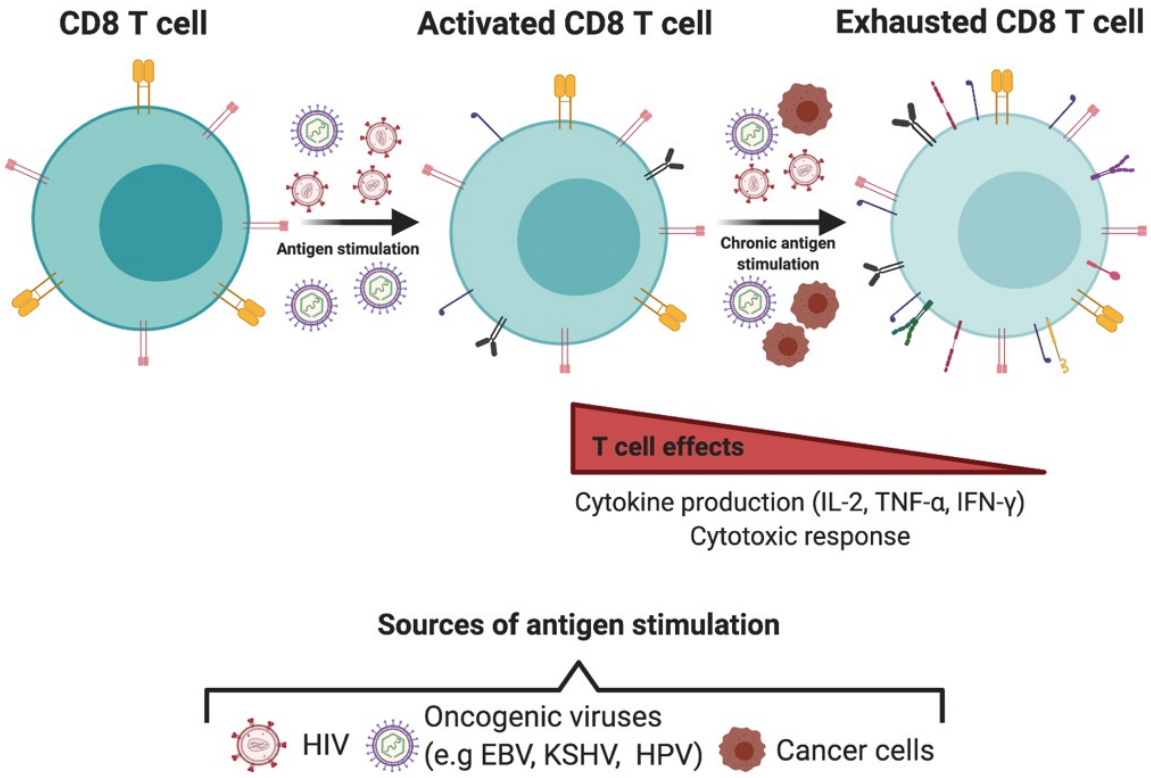
Viral and immune etiology of lymphoma subtypes



Pai, Lurain & Yarchoan 2021 ASH Education Book

HIV effects on T cells

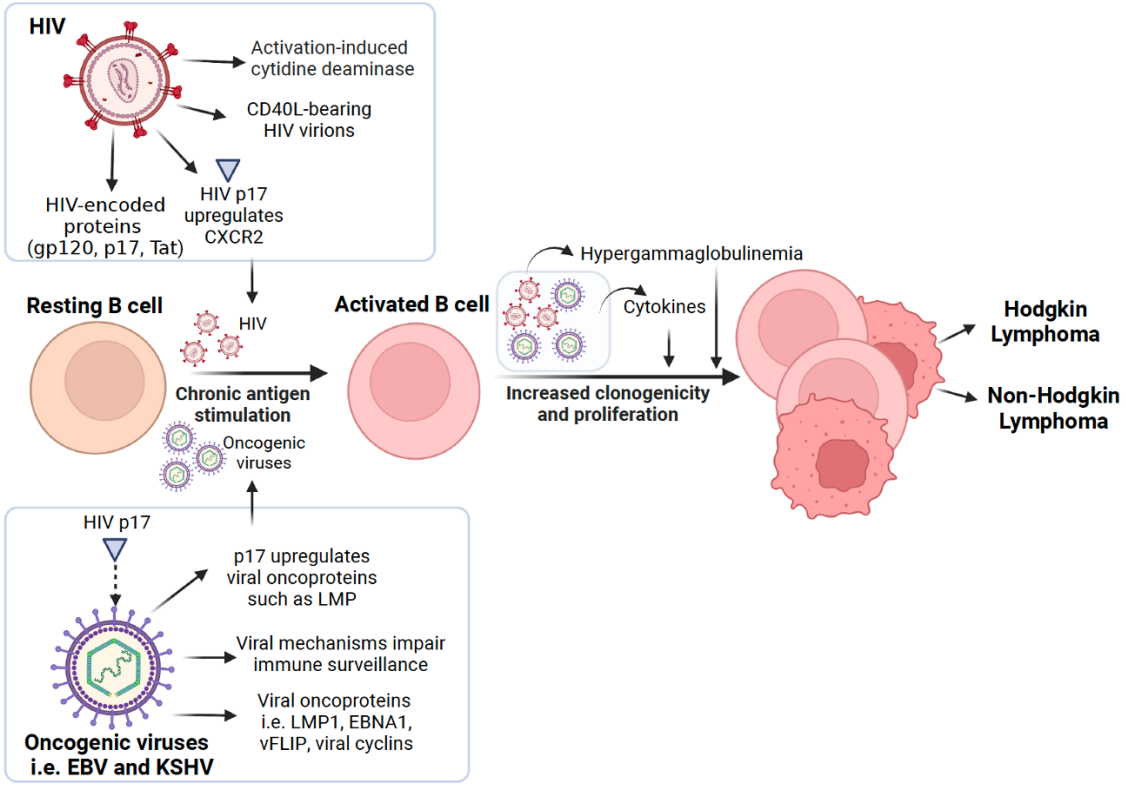
- $CD4^+$ T cell lymphopenia
- Chronic viral stimulation
- Decreased cytokine production
- T cell exhaustion



Lurain et al. *Current HIV/AIDS Reports* 2020 Oct;17(5):547-556

Effects of HIV, EBV, and KSHV on lymphomagenesis

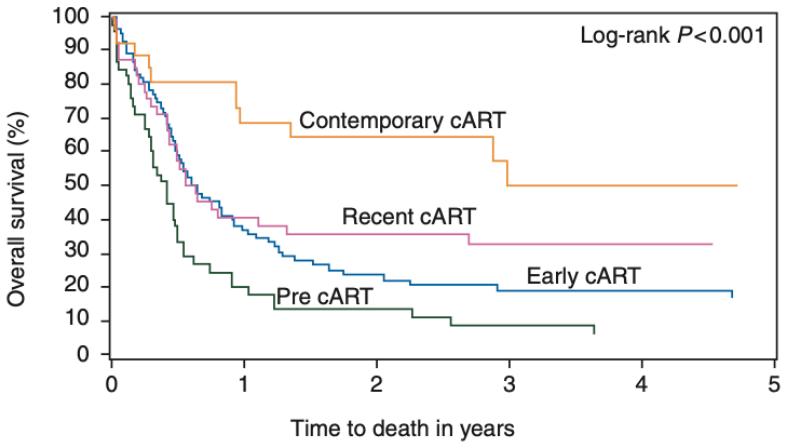
- Chronic antigenemia causes polyclonal B cell hyperactivity
- HIV, EBV, and KSHV stimulate cytokine production and B cell proliferation
- Viral homologues of cellular proteins
- Despite activation B cells are poorly immune responsive



Lurain et al. *Seminars in Hematology* 2022. *In press*

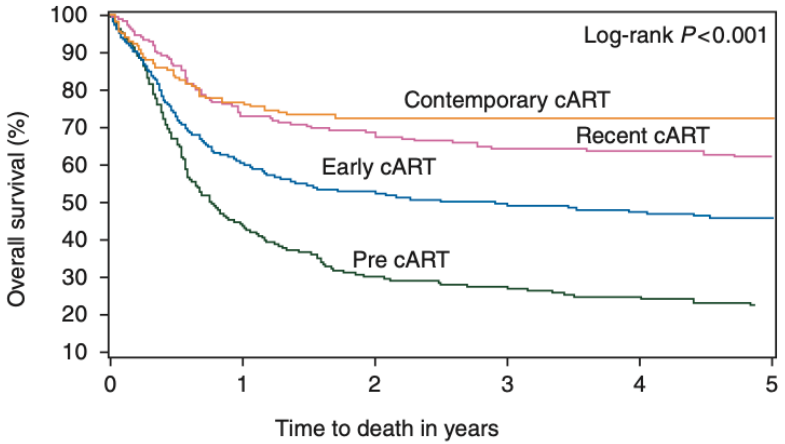
Outcomes for HIV+ lymphomas have improved overtime

Survival in Patients with CD4 <50 cells/mm^3



Number at risk:						
Contermporary	26	17	14	7	5	3
Recent	46	17	14	12	12	8
Early	83	28	16	12	11	10
Pre	45	9	6	4	3	3

Survival in Patients with CD4 >50 cells/mm^3



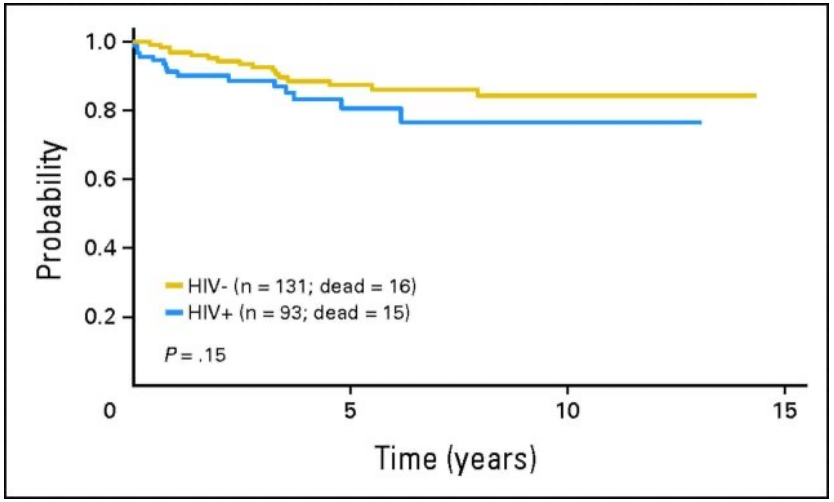
Number at risk:						
Contermporary	150	108	91	68	46	18
Recent	226	144	125	96	85	64
Early	522	303	250	222	160	99
Pre	338	145	98	87	76	66

**HIV-related factors not prognostic in the clinical trial setting*

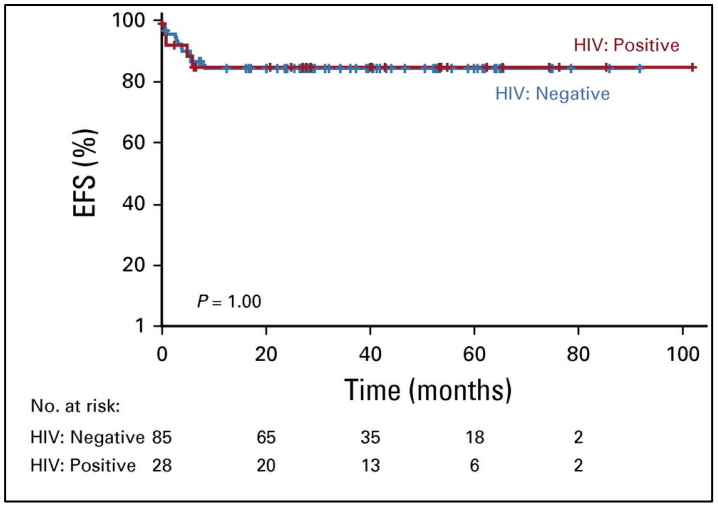
Barta et al. *Annals of Oncology* 2015. 26: 958–966

HIV does not influence outcomes in Burkitt and Hodgkin lymphoma*

OS in Hodgkin Lymphoma by HIV Status



EFS in Burkitt Lymphoma by HIV Status



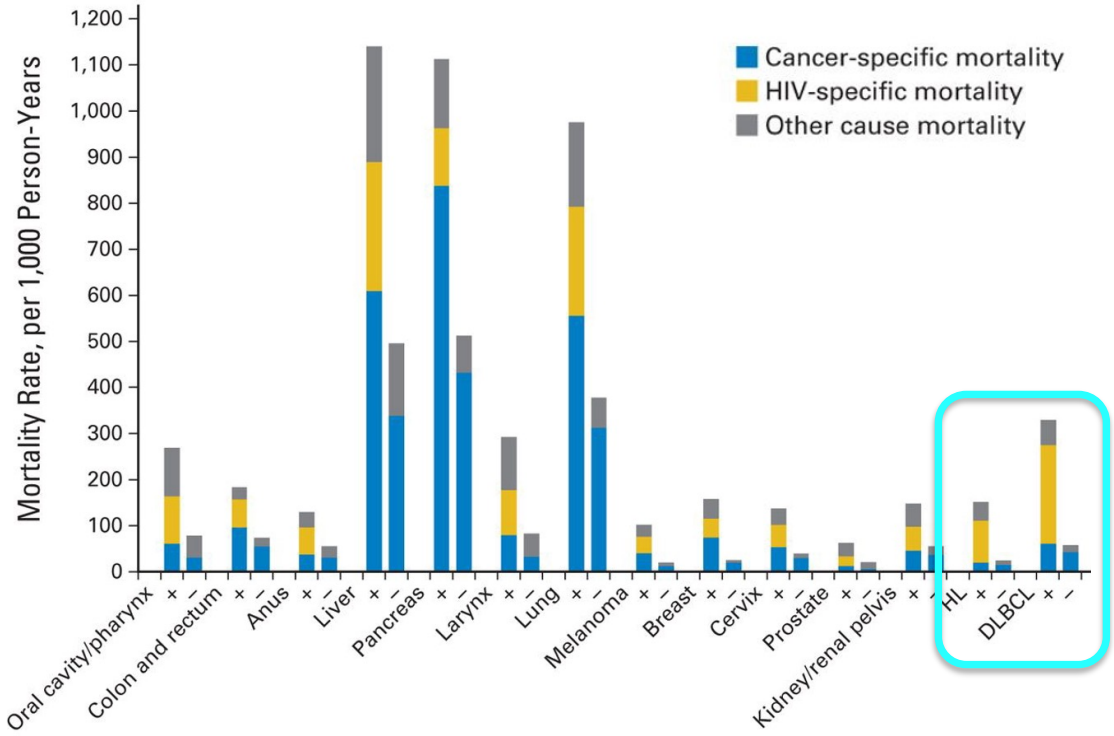
**When PLWH receive same therapy as immunocompetent patients*

Roschewski et al. *JCO* 2020 Aug 1; 38(22): 2519-2529.

Montoto et al. *JCO* 2012 Nov 20; 30(33): 4111–4116.

However, PLWH and lymphoma have higher mortality overall in modern ART era

- Many do not receive standard cancer treatment
- Excluded from clinical trials
- Stigma against HIV and sexual and gender minorities



Coghill et al. *JCO* 2015; 33(21):2376-2383

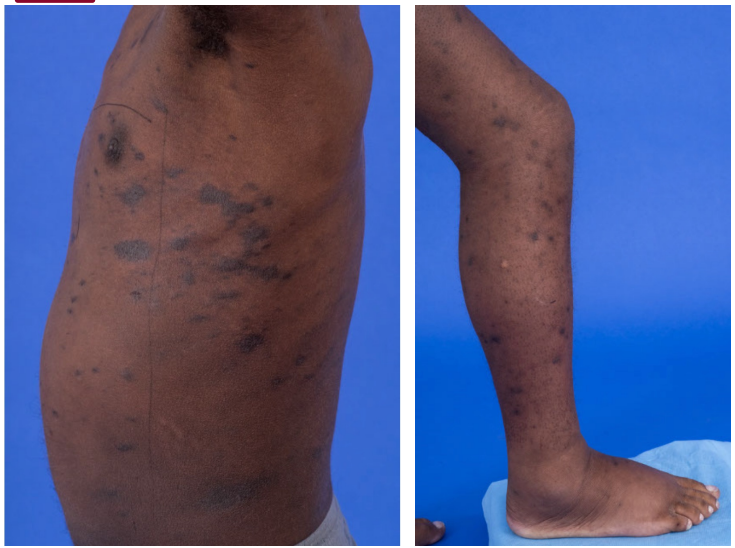
Case presentation

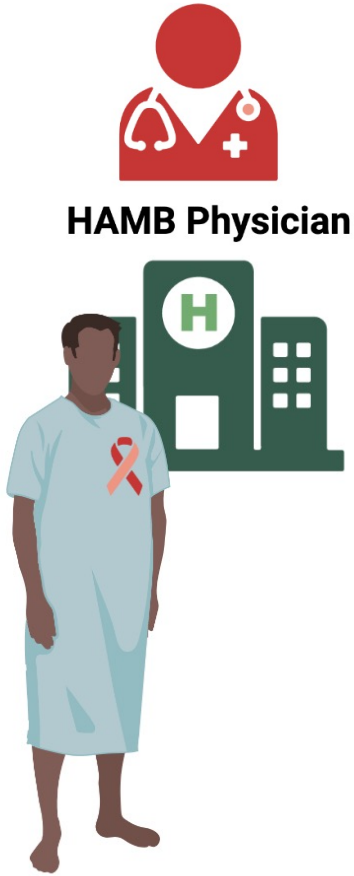
Call from an outside facility

Typical patient referral to the HIV/AIDS Malignancy Branch (HAMB)

CD4 111 cells/uL, VL<20

29 yo African-American male who was diagnosed with HIV and Kaposi sarcoma in the last 3 months





Patient reports

- Diarrhea
- Dyspnea
- Fevers
- Swollen lymph nodes

Laboratory findings

↑ C-reactive protein
KSHV/HHV8 viral load

↓ Hemoglobin, platelets, albumin

Patient work up at HAMB

Patient reports

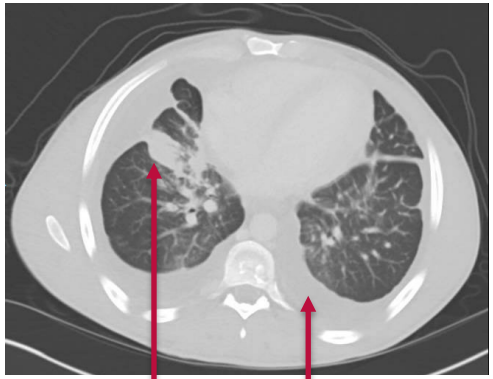
- Diarrhea
- Dyspnea
- Fevers
- Swollen lymph nodes

Laboratory findings

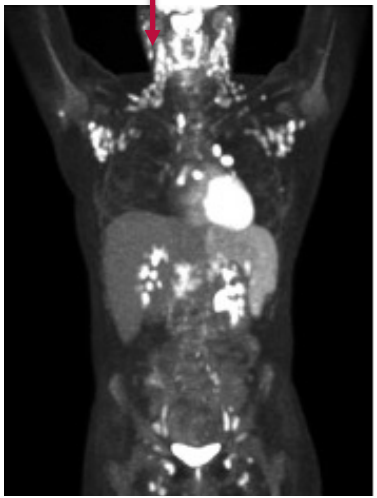
↑ C-reactive protein
KSHV/HHV8 viral load

↓ Hemoglobin, platelets, albumin

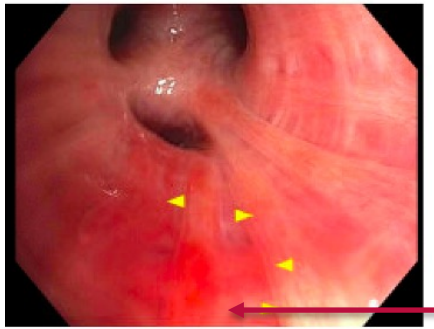
Scans

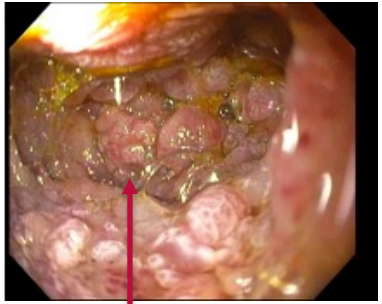


Avid lymph nodes



Scopes





Kaposi sarcoma

Where we started and where we are in the 21st Century

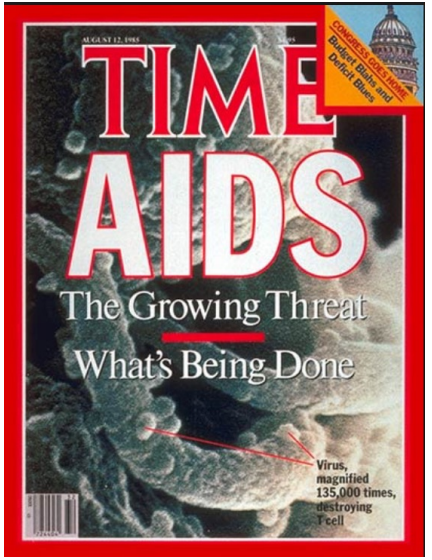
HIV and KS: A close association

THE NEW YORK TIMES,
FRIDAY, JULY 3, 1981

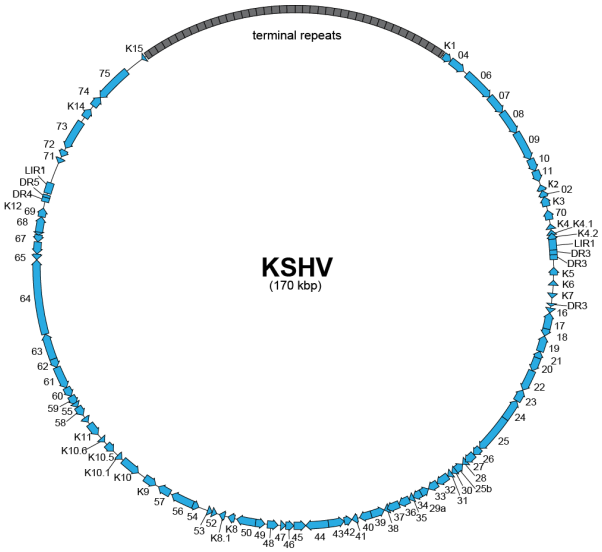
A20 L

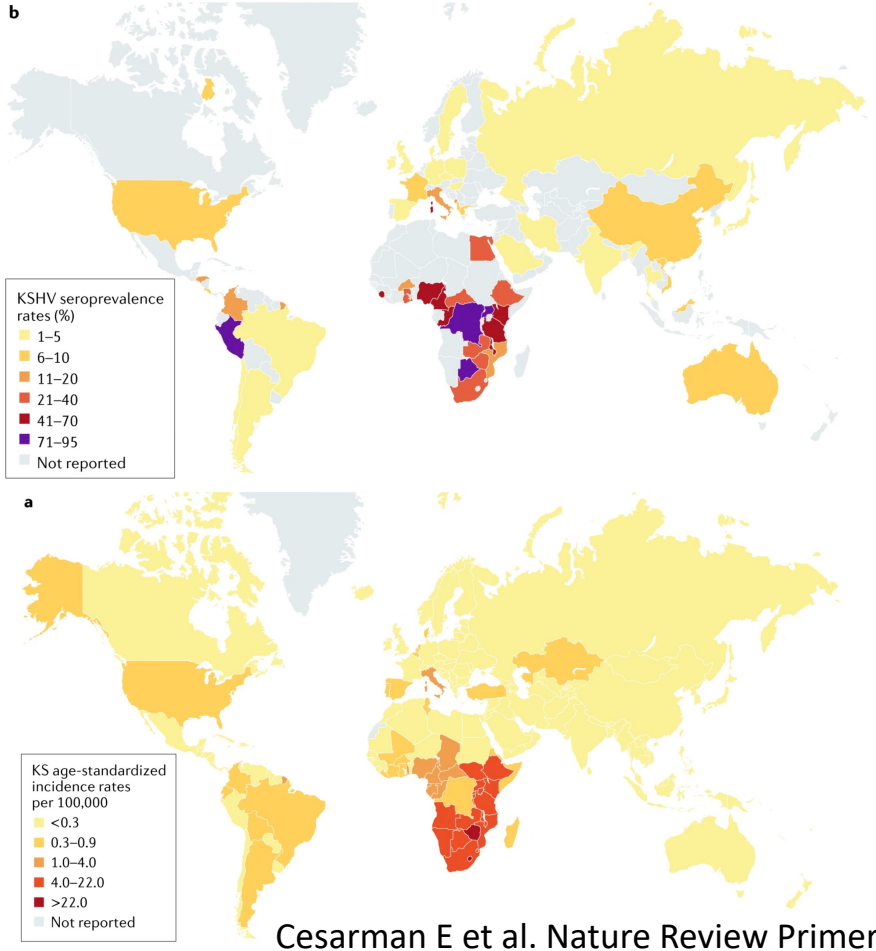
RARE CANCER SEEN IN 41 HOMOSEXUALS

Outbreak Occurs Among Men in New York and California —8 Died Inside 2 Years



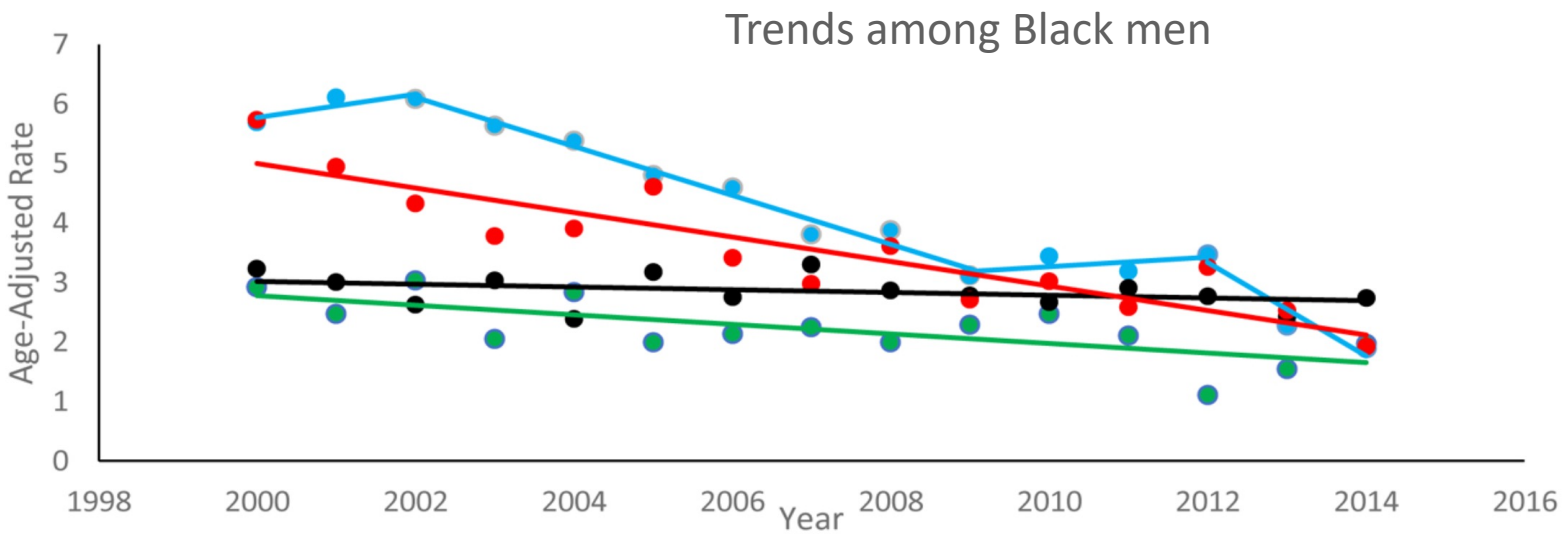
KSHV/HHV8 prevalence and impact worldwide





Cesarman E et al. Nature Review Primers (2019)

Decreasing KS incidence but hot spots in United States remain



White DL, et al. JAIDS (2019)

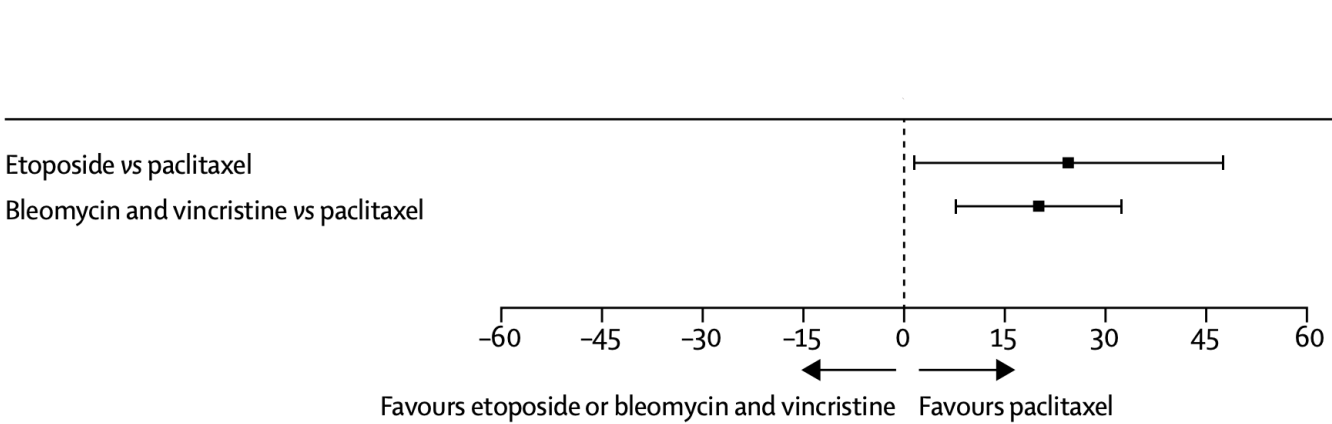
KS treatment and impact

Antiretroviral therapy

Liposomal doxorubicin

Paclitaxel

Progression or death rates



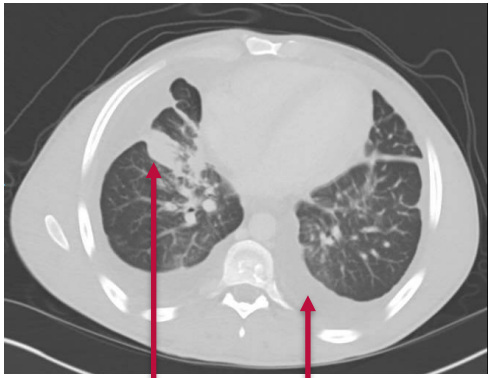
Krown S, et al Lancet (2020)

Back to our case

More than just Kaposi sarcoma

Diagnoses of other KSHV-associated diseases

Scans

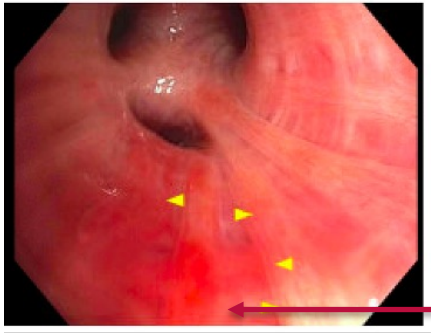


Infiltrates, nodules

Effusion

Avid lymph nodes

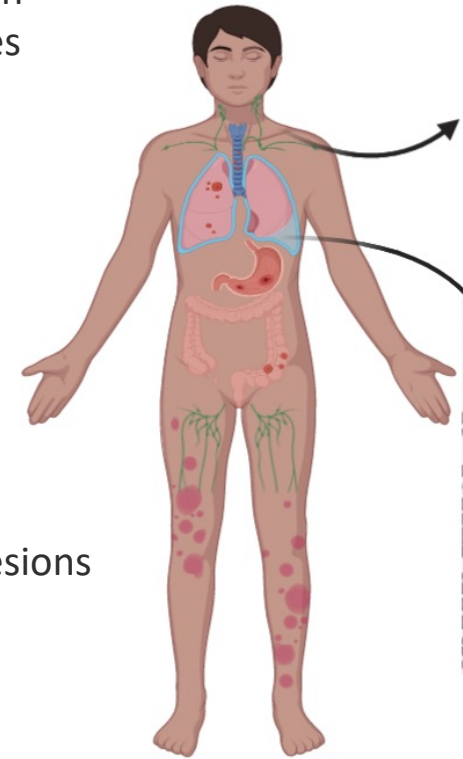
Scopes



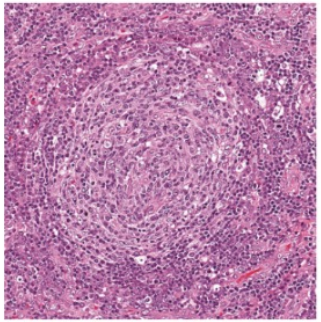
KS lesions

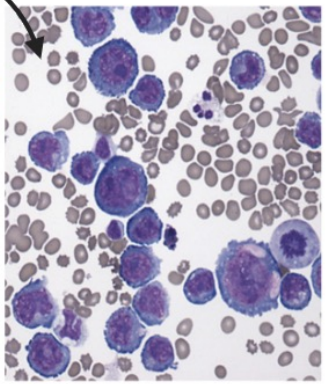
KS lesions

Pathology



Multicentric Castleman Disease (MCD)

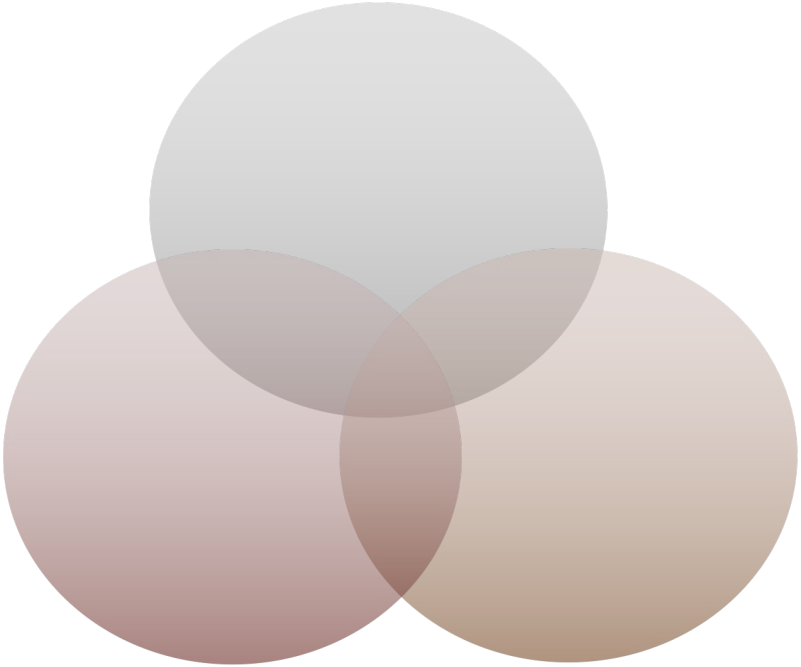


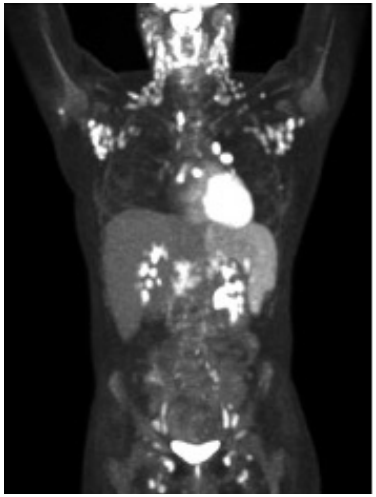


Primary Effusion Lymphoma (PEL)

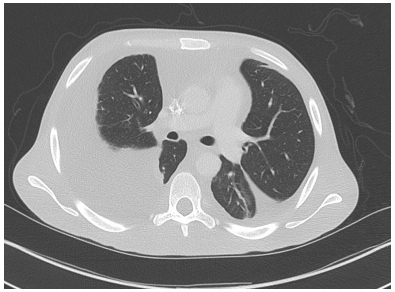
Concurrent KSHV-associated diseases

Kaposi Sarcoma





Multicentric Castleman Disease

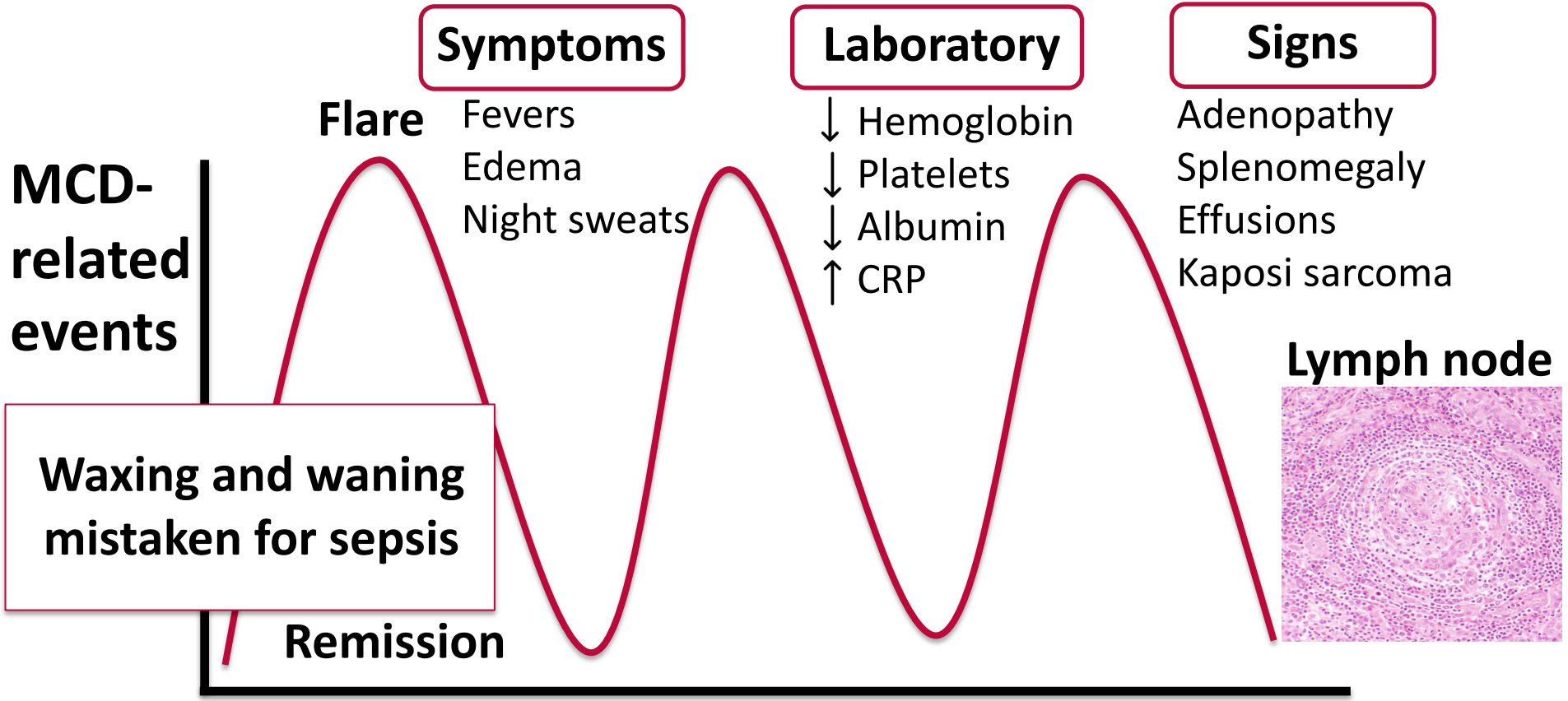


Primary Effusion Lymphoma

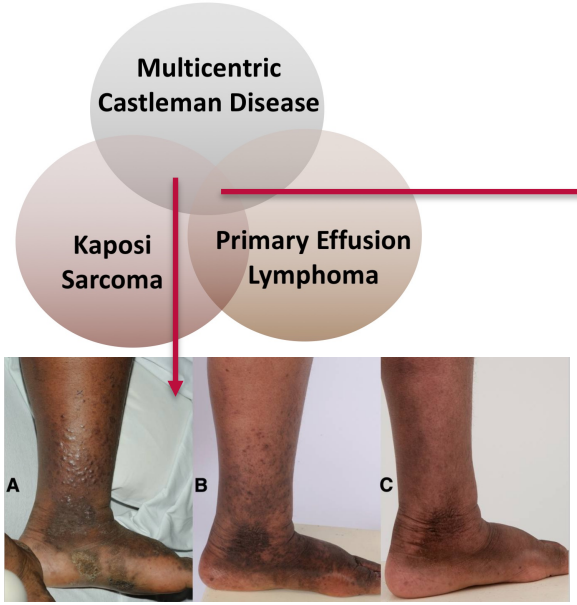
Diagnosing more than just KS

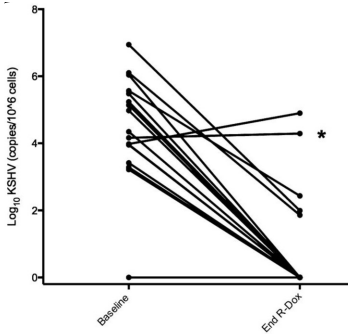
Managing concurrent KSHV-associated diseases

KSHV-associated multicentric Castleman disease (MCD)



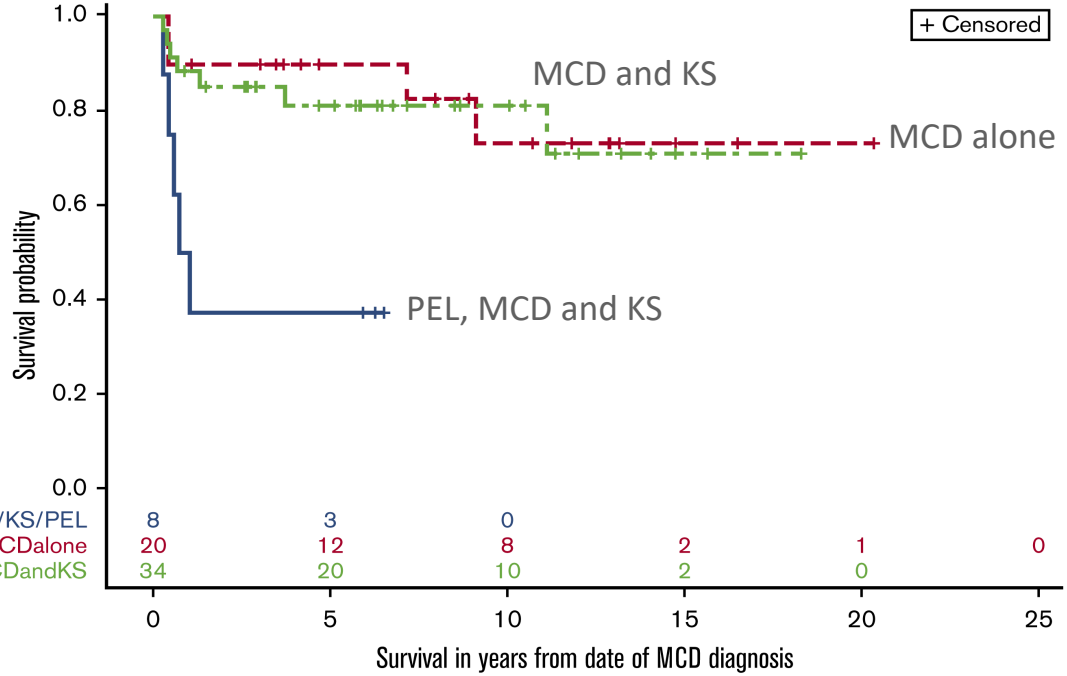
Treatment and outcomes in MCD





Uldrick TS, et al. Blood (2014)

Cohort of 62 participants with HIV and MCD

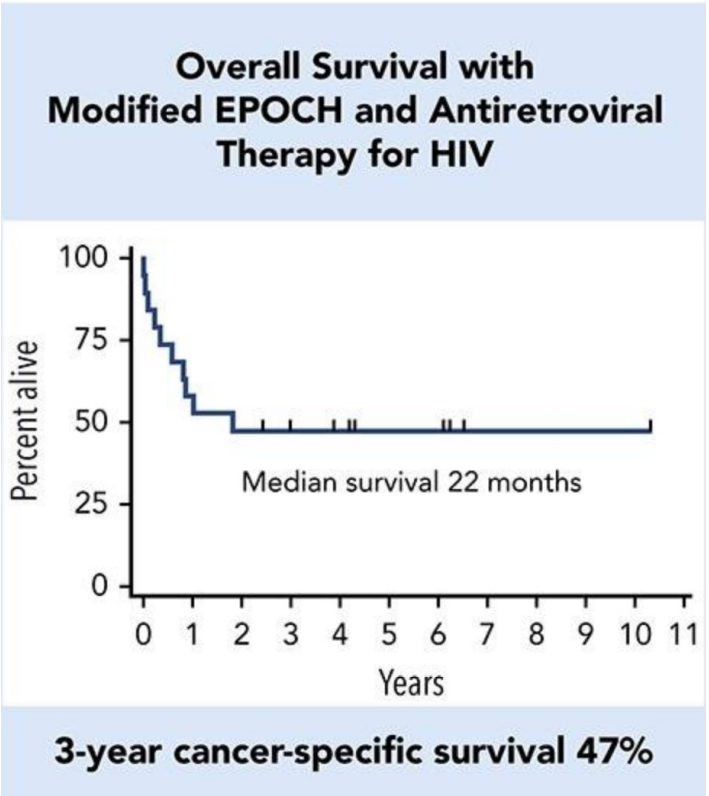


Ramaswami R, et al. Blood Advances (2021)

Management and prognosis of primary effusion lymphoma (PEL)

Baseline

After 6 Cycles



Treatment with CURATIVE intent

Prognostic factors

Negatively impacts survival
Elevated IL6
Elevated IL10

Positively impacts survival
EBV coinfection

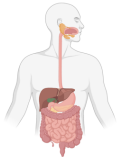
Lurain K, et al. Blood (2019)

KSHV inflammatory cytokine syndrome (KICS)

1. No diagnosis of MCD or PEL

2. Symptoms

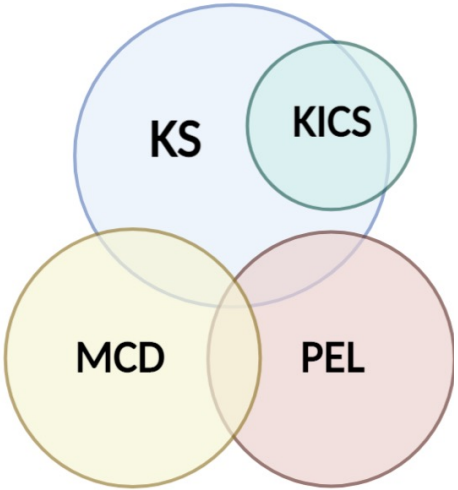
B symptoms



GI symptoms

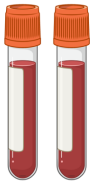
Respiratory symptoms

Edema, cachexia etc



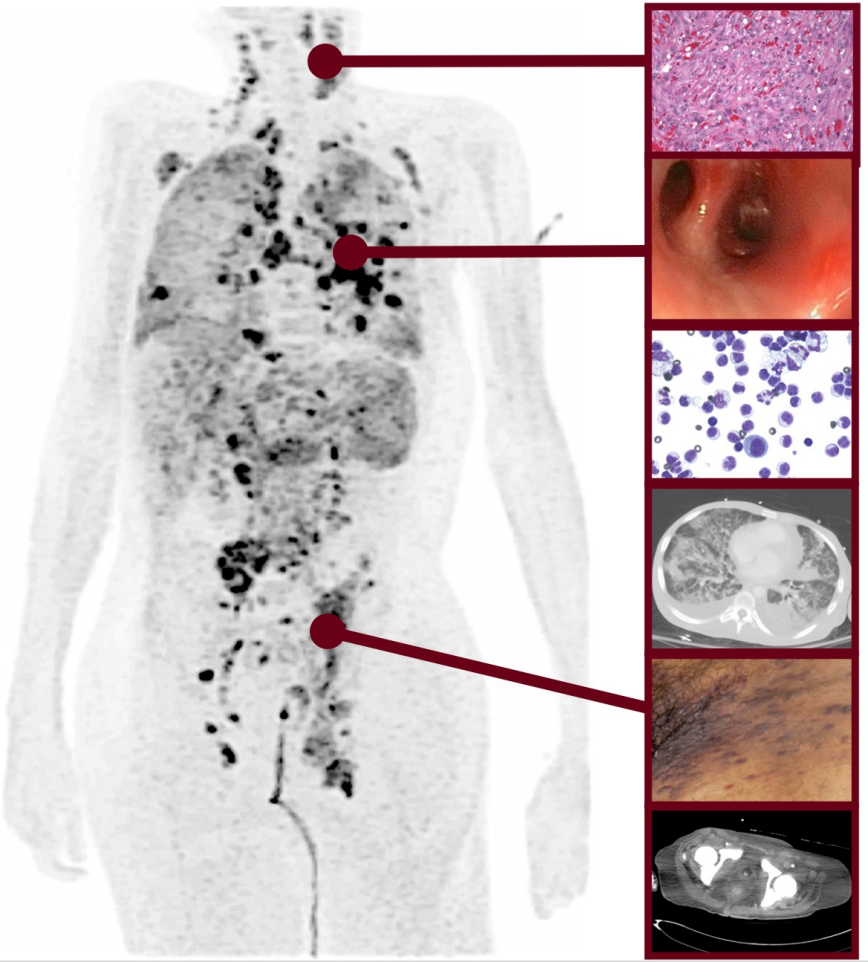
3. Laboratory

Anemia
Thrombocytopenia
Hypoalbuminemia
Hyponatremia



4. Elevated C-reactive protein

5. Elevated HHV8/KSHV VL



Patients in intensive care with KS may not have KS alone

42 patients admitted to the intensive care unit (ICU) with KSHV-associated diseases.

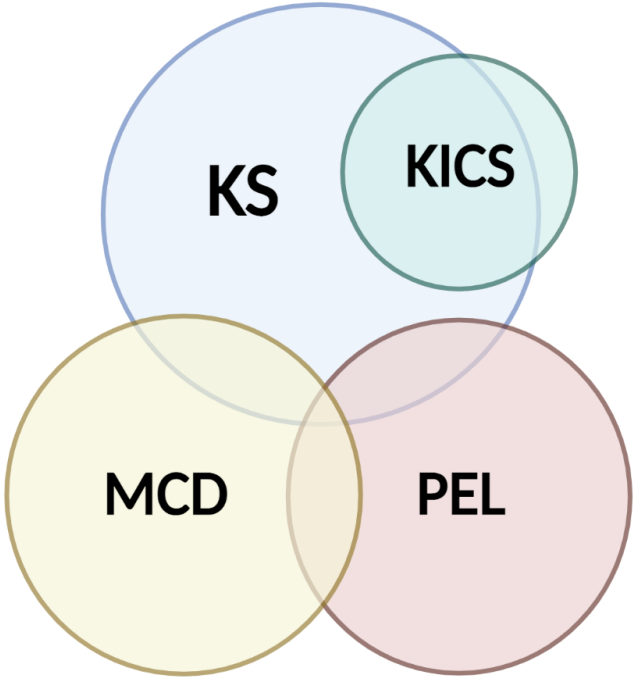
8 of 22 patients with presumed KICS +/- KS had MCD and/or PEL diagnosed in the ICU

Important to keep seeking additional diagnoses beyond the initial KSHV diagnosis

This can impact management and outcomes

Hansen ME, …Ramaswami R, AIDS (2022)

Summary of treatment of KSHV-associated diseases



KS alone
Liposomal doxorubicin
Paclitaxel
Pomalidomide

KS + KICS (exclude PEL and MCD)
No standard first line, consider MCD treatments or clinical trial options

KS + MCD
Rituximab + liposomal doxorubicin

KS + PEL +/- MCD
EPOCH+/-Rituximab

Consider clinical trials for all groups

Ramaswami R et al. JCO (2022)

How can we improve outcomes for PLWH and cancer?

- Multidisciplinary and gender-inclusive care
  - Oncologists, HIV specialists, pharmacists, nurses, social workers, patient navigator
- Antiretroviral therapy is an important part of lymphoma treatment
- Supportive care and prophylaxis against opportunistic infections
- Give standard therapies at standard doses where indicated

How can we improve outcomes for PLWH and cancer?

- Exploit unique aspects of pathogenesis
  - T cell-sparing regimens
  - Reverse immune suppression/dysregulation
  - Target oncogenic viruses

The hope of cure in multiple disciplines

The HIV and AIDS Malignancy Branch

NATIONAL
CANCER
INSTITUTE

www.cancer.gov

www.cancer.gov/espanol