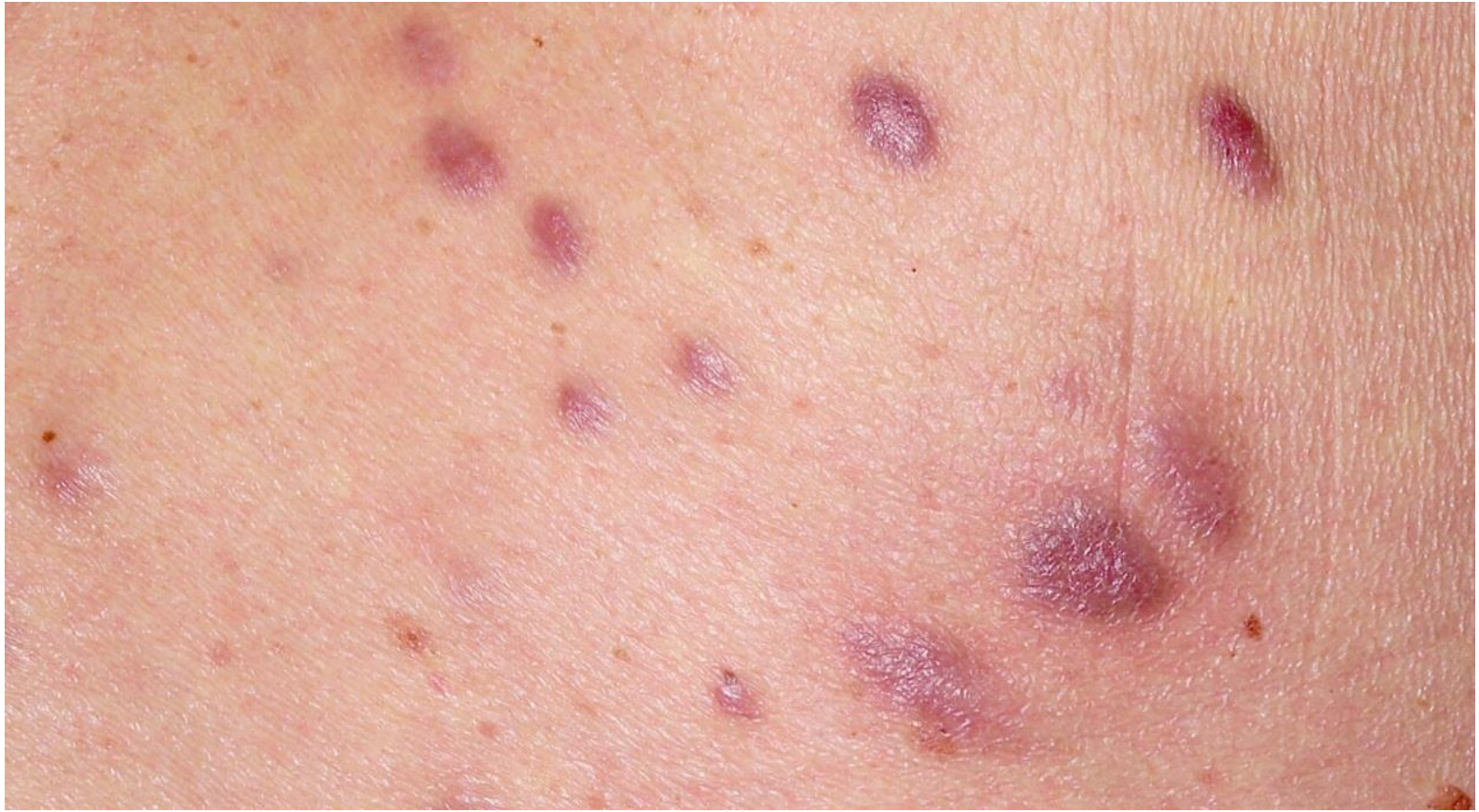
KS and Lymphoma – ghosts from the past and the challenges ahead

Duncan Churchill



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MORBIDITY AND MORTALITY WEEKLY REPORT

Epidemiologic Notes and Reports

Kaposi's Sarcoma and *Pneumocystis* Pneumonia Among Homosexual Men – New York City and California

During the past 30 months, Kaposi's sarcoma (KS), an uncommonly reported malignancy in the United States, has been diagnosed in 26 homosexual men (20 in New York City [NYC], 6 in California). The 26 patients range in age from 26-51 years (mean 39 years). Eight of these patients died (7 in NYC, 1 in California)–all 8 within 24 months after KS was diagnosed. The diagnoses in all 26 cases were based on histopathological examination of skin lesions, lymph nodes, or tumor in other organs. Twenty-five of the 26 patients were white, 1 was black. Presenting complaints from 20 of these patients are shown in Table 1.

Prevalence of KS

- KS >20,000x more frequent if HIV+

- By March 1989, 15% of PWA in USA (n=13,616)
  - 21% in MSM
  - 1% in haemophiliacs

Beral et al., Lancet 1990 Jan 20;335(8682):123-8

1994: discovery of causative agent

- KSHV (HHV-8)

- Also implicated in:
  - Multicentric Castleman's Disease
  - Primary Effusion Lymphoma

Chang et al. Science. **1994** Dec 16;266(5192):1865-9

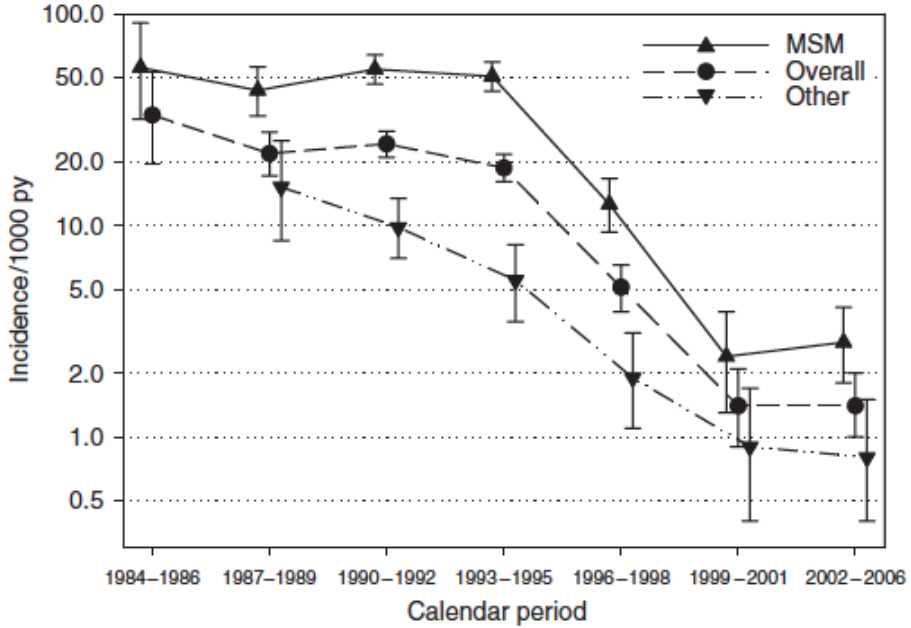


Figure 1 Incidence rates of KS by calendar period, overall and according to HIV transmission category. Rates were standardised (direct method) on age and gender, based on Swiss HIV Cohort Study participants. Vertical bars represent 95% CI. MSM: men having sex with men.

Franceschi et al, Br J Cancer 2008; 99: 800-4

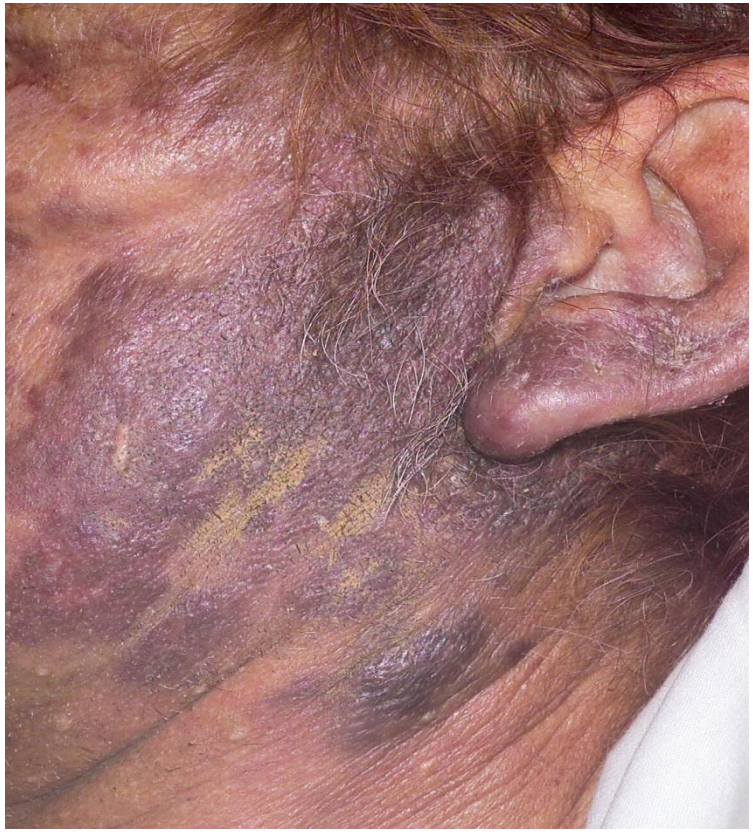
KS in 2018

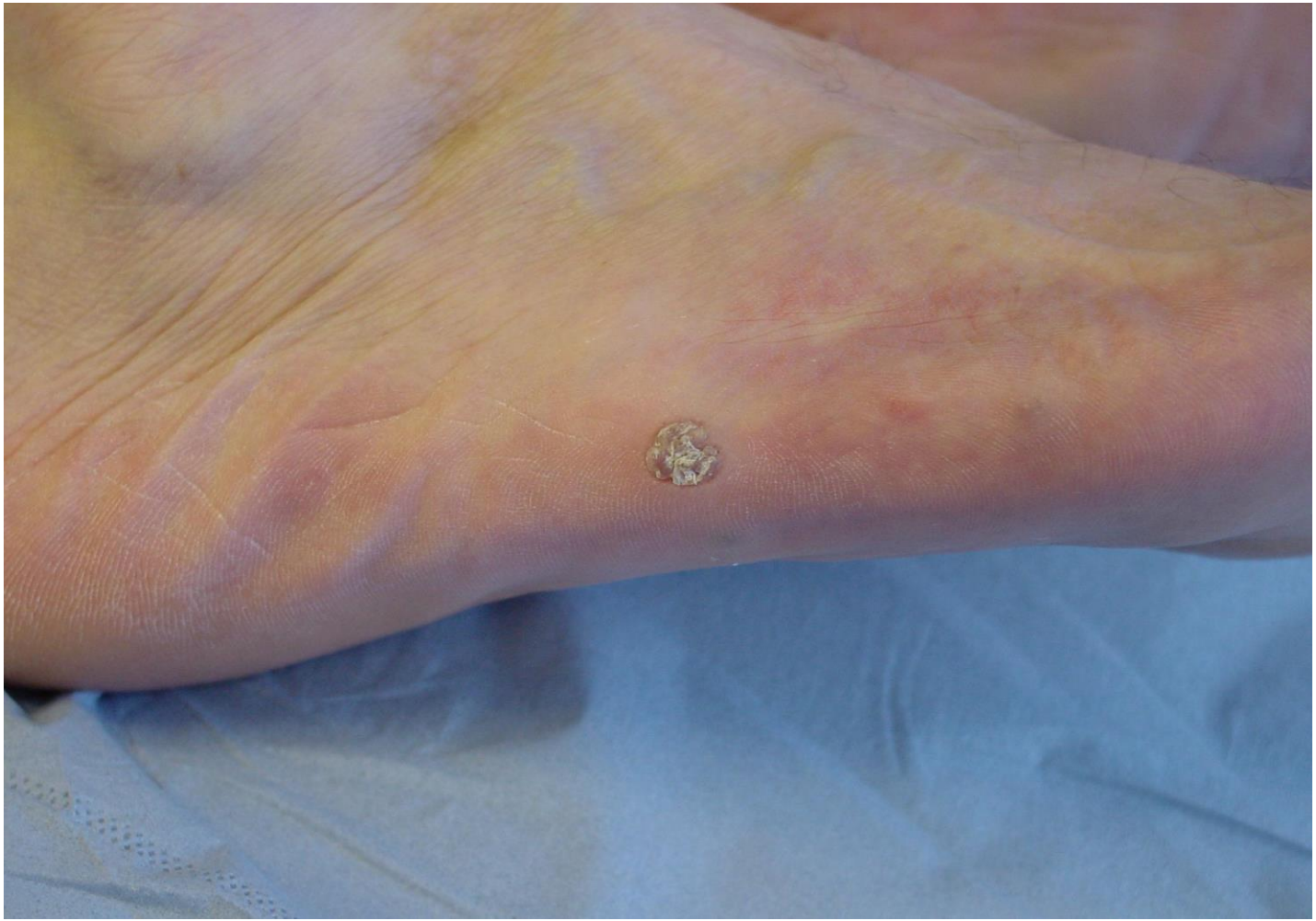
- Incidence reduced
- Occurs at higher CD4 counts

Approach to management

Ideally joint management between HIV physician and oncologist

1. Confirm the diagnosis histologically



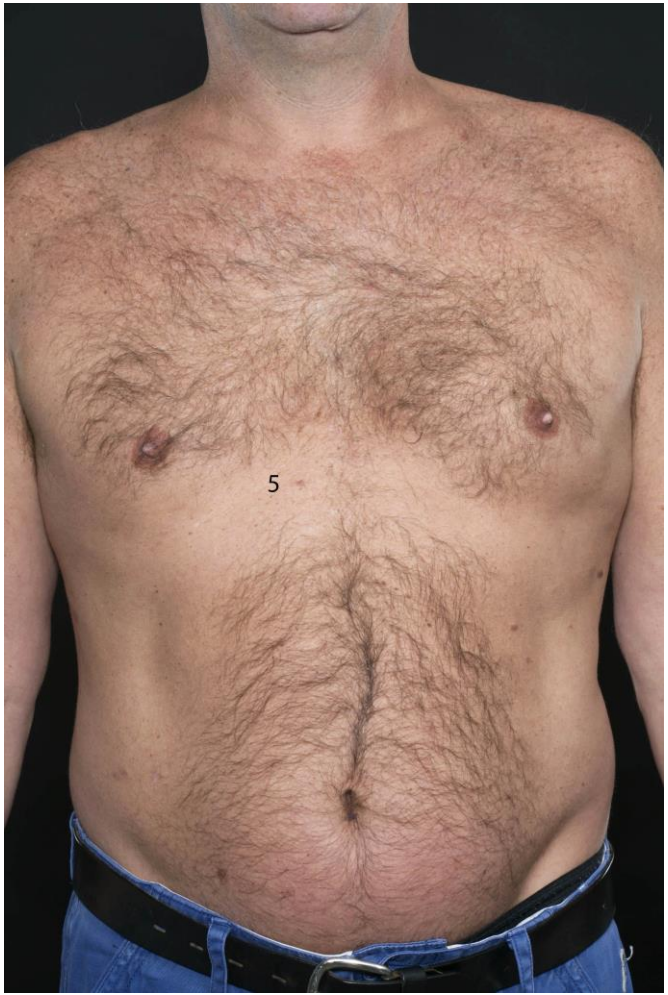


Approach to management

1. Confirm the diagnosis
2. Start ART

Approach to management

1. Confirm the diagnosis
2. Start ART
3. Take photographs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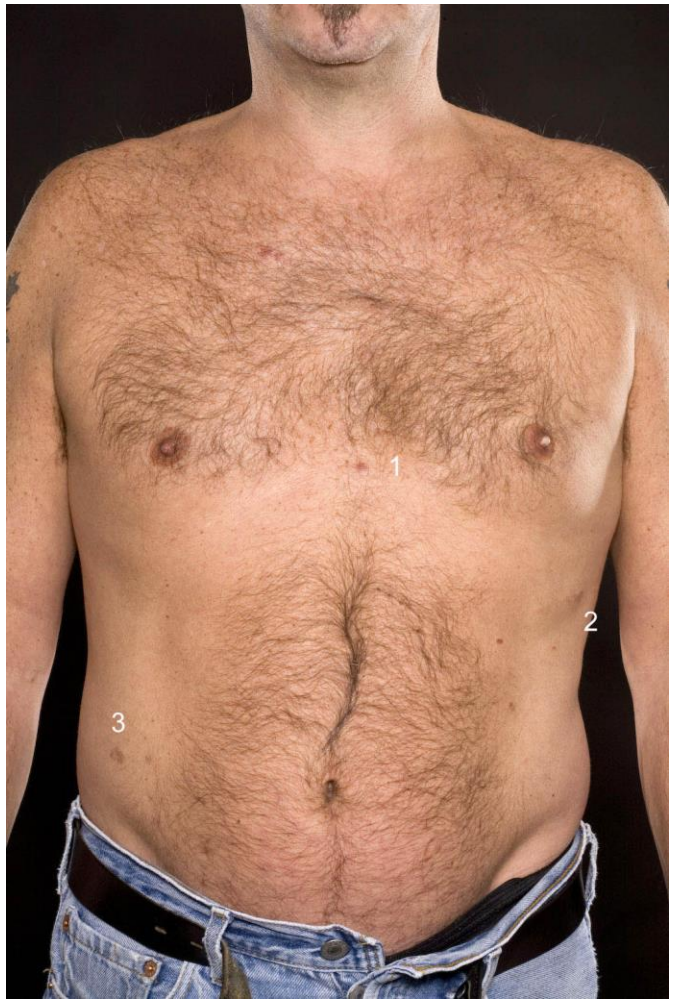
1
2
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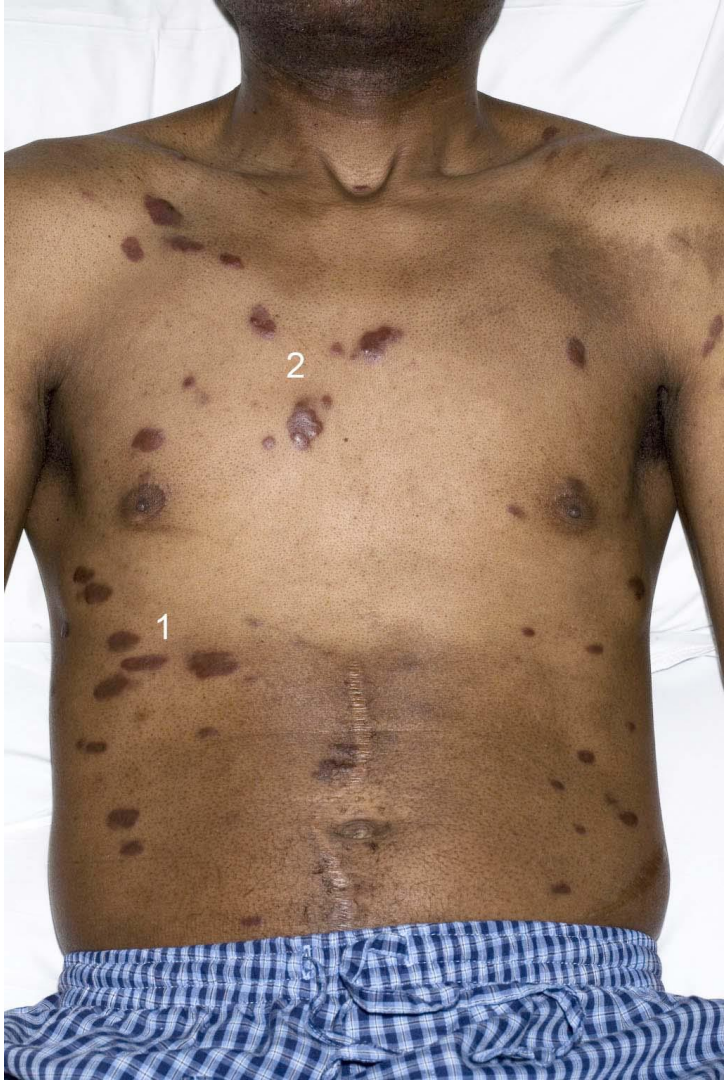
Approach to management

1. Confirm the diagnosis
2. Start ART
3. Take photographs
4. Staging
   - Is there an indication for chemotherapy?

Table 3.1 The modified AIDS Clinical Trials Group staging of KS [3,4]

TIS staging of KS	Good risk (all of the following)	Poor risk (any of the following)
(T) Tumour	Confined to skin, lymph nodes or minimal oral disease	Tumour-associated oedema or ulceration Extensive oral KS Gastrointestinal KS KS in other non-nodal viscera
(I) Immune status	CD4 cell count >150 cells/μL	CD4 cell count <150 cells/μL
(S) Systemic illness	Karnovsky performance status >70	Karnovsky performance status <70 or other HIV-related illness

Visceral disease: 14% of patients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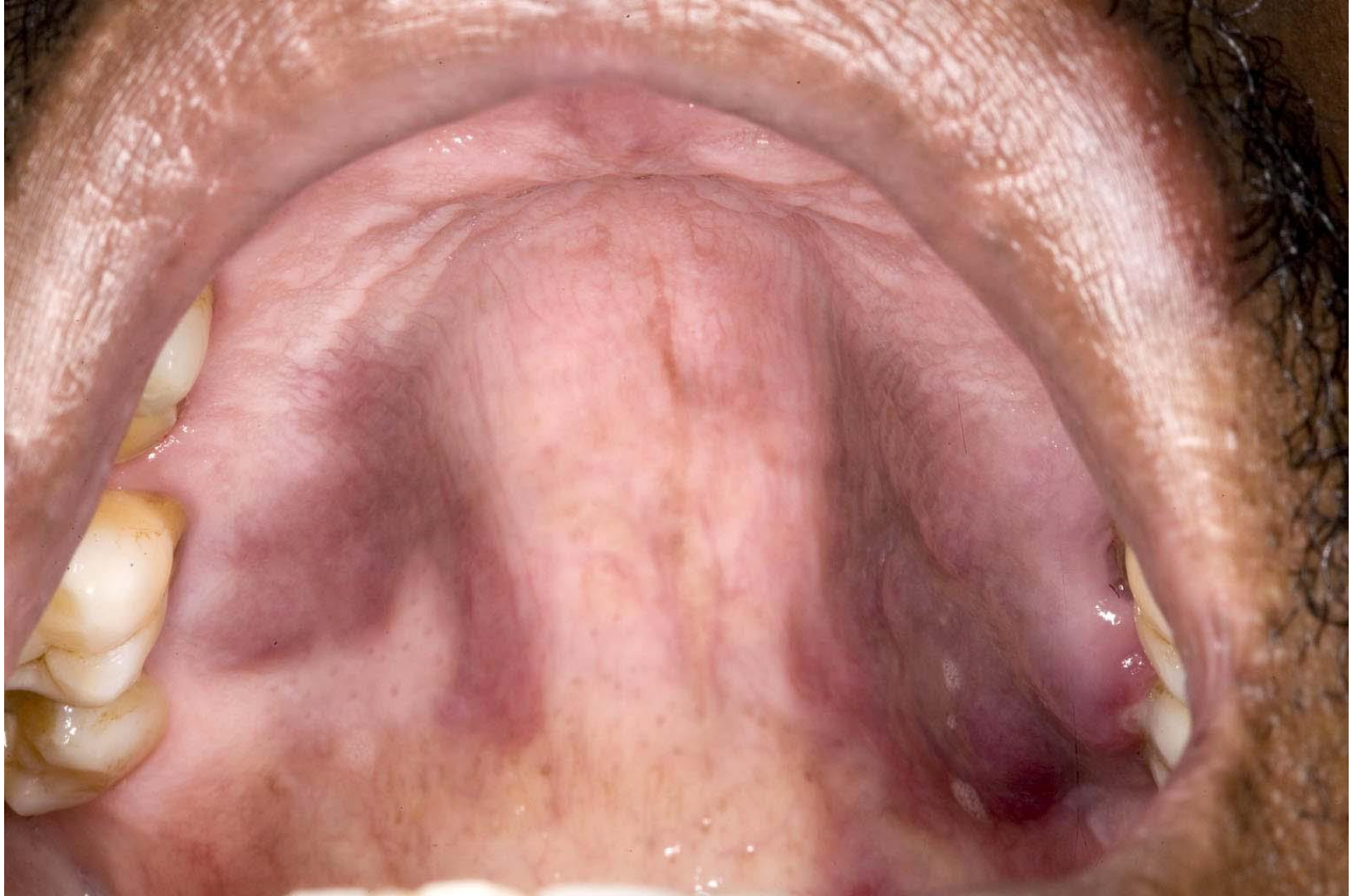

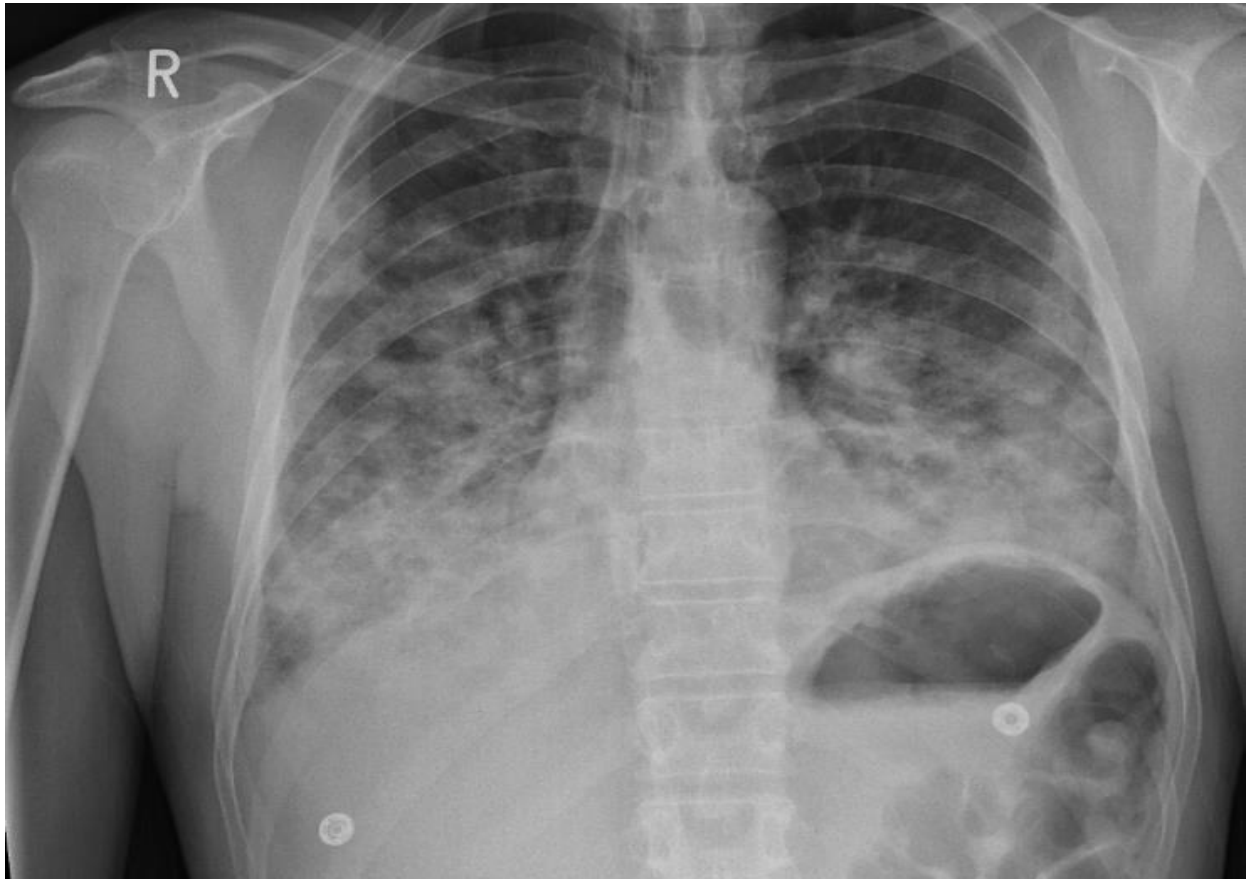
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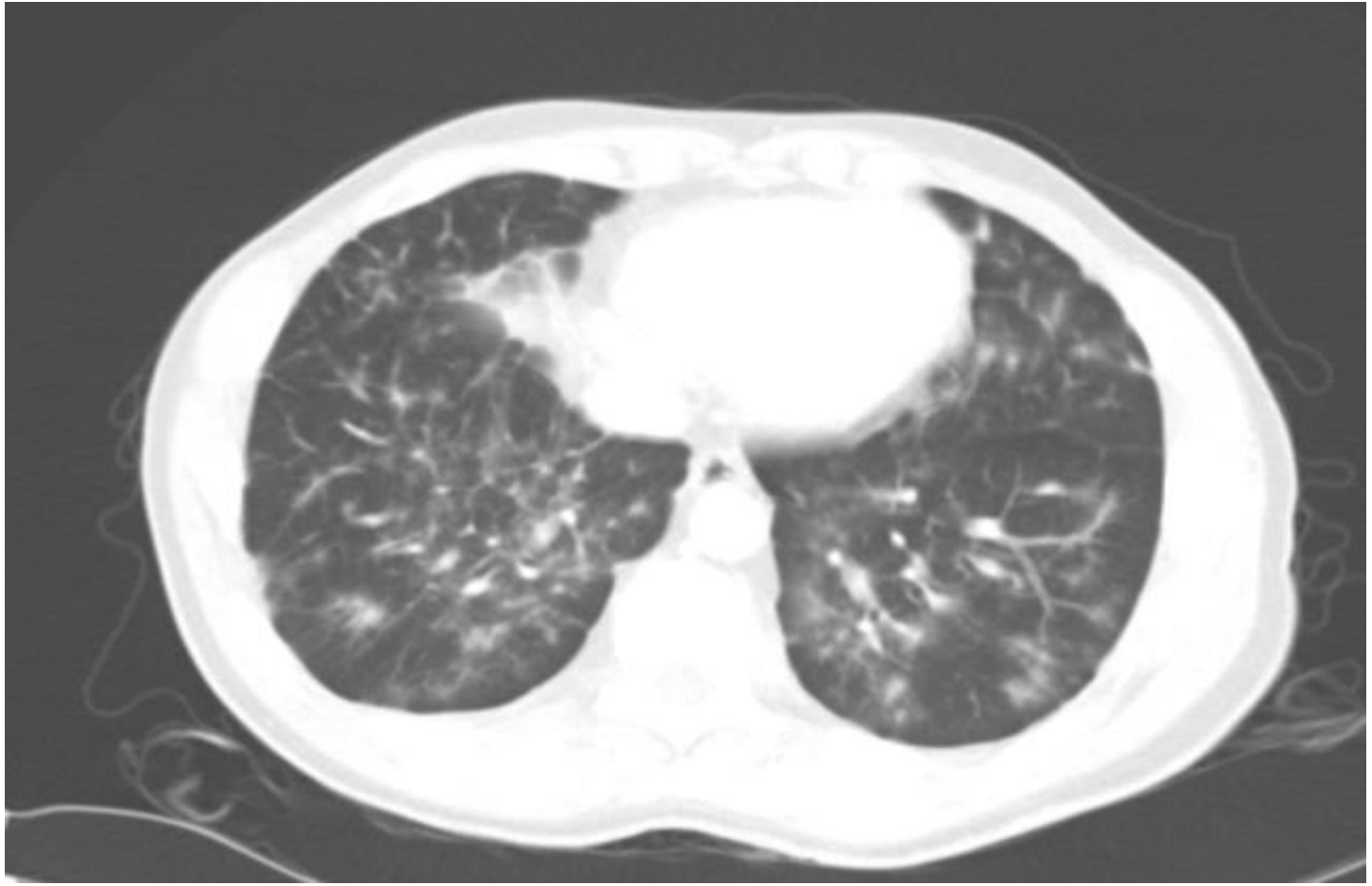
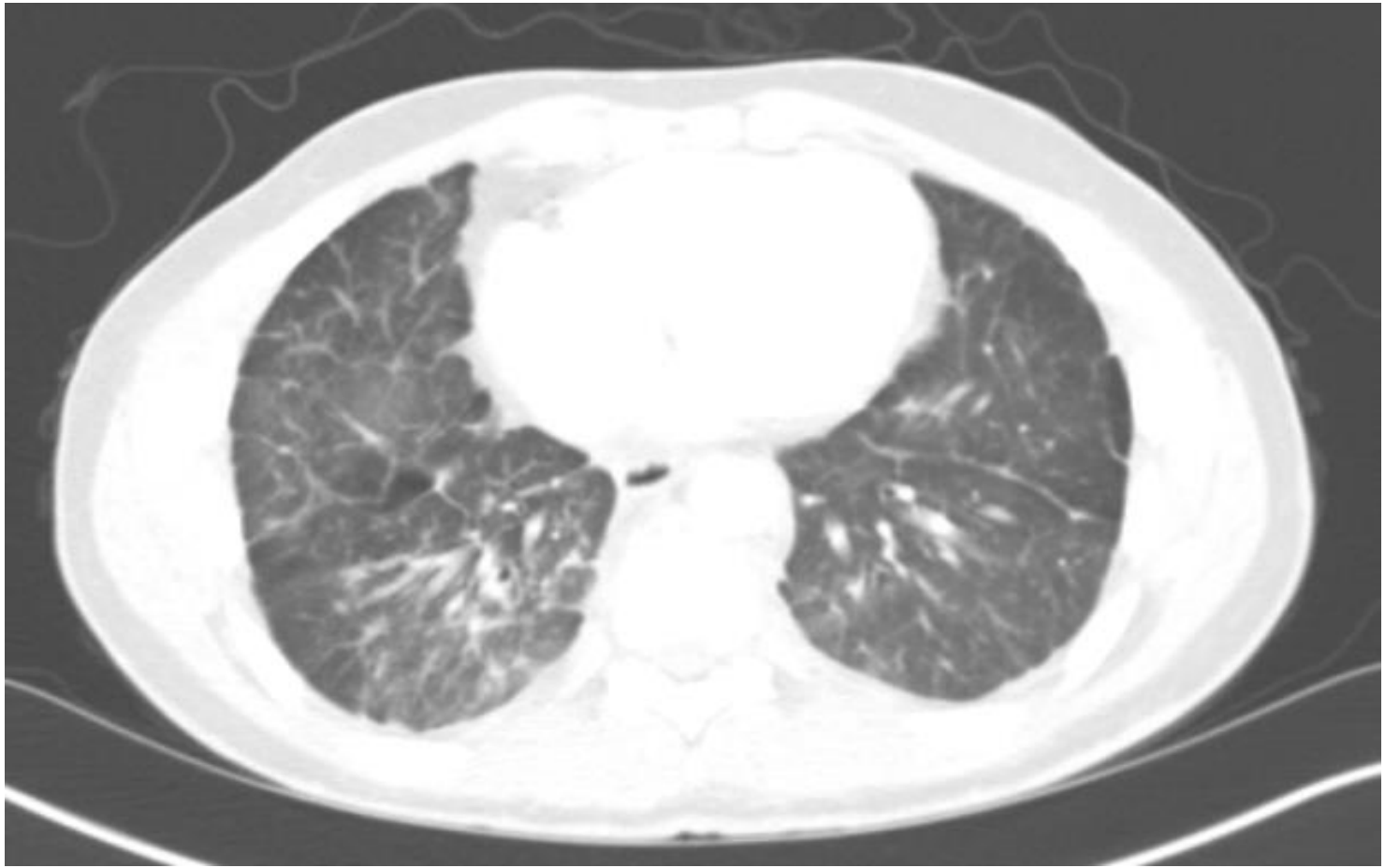


Chemotherapy

- Visceral disease
- Extensive cutaneous disease (despite ART)

- Liposomal doxorubicin (every 3 weeks)
- Paclitaxel (every 2 weeks)



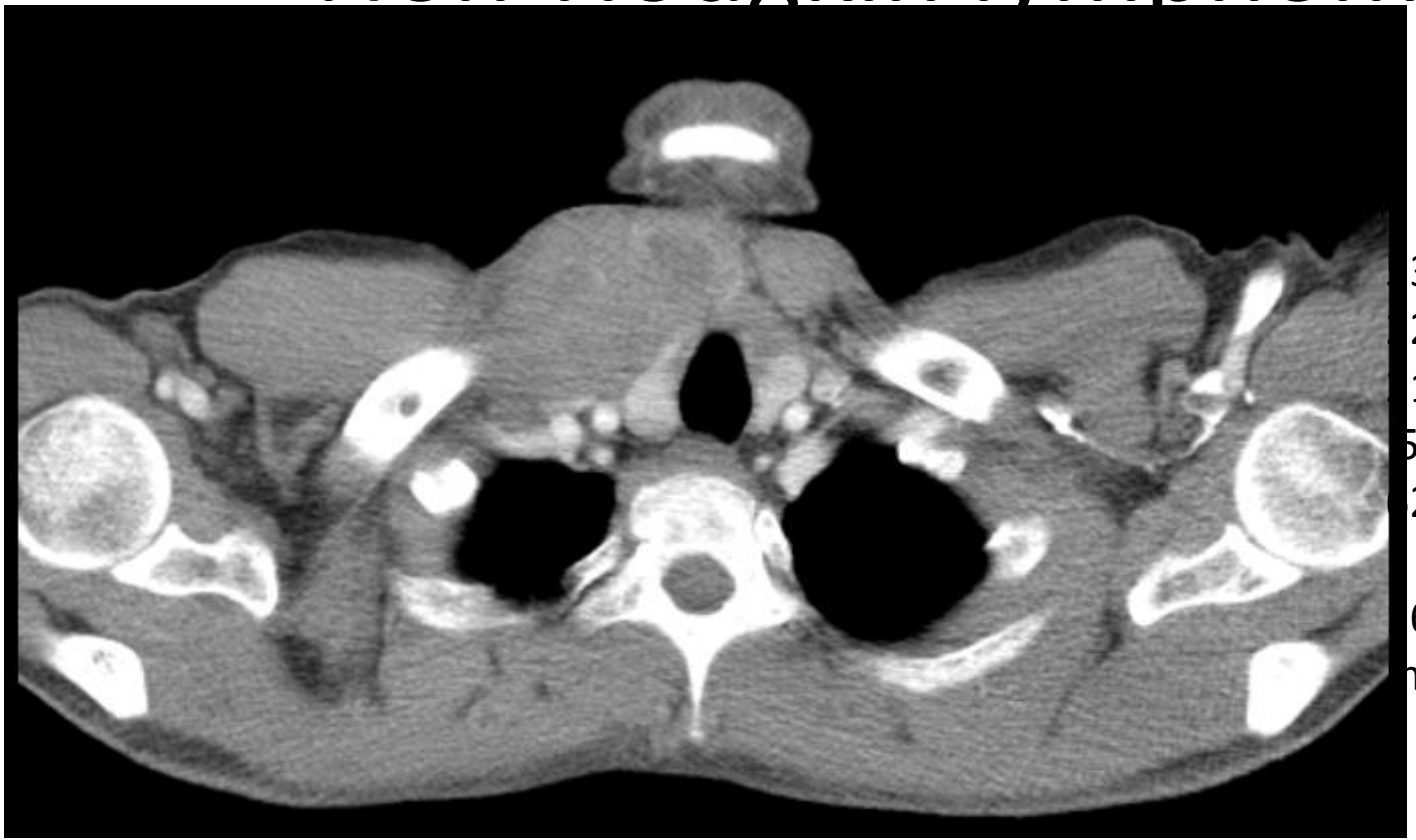
Approach to management

1. Confirm the diagnosis
2. Start ART
3. Take photographs
4. Staging
   - Is there an indication for chemotherapy?
5. Chemotherapy (or radiotherapy) in a minority

Ideally joint management between HIV physician and oncologist

Lymphoma

Non-Hodgkin lymphoma



3605 patients
2 European cohorts
12042 PY FU
521 NHL
2 PCNSL

65-fold increased
ncidence in HIV+

Bohlius et al., Antivir Ther 2009

Presentation

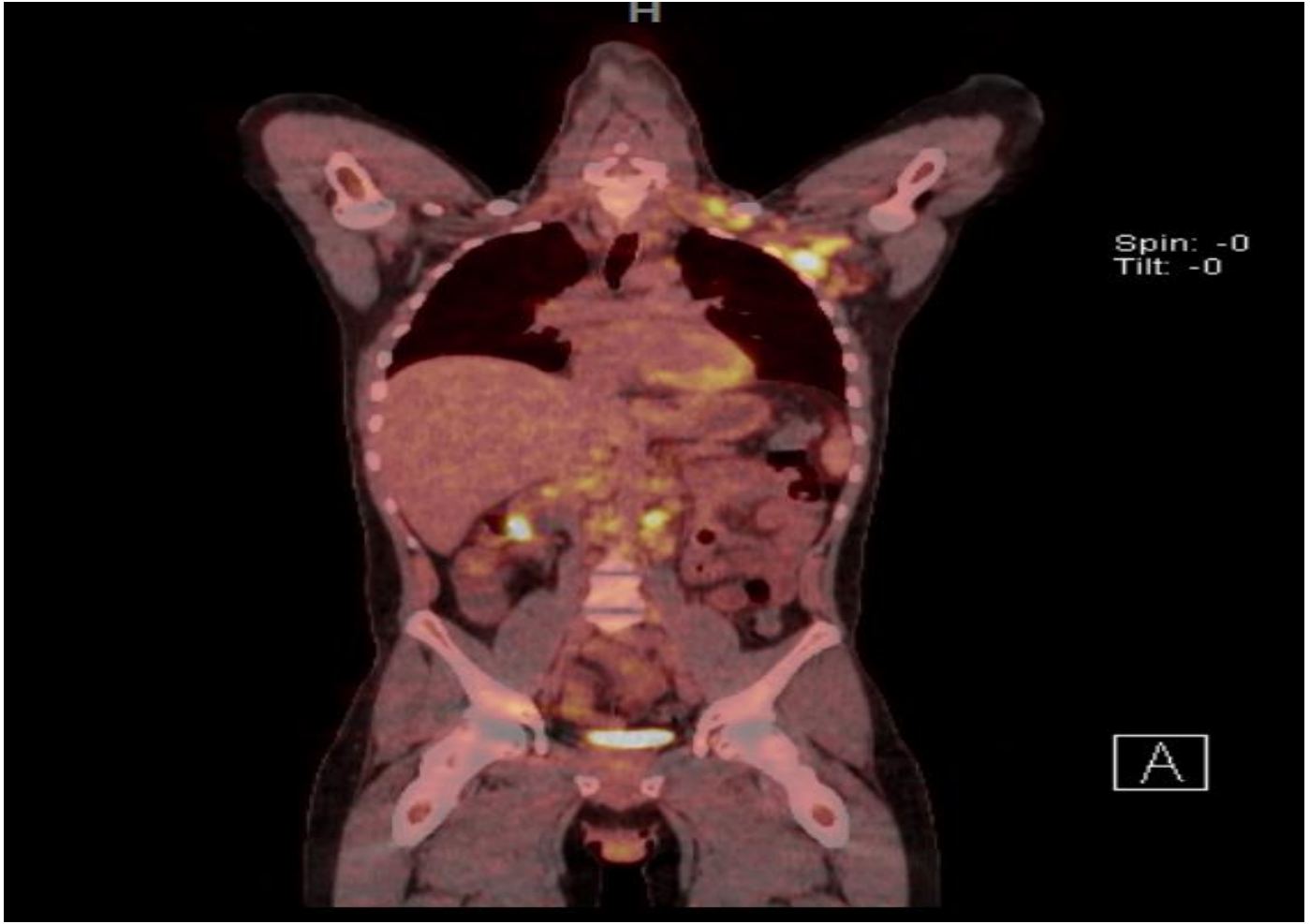
- Lump
- Systemic symptoms
  - Fever, sweats
  - Weight loss
  - Anaemia, raised C-RP

Is it lymphoma?

- Tissue biopsy
  - Excision vs. needle biopsy

Lymphoma – approach to management

1. Obtain tissue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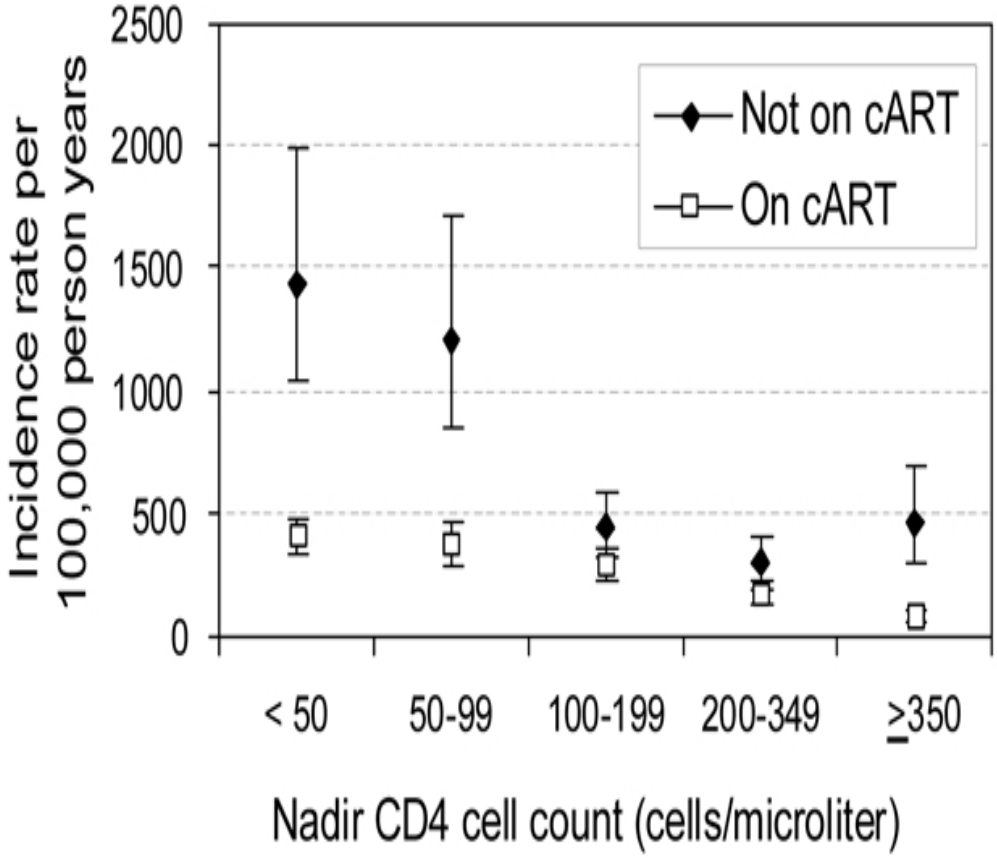
Incidence rate per 100,000 person years
2500
2000
1500
1000
500
0
Not on cART
On cART
< 50
50-99
100-199
200-349
≥350
Nadir CD4 cell count (cells/microliter)

Lymphoma – approach to management

1. Obtain tissue
2. Confirm diagnosis and type

- Hodgkin lymphoma
- Non-Hodgkin lymphoma
  - DLBCL
  - Burkitt-type (histological/ c-MYC rearrangement)
  - Plasmablastic
  - Primary effusion lymphoma
- Primary CNS lymphoma

Hodgkin lymphoma

- 10-20x increase in incidence if HIV+
- Incidence has not fallen markedly with ART

- ABVD 4-6 cycles
- Outpatient-based

Good prognosis

- 23 consecutive patients with Hodgkin lymphoma from 6 centres 2007-2010
- All treated with ART and ABVD
- 100% 2 year survival for patients with negative PET-CT after 2/3 cycles

Okosun et al., AIDS 2012, 26: 861-5

DLBCL

- R-CHOP 6-8 cycles
- Outpatient-based

- 78% overall survival
  - 97 patients (2003-11)

Coutinho et al. AIDS 2014 Mar 13;28(5):689-97

Burkitt-type

- More aggressive
- Higher risk of CNS disease

- CODOX-M/IVAC
- Inpatient-based

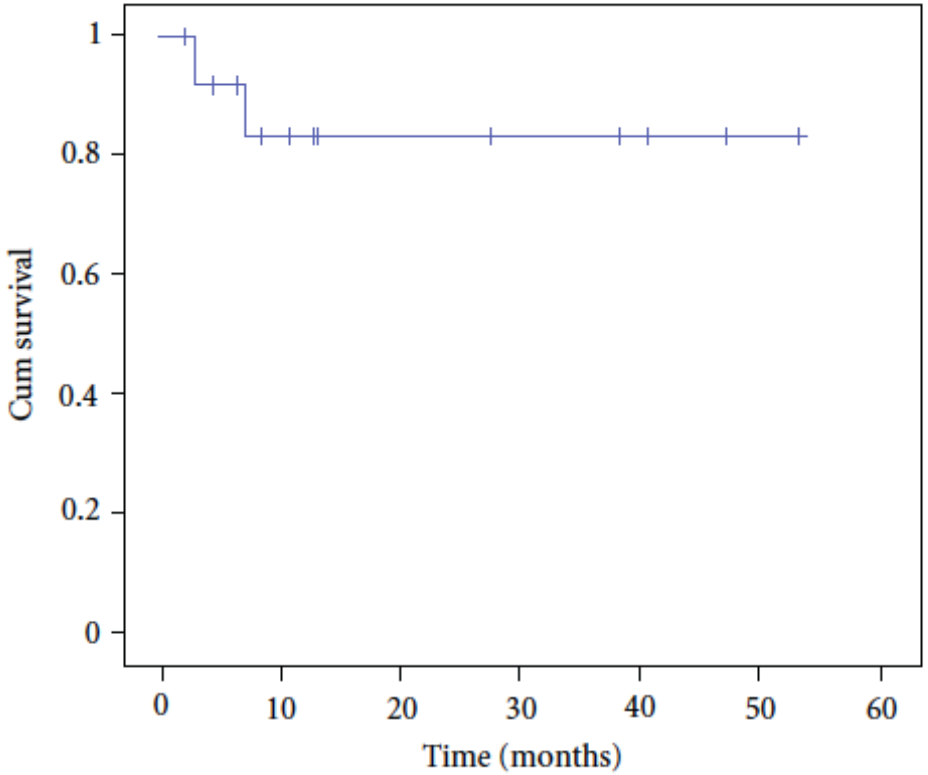

FIGURE 1: Overall survival of 14 patients with HIV-associated Burkitt lymphoma receiving CODOX-M/IVAC chemotherapy, 13 with HAART and 10 with rituximab.

Rodrigo et al., 2012

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Low-Intensity Therapy in Adults with Burkitt's Lymphoma

Kieron Dunleavy, M.D., Stefania Pittaluga, M.D., Ph.D., Margaret Shovlin, R.N., Seth M. Steinberg, Ph.D., Diane Cole, M.S., Cliona Grant, M.D., Brigitte Widemann, M.D., Louis M. Staudt, M.D., Ph.D., Elaine S. Jaffe, M.D., Richard F. Little, M.D., and Wyndham H. Wilson, M.D., Ph.D.

ABSTRACT

RESULTS

A total of 30 consecutive patients were treated; 19 patients were in the DA-EPOCH-R group, and 11 in the SC-EPOCH-RR group. The overall median age of the patients was 33 years, and 40% were 40 years of age or older; 73% of the patients had intermediate-risk disease, and 10% had high-risk disease. The principal toxic events, fever and neutropenia, were observed during 22% of the DA-EPOCH-R treatment cycles and 10% of the SC-EPOCH-RR treatment cycles. The tumor lysis syndrome developed in 1 patient; no treatment-related deaths occurred. The median cumulative doses of doxorubicin–etoposide and cyclophosphamide administered in the SC-EPOCH-RR group were 47% and 57% lower, respectively, than those administered in the DA-EPOCH-R group. With median follow-up times of 86 months in the DA-EPOCH-R group and 73 months in the SC-EPOCH-RR group, the rates of freedom from progression of disease and overall survival were, respectively, 95% and 100% with DA-EPOCH-R and 100% and 90% with SC-EPOCH-RR. None of the patients died from Burkitt's lymphoma.

CONCLUSIONS

In this uncontrolled prospective study, low-intensity EPOCH-R–based treatment was highly effective in adults with sporadic or immunodeficiency-associated Burkitt's lymphoma. (Funded by the National Cancer Institute; ClinicalTrials.gov numbers, NCT00001337 and NCT00006436.)

HIV-associated plasmablastic lymphoma

- 50 patients from 13 institutions over 10 years

- Median CD4 206 cells/mm3
- 90% extranodal disease, 27% oral involvement
- myc rearrangements in 41%
- CR 66%; median overall survival 11 months
- Intensive chemotherapy didn’t improve survival

Castillo et al. Cancer 2012, epub17 APR 2012 DOI: 10.1002/cncr.27551

Primary CNS lymphoma

- High-dose methotrexate + rituximab

+/-Autologous stem cell transplantation

Lymphoma – approach to management

1. Obtain tissue
2. Confirm diagnosis and type
3. Start ART
4. Staging (?CNS disease; baseline PET)
5. Start chemoprophylaxis
6. Chemotherapy
7. Follow up for relapse

Role of the HIV physician

1. Optimise ART
   - Integrase inhibitors
   - Avoid ritonavir and cobicistat
   - ?Avoid TDF in aggressive chemotherapy regimens

2. Prophylaxis
   - Co-trimoxazole
   - Fluconazole
   - Aciclovir
   - TDF/TAF + FTC if Hepatitis B cAb+
   - Azithromycin (?caution if stem cell transplantation)

3. Co-ordination/morale