KAPOSI SARCOMA – MEDICAL TREATMENT

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10/04/2021

08/12/2023

Disclosures

- No disclosure

Plan

- **Introduction**
  - Classification and staging of Kaposi sarcoma
  - General principles of treatment

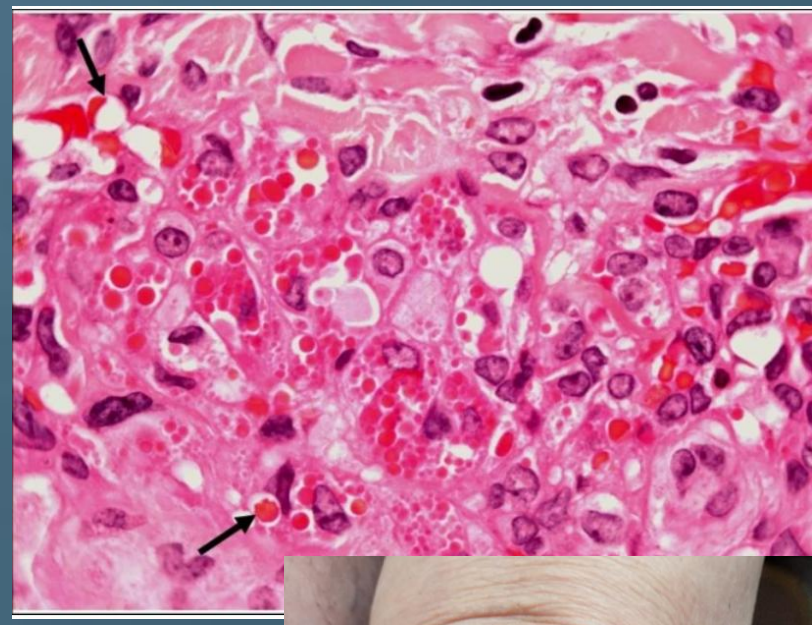
- **Systemic therapy of Kaposi sarcoma**
  - Chemotherapy
  - **New targeted agents**
  - **Immunotherapy**

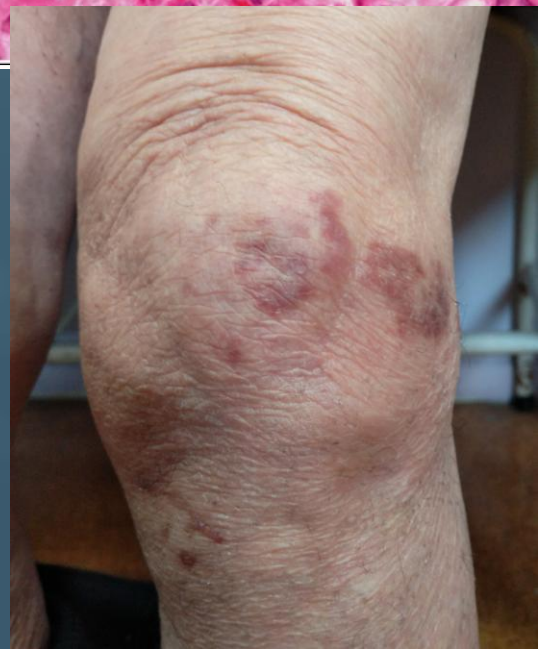
- **Open questions**

Introduction

Kaposi sarcoma: General overview

- Multifocal malignancy of endothelial cells
- Characteristic red or brown papules
- In 95%-98% of cases serologic confirmation of human herpesvirus-8 (**HHV-8**) infection = **Kaposi sarcoma-associated herpesvirus** (KSHV) infection





Hiatt et al., Mod Pathol. 2008

Subclassification of Kaposi sarcoma

1. **AIDS-related** (risk x3640 before antiretroviral therapy)
2. **Classic** (men, 74 years old, lower extremities)
3. **Iatrogenic or transplant-associated** (males, 2-8 months after immunosuppresion, can involve LN, mucosa and visceral organs)
4. **Endemic** (<40 years old, equatorial Africa, more aggressive)
5. **MSM** (men who have sex with men, without HIV infection, often young or middle aged)

Openshaw et al., J of Translat Med 2023

Initial Workup

- History of immunosuppressive drugs (corticoids..)
- Physical examination (complete skin, oral, and lymph node examinations, documentation of edema)
- Photography of the lesions
- HIV testing
- Chest x-ray if advanced cutaneous, oral, visceral, or nodal disease, or any pulmonary symptoms
- Chest CT with contrast and bronchoscopy if unexplained pulmonary symptoms or abnormalities on chest x-ray
- Abdomen/pelvis CT with contrast (or MRI) and endoscopy if GI symptoms or positive hemoccult

AIDS-related Kaposi sarcoma

STAGING CLASSIFICATION FOR KS[a]

	Good risk (all of the following)	Poor risk (any of the following)
Tumor, T	**T0: Confined to skin and/or lymph nodes and/or minimal oral disease (non-nodular KS confined to palate)**	**T1: Tumor-associated edema or ulceration Extensive oral KS Gastrointestinal KS KS in organs other than lymph nodes**
Immune system, I[1]	**I0: CD4+ T-cell count ≥150/μL**	**I1: CD4+ T-cell count <150/μL**
Systemic disease, S	**S0: No history of opportunistic infection or thrush No "B" symptoms[2] Karnofsky Performance Status ≥70**	**S1: History of opportunistic infection and/or thrush "B" symptoms present Karnofsky Performance Status <70 Other HIV-related illness (eg, neurologic disease, lymphoma)**

[1]I stage has less prognostic value than T or S stages in patients on ART therapy.
[2]"B" symptoms are unexplained fever, night sweats, >10% involuntary weight loss, or diarrhea persisting >2 weeks.

Staging for non AIDS-related

- **Limited cutaneous disease**: absence of established criteria (in the different trials: 5 index lesions or <5% body surface area involvement). Clinical judgement is required.

→ local therapies (topicals, cryotherapy, intralesional chemo..)

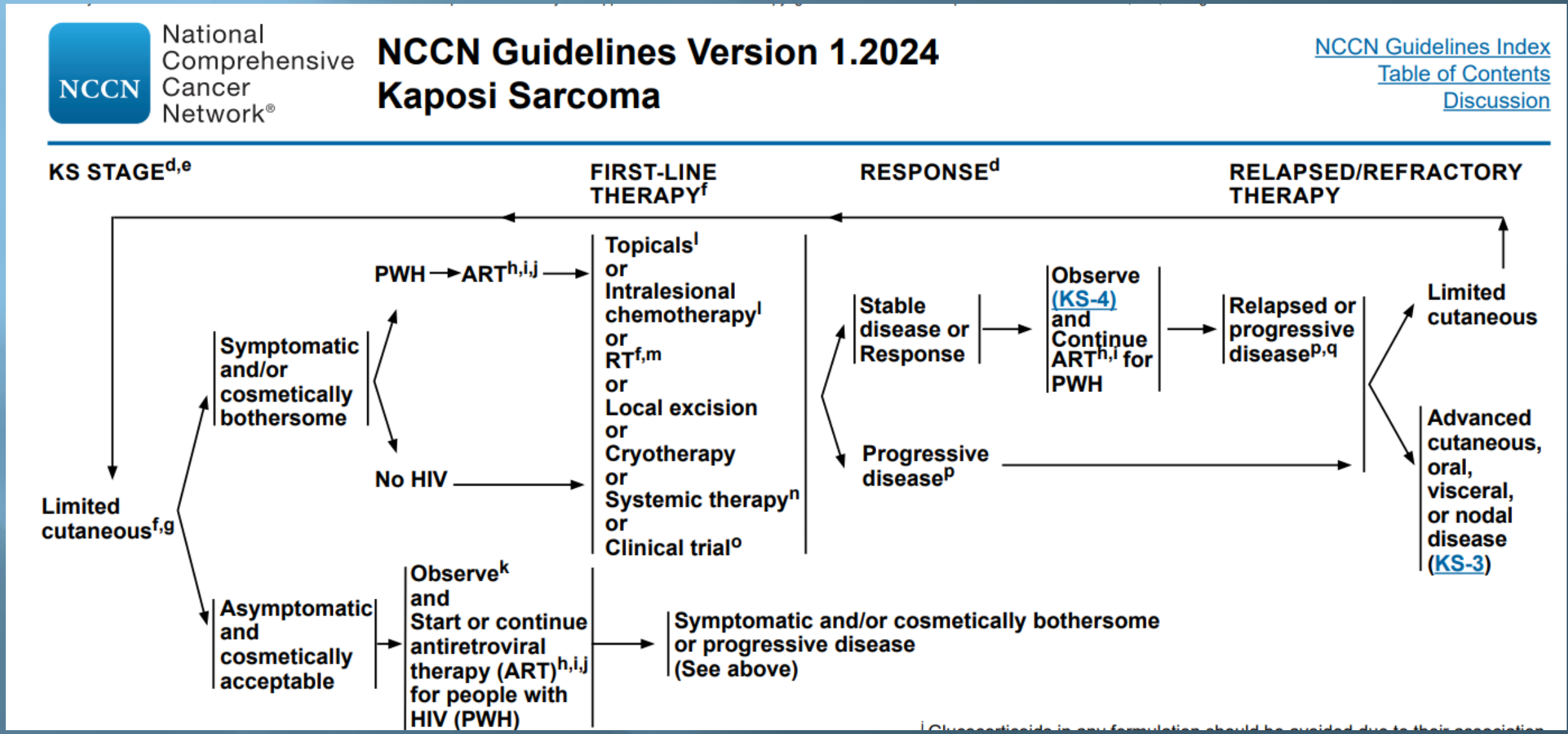
- **Advanced cutaneous, oral, visceral, or nodal disease**

→ systemic therapy

General principles during treatment

- Concomitant diseases: infections (HIV or opportunistic), lymphoma, multicentric Castleman disease
- HIV: viral load, T-cell subsets. Cooperation with infectiologist, drugs interactions!
- Risk for lymphedema (especially after RT), cellulitis and deep soft tissue infections
- Fever: Castleman d. or KSHV-associated inflammatory cytokine syndrome

Limited cutaneous Kaposi sarcoma



Advanced cutaneous or extra-cutaneous disease

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2024
Kaposi Sarcoma

NCCN Guidelines Index
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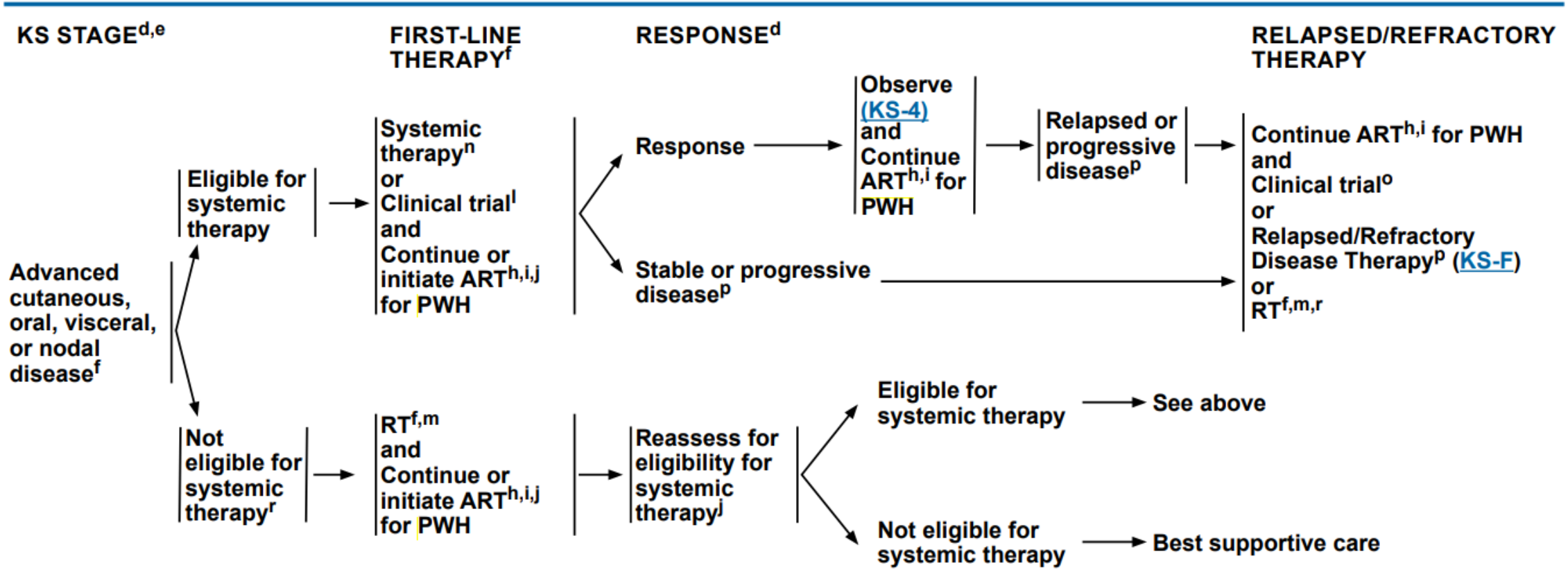
Discussion



RESPONSE DEFINITIONS FOR KS[a]

Complete response (CR)	**The absence of any detectable residual disease, including tumor-associated (local) edema, persisting for at least 4 weeks. Patients known to have had visceral disease should have restaging with appropriate endoscopic or radiographic procedures relevant to sites involved at baseline.**
Partial response (PR)	**No new mucocutaneous lesions, visceral sites of involvement, or the appearance or worsening of tumor-associated edema or effusions; AND** **▸ A 50% or greater decrease in the number of all previous existing lesions lasting for at least 4 weeks; OR** **▸ Complete flattening of at least 50% of all previously raised lesions (ie, 50% of all previously nodular or plaque-like lesions become macules); OR** **▸ A 50% decrease in the sum of the products of the largest perpendicular diameters of at least 5 measurable lesions.** **NOTE: When there is residual tumor-associated edema or effusion, but disease otherwise meets criteria for complete response, response should be classified as "partial."**
Stable disease (SD)	**Any response that does not meet the criteria for progressive diease or PR.**
Progressive disease (PD)	**An increase of ≥25% in the size of pre-existing lesions and/or the appearance of new lesions or sites of disease and/or a change in the character of the skin or oral lesions from macular to plaque-like or nodular of ≥25%. If new or increasing tumor-associated edema or effusion develop, disease is considered to be progressive.**

[a] Adapted from Krown SE, Metroka C, Wernz JC. Kaposi's sarcoma in the acquired immune deficiency syndrome: a proposal for uniform evaluation, response, and staging critera. AIDS Clinical Trials Group Oncology Committee. J Clin Oncol 1989;7:1201-1207.

Systemic therapies for Kaposi sarcoma

NCCN Guidelines Version 1.2024
Kaposi Sarcoma

treatments can be repeated if they were tolerated and the response was durable (≥3 months)

SYSTEMIC THERAPY[a]

First-line systemic therapy options

- Preferred regimens
  - Liposomal doxorubicin[c]
  - For transplant KS, sirolimus[d]
- Other recommended regimen
  - Paclitaxel

Relapsed/ refractory systemic therapy[b] options (advanced cutaneous, oral, visceral, or nodal disease)

If tolerated and durable response (≥3 months) to first-line systemic therapy → **Repeat of first-line systemic therapy or Alternate first-line systemic therapy** → **Progression**

If no response to first-line systemic therapy → **Alternate first-line systemic therapy[e]** → **Progression**

Systemic Therapy Dosing (KS-F 2 of 4)

- Subsequent systemic therapy options for relapsed/ refractory therapy[f]
  - Preferred regimen
    - ◊ Pomalidomide[g]
  - Other recommended regimens (in alphabetical order)
    - ◊ Bortezomib
    - ◊ Gemcitabine
    - ◊ Lenalidomide
    - ◊ Vinorelbine
  - Useful in certain circumstances (in alphabetical order)
    - ◊ Albumin-bound paclitaxel (if paclitaxel intolerant)
    - ◊ Etoposide
    - ◊ Imatinib
    - ◊ Ipilimumab + nivolumab (for classic KS)[h]
    - ◊ Pembrolizumab (for endemic and classic KS)[h]
    - ◊ Sirolimus[d] (for transplant KS)
    - ◊ Thalidomide (for patients with IRIS)

[a] References for regimens on KS-F (4 of 4).

[b] Consider repeating any prior systemic therapy that was tolerated and resulted in

[e] If both first-line options have already been given, the patient should proceed to

Liposomal Pegylated Doxorubicin

Clinical Trial > J Clin Oncol. 1998 Feb;16(2):683-91. doi: 10.1200/JCO.1998.16.2.683.

Randomized comparative trial of pegylated liposomal doxorubicin versus bleomycin and vincristine in the treatment of AIDS-related Kaposi's sarcoma. International Pegylated Liposomal Doxorubicin Study Group

S Stewart [1], H Jablonowski, F D Goebel, K Arasteh, M Spittle, A Rios, D Aboulafia, J Galleshaw, B J Dezube

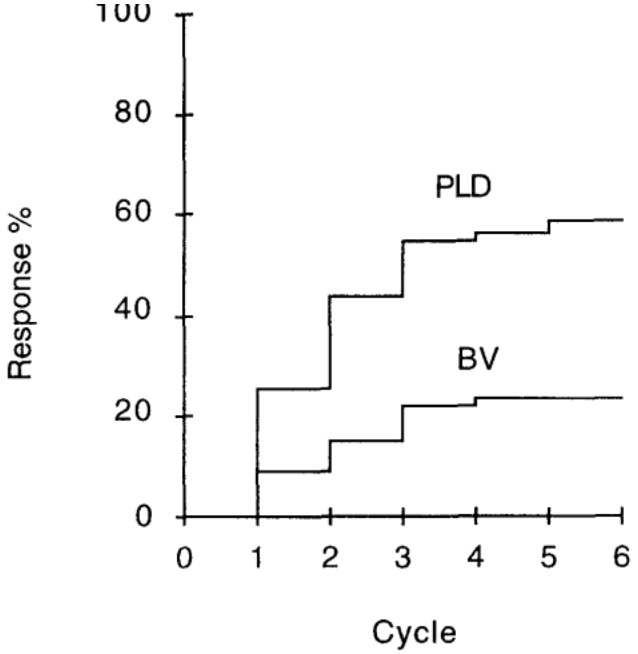


Fig 1. Cumulative response rate for BV and PLD.

Table 3. Comparison of the Response of Kapsosi's Sarcoma to PLD and BV

	PLD		BV		
	No.	%	No.	%	P
No. of patients	121		120		
Best response during treatment					
Clinical complete response*	7	5.8	1	0.8	< .001†
Partial response	64	52.9	27	22.5	
Stable disease	46	38.0	81	67.5	
Progression	0		5	4.2	
Not evaluated	4	3.3	6	5.0	
Overall response	71	58.7	28	23.3	< .001‡
Best response at the end of treatment					
Clinical complete response*	4	3.3	0		< .001†
Partial response	43	35.5	17	14.2	
Stable disease	39	32.2	54	45.0	
Progression	12	9.9	26	21.7	
Not evaluated	23	19.0	23	19.2	
Overall response	47	38.8	17	14.2	< .001‡
Time to response, days					
Mean, SE	48.6, 2.7		57.3, 3.5		
Median	44.0		64.0		< .025§
Duration of response					
Mean, SE	160.4, 18.3		156.7, 24.6		
Median	142.0		123.0		< .572§

*Clinical complete response denotes the clinical complete response criteria observed in this study and not the biopsy-proven complete response defined by the ACTG.

†Cochran-Mantel-Haenszel row mean scores test.

‡Fisher's exact test.

§Log-rank test.

Clinical Trial > J Clin Oncol. 1998 Jul;16(7):2445-51. doi: 10.1200/JCO.1998.16.7.2445.

Pegylated-liposomal doxorubicin versus doxorubicin, bleomycin, and vincristine in the treatment of AIDS-related Kaposi's sarcoma: results of a randomized phase III clinical trial

D W Northfelt [1], B J Dezube, J A Thommes, B J Miller, M A Fischl, A Friedman-Kien, L D Kaplan, C Du Mond, R D Mamelok, D H Henry

- N=258
- pegylated-liposomal doxorubicin (20 mg/m^2) or doxorubicin (20 mg/m^2), bleomycin (10 mg/m^2) and vincristine (1 mg) q2w for six cycles
- ORR: 50% v. 25% ($p < .001$)
- Less toxicity with pegylated liposomal doxorybicin

Pomalidomide

VOLUME 34 · NUMBER 34 · DECEMBER 1, 2016

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Pomalidomide for Symptomatic Kaposi's Sarcoma in People With and Without HIV Infection: A Phase I/II Study

Mark N. Polizzotto, Thomas S. Uldrick, Kathleen M. Wyvill, Karen Aleman, Cody J. Peer, Margaret Bevans, Irini Sereti, Frank Maldarelli, Denise Whitby, Vickie Marshall, Priscila H. Goncalves, Vikram Khetani, William D. Figg, Seth M. Steinberg, Jerome B. Zeldis, and Robert Yarchoan

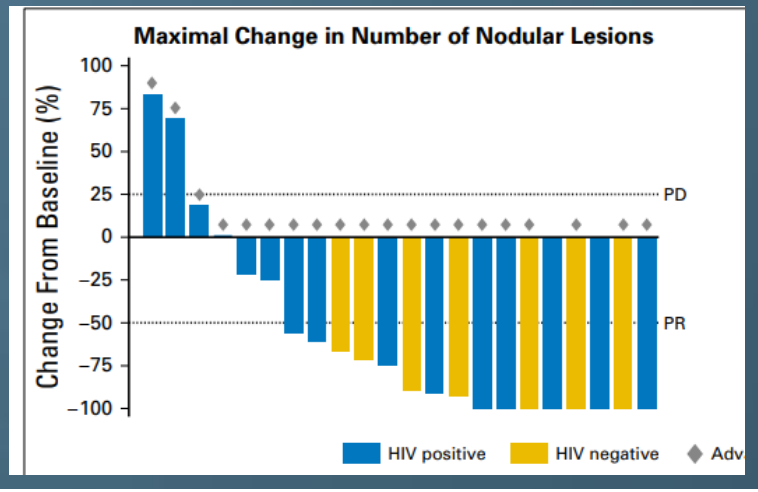


Table 2. Objective Responses and Timing of Responses

Group	Patients Enrolled (assessable)	Overall Response (CR + PR), No. (%)	CR, No. (%)	PR, No. (%)	SD, No. (%)	PD, No. (%)	Time to Response, Median (range), Weeks
All patients	22 (22)	16 (73)	4 (18)	12 (55)	3 (14)	3 (14)	4 (4–36)
HIV-positive patients	15 (15)	9 (60)	3 (20)	6 (40)	3 (20)	3 (20)*	8 (4–32)
HIV-negative patients	7 (7)	7 (100)	1 (14)	6 (86)	0	0	4 (4–36)

NOTE. Complete and partial responses are objective tumor responses by modified AIDS Clinical Trial Group Criteria for Kaposi's sarcoma; CR requires pathologic confirmation.

Abbreviations: CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease.

*Includes one patient who became nonadherent to antiretroviral therapy and protocol therapy.

- Grade 3-4 AE: neutropenia, infection, edema

Bortezomib in AIDS-associated KS

- AMC-063 pilot dose-escalation st.
- median plasma KSHV DNA copy number decreased compared with baseline only in patients with SD
- N=17, No DLT
- Diarrhea, fatigue, nausea

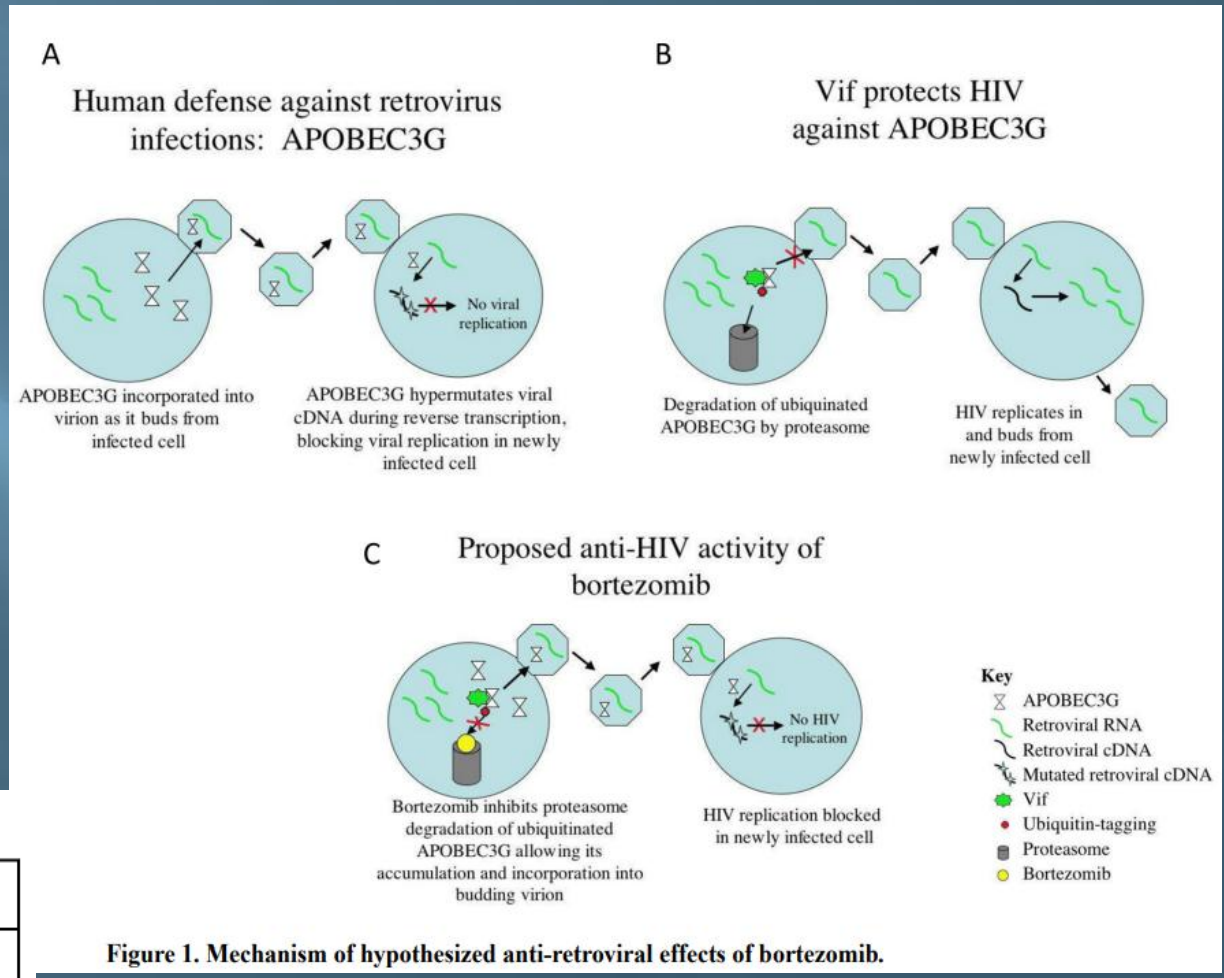


Figure 1. Mechanism of hypothesized anti-retroviral effects of bortezomib.

Best Response*

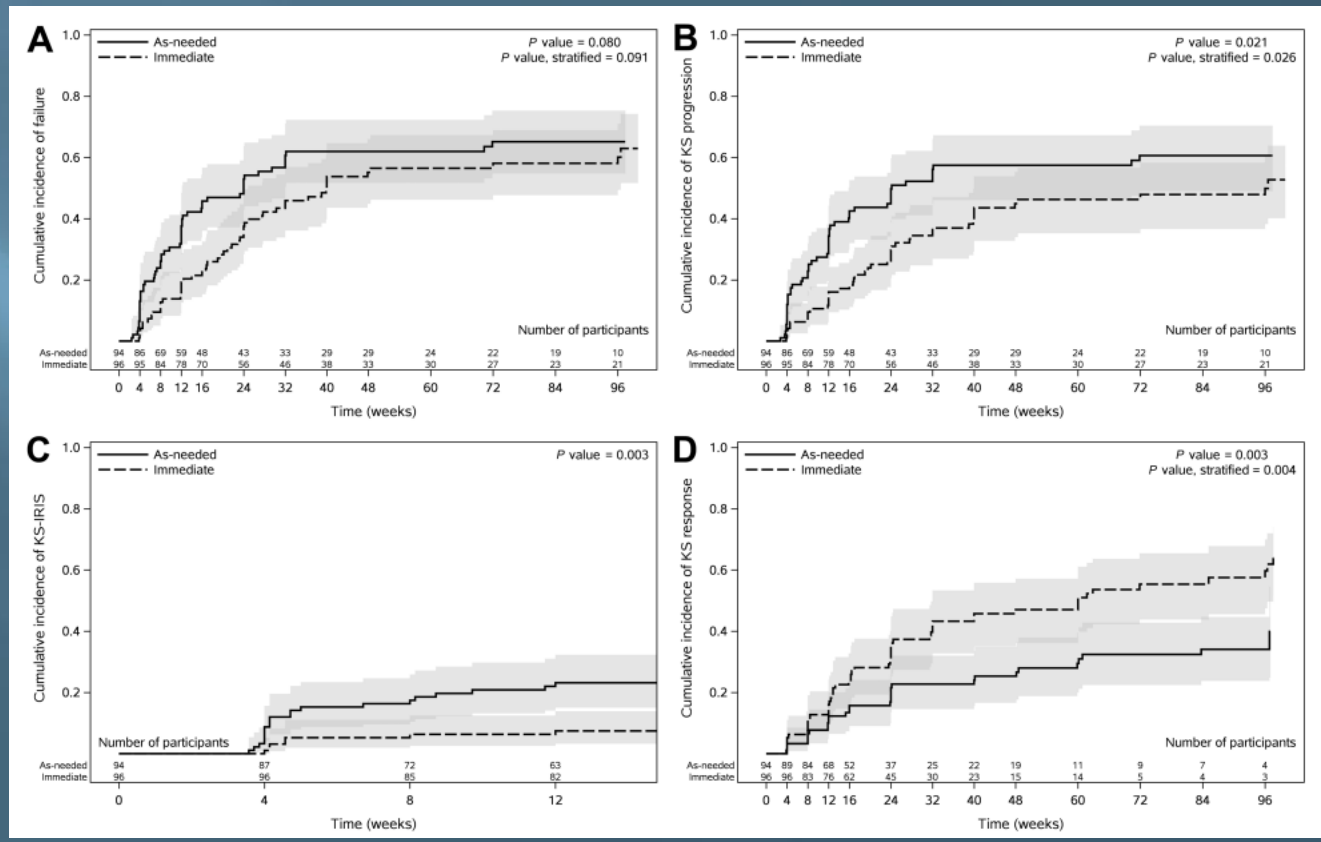
	Bortezomib 0.75 mg/m² N=3	Bortezomib 1.0 mg/m² N=3	Bortezomib1.3 mg/m² N=3	Bortezomib 1.6 mg/m² N=6	All Doses N=15
Partial Response, n (%)	1 (33)	3 (100)	0 (0)	5 (83)	9 (60)
Stable Disease, n (%)	2 (67)	0 (0)	3 (100)	1 (17)	6 (40)

*Note: Two patients (not shown above) were not evaluable for response as they did not complete 2 cycles of therapy. Intra-patient dose escalation to the next dose level was permitted in patients without DLTs after cycle 2. One patient in cohort 1 and 2 patients in cohort 2 dose-escalated to the next higher dose level for their final 2 cycles of protocol therapy.

Reid et al., Clin Cancer Res. 2020

Etoposide in AIDS-related KS

- Multiple phase II trials of patients with AIDS-related KS
- Clinical activity of oral etoposide, well tolerated (neutropenia)
- A5264/ AMC-067 R trial: N=190, mild-to-moderate AIDS-related KS, ART alone with etoposide as needed v. ART + immediate etoposide



Hosseinipour et al., Clin Inf Dis. 2018
Tas et al., J Eur Acad Dermatol Venereol 2013

Lenalidomide in AIDS-related KS

- oral anti-inflammatory, antiangiogenic, and immunomodulatory agent
- AMC070 Ph.I (N=15)/II (N=23) trial
- 4 dose levels, 21 days/28 → no MDT, 60% ORR
- AE: neutropenia, fatigue, leukopenia, and diarrhea
- ↑ T-regulatory cells, less inflammatory pattern of plasma cytokines

- Also: phase II ANRS 154 Lenakap trial (N=12)

Reid et al., Clin Cancer Res. 2022
Pourcher et al., AIDS Res Hum Retrov 2017

Nab-paclitaxel in classic KS

Annals of Oncology 27 (Supplement 4): iv107–iv125, 2016
doi:10.1093/annonc/mdw345.63

miscellanea

S63 **Treatment of Kaposi's Sarcoma (KS) with nab-paclitaxel**

S. Fortino, M. Santoro, E. Iuliano, M. Luci, A. Perricelli, A. Pomillo
Hospital N.Giannettasio, Rossano

Background: Kaposi's sarcoma (KS) is a potentially life-threatening multifocal neoplasm that may represent a difficult therapeutic challenge in disseminated stages. Liposomal anthracyclines, or combination chemotherapy are widely used to treat this kind of patients. The efficacy of taxanes (paclitaxel and docetaxel), as agents with antiangiogenic properties, has been described previously in the treatment of KS patients butthe length of the infusion, the need for pre-medication with steroids and toxicity caused by solvents - Cremophor EL (CrEL) and polysorbate 80 (Tween80) - can limit their utilization, especially in elderly patients.Nab-paclitaxel has efficacy comparable with solvent-based taxanes without need for steroid premedication which can make it easier to tolerate .At the moment there are no studies on its efficacy and safety in older KS patients.

Methods: After written informed consent was obtained a phase II trial was conducted with nab-paclitaxel in 6 patients with advanced-stage KS to assess its safety and antitumor activity. The mean age of patients was 74,8 years(range 71-83). Nab-paclitaxel was administered at a fixed dose of 100 mg intravenously over 30 minutes administered weekly on days 1, 8, and 15 of each 4-week cycle for 4 cycles. No premedication to prevent hypersensitivity r administration. Thereafter, if the patient ex treatment doses were given every two week progression, or unacceptable toxicity occur

Results: All patients improved dramatically (n = 2) or complete desinfiltration (n = 4) c observed with marked improvement of lym and thrombocytopenia were observed in th respectively. It was not observed any grade

Conclusions: Classic KS predominantly aff whom do not tolerate aggressive chemothe comorbidity and diminished cardiovascula has a good and rapid efficacy in our experi difficult to manage.

All 6 patients PR or CR

Meeting Abstract | 2016 ASCO Annual Meeting I

SARCOMA

Weekly nab-paclitaxel in elderly patients with classic Kaposi sarcoma.

Check for updates

Francesco Iuliano, Gian Luca Cervo, Eleonora Iuliano, Alessia Perricelli, Maria Luci, Angelo Pomillo, ...

Show More

Abstract Disclosures

Abstract

e22539

Imatinib

VOLUME 32 · NUMBER 5 · FEBRUARY 10 2014

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Phase II Trial of Imatinib in AIDS-Associated Kaposi's Sarcoma: AIDS Malignancy Consortium Protocol 042

Henry B. Koon, Susan E. Krown, Jeannette Y. Lee, Kord Honda, Suthee Rapisuwon, Zhenghe Wang, David Aboulafia, Erin G. Reid, Michelle A. Rudek, Bruce J. Dezube, and Ariela Noy

See accompanying editorial on page 373 and article on page 409

- Activating mutations in PDGF-R and c-kit were not found at baseline or at disease progression
- no correlation with response with changes in any of the candidate cytokines (IFN, Rantes, IL-6, and bFGF)

Table 3. Clinical Effect

Effect	No. of Patients	%
Best response		
Partial response	10	33.3
Stable disease	6	20.0
Progressive disease	7	23.3
Unevaluable*	7	23.3
Time to response, weeks	10	
Median	21.0	
Min-max	3.0-40.1	
Response duration, weeks	10	
Censored	7	70
Median	36	
95% CI for median	14.0–not reached	

Abbreviations: AE, adverse event; max, maximum; min, minimum.
*Three patients withdrew because of AEs (nausea and vomiting, n = 2; hives/angioedema, n = 1). Four patients were discontinued from study because of their inability to keep up with scheduled visits.

Sorafenib in AIDS-related Kaposi sarcoma

- VEGFR2-3, PDGFR and c-kit: implicated in KS pathogenesis and inhibited by sorafenib
- antiretroviral drug ritonavir (R) inhibits CYP3A4
- Phase I study of sorafenib in 10 pts
- 20% PR, clinical improvement in the remaining pts
- But adverse events, DLT…

Uldrick et al., ASCO Annual Meeting 2022

Immunotherapy in Kaposi sarcoma

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

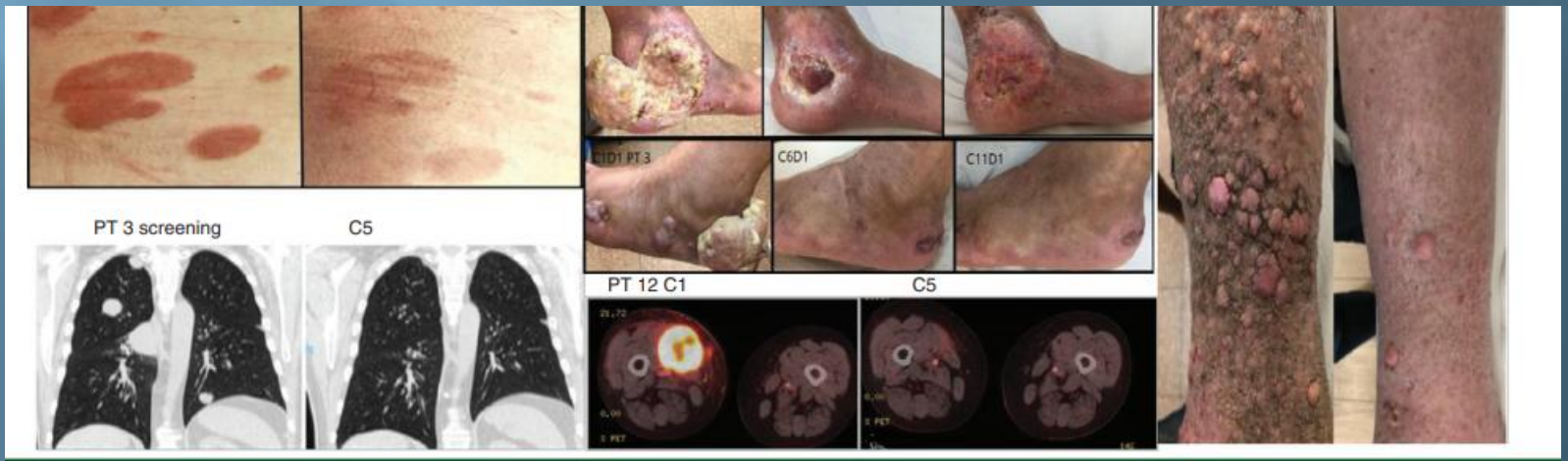
ANNALS OF ONCOLOGY driving innovation in oncology

ORIGINAL ARTICLE

Phase II single-arm study of nivolumab and ipilimumab (Nivo/Ipi) in previously treated classical Kaposi sarcoma (cKS)☆

A. Zer[1*], O. Icht[2], L. Yosef[2], D. Avram[2], O. Jacobi[2], E. Fenig[2], N. Kurman[2], I. Peretz[2], S. Shamai[3], O. Merimsky[3], E. Ben-Ami[4], R. Shapira Frommer[4], A. E. Schwarzbach[5], H. Bernstine[6], R. Weitzen[7], O. Vornicova[8], G. Bar-Sela[8], S. M. Stemmer[2] & M. Lotem[9]

- Nivolumab 240 mg D1,D15,D28 + Ipilimumab 1 mg/kg D1 q42d for ≤24m.
- ≥1 prior therapies
- N=17(HIV-negative)
- **Biomarker analysis**: low TMB, MSS, no HRD, no PDL1, low TILs, biallelic copy number loss of the FOX1A gene (most frequent alteration)
- mPFS not reached
- ORR = clinical 78%, radiological 87%



Zer et al., Ann Oncol 2022

Pembrolizumab in Kaposi sarcoma

PD-1 blockade with pembrolizumab in classic or endemic Kaposi's sarcoma: a multicentre, single-arm, phase 2 study

Julie Delyon, Lucie Biard, Marion Renaud, Matthieu Resche-Rigon, Jérôme Le Goff, Stéphane Dalle, Valentine Heidelberger, Laetitia Da Meda, Laurie Toullec, Guislaine Carcelain, Samia Mourah, Sophie Caillat-Zucman, Vincent Allain, Maxime Battistella, Céleste Lebbe

- 47% classic, 53% endemic (sub-Saharan Africa and the Caribbean)
- 200 mg IV q21d for 6 months
- Different lines of treatment
- Median T to progressin = 24 m.

	Best overall response (n=17)	Response at 3 months (n=17)	Response at 6 months (n=17)
ACTG criteria			
Complete response	2 (12%)	1 (6%)	2 (12%)
Partial response	10 (59%)	8 (47%)	10 (59%)
Stable disease	5 (29%)	7 (41%)	2 (12%)
Progression	0	1 (6%)	3 (18%)
PGA criteria			
Complete response (PGA 0)	4 (24%)	2 (12%)	4 (24%)
Partial response (PGA 1–3, improvement >50%)	8 (47%)	8 (47%)	8 (47%)
Stability (PGA 4–5)	5 (29%)	7 (41%)	2 (12%)
Progression (PGA 6)	0	0	3 (18%)

Data are n (%). Tumour response is presented as the best overall response obtained from baseline to end of study at 6 months, tumour response at 3 months, and tumour response at 6 months. ACTG=AIDS Clinical Trial Group. PGA=Physician Global Assessment.

Table 2: **Tumour responses during study treatment**

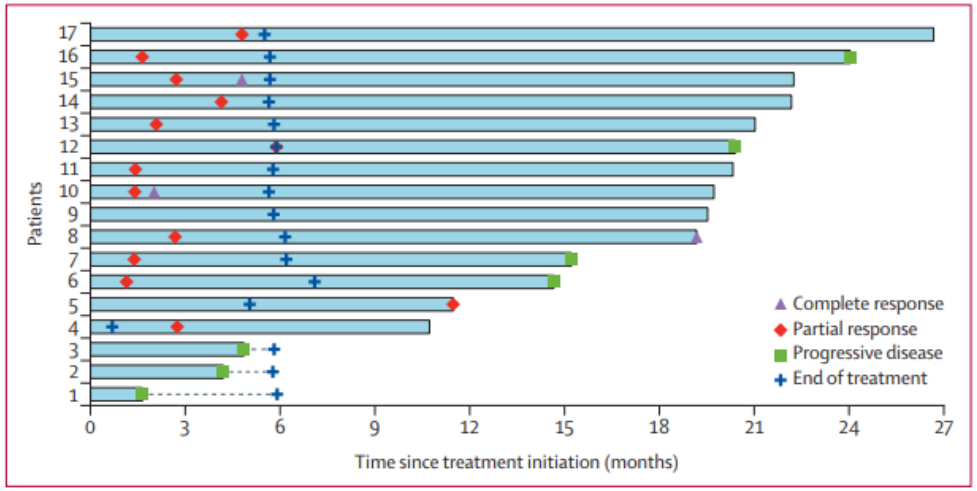


Figure 2: **Clinical efficacy of pembrolizumab**

SYSTEMIC THERAPY DOSING[a,i]

FIRST-LINE SYSTEMIC THERAPY DOSING

Preferred regimens

- Liposomal doxorubicin[c]
  - 20 mg/m² IV every 2 to 3 weeks
- Sirolimus (for transplant KS)
  - Loading dose 0.15 mg/kg PO followed by 0.04–0.06 mg/kg/day to maintain trough blood levels of 6–10 ng/mL or 2 mg PO daily (adjust to maintain trough levels of 6–10 ng/mL)
  - For PWH on ART, providers should consult with an ID pharmacist prior to dosing sirolimus

Other recommended regimen

- Paclitaxel
  - Premedication with dexamethasone may not be needed; if used, the dose should be minimized and tailored to patient needs.
  - Dose schedule options:
    - ◊ 60 mg/m² IV weekly
    - ◊ 100 mg/m² IV every 2 weeks
    - ◊ 100 mg/m² IV every 3 weeks
    - ◊ 135 mg/m² IV every 3 weeks

SUBSEQUENT SYSTEMIC THERAPY OPTIONS FOR RELAPSED/REFRACTORY THERAPY DOSING

Preferred regimen

- Pomalidomide[j]
  - 4 or 5 mg/day PO for 21 days of each 28-day cycle[k]

Other recommended regimens (in alphabetical order)

- Bortezomib
  - 1.6 mg/m² IV/SC on days 1, 8, and 15 of each 28-day cycle
- Gemcitabine
  - 1000 mg/m² IV every 2 weeks
  - Or 1000 mg/m² IV on days 1 and 8 every 21 days
- Lenalidomide[j]
  - 25 mg/day PO for 21 days of each 28-day cycle
- Vinorelbine
  - 30 mg/m² IV every 2 weeks

Useful in certain circumstances (in alphabetical order)

- Albumin-bound paclitaxel (if paclitaxel intolerant)
  - 100 mg IV on days 1, 8, and 15 of each 28-day cycle
- Etoposide
  - 50 mg/day PO for 7 days of each 14-day cycle. After 2 cycles, escalate dose to 100 mg/day PO for 7 days of each 14-day cycle in patients without PR or CR and no toxicity >Grade 2. Dose can be further escalated to 150 mg/day based on tolerance and response
- Imatinib
  - 400 mg/day PO
- Ipilimumab + nivolumab (for classic KS)[h]
  - Ipilimumab 1 mg/kg IV every 6 weeks and nivolumab 240 mg IV every 2 weeks
- Pembrolizumab (for endemic and classic KS)[h]
  - 200 mg IV every 3 weeks for up to 6 months
- Sirolimus (for transplant KS)
  - Loading dose 0.15 mg/kg PO followed by 0.04–0.06 mg/kg/day to maintain trough blood levels of 6–10 ng/mL or 2 mg PO daily (adjust to maintain trough levels of 6–10 ng/mL).
  - For PWH on ART, providers should consult with an ID pharmacist prior to dosing sirolimus
- Thalidomide (for patients with IRIS)[j]
  - 200 mg/day orally (starting dose, titrated to effect and tolerability)

Footnotes on KS-F 3 of 4

Open questions

- Optimal staging for cutaneous disease
- Initial workup: CT scan, endoscopy ?
- How many cycles of L1 therapy?
- If relapse >3 months, how many times to use L1 chemo (liposomal pegylated doxorubicin)?
- What is the best L2 regimen?
- ……

Conclusions

- Rare disease, usually not life-threatening
- Very limited prospective data concerning systemic therapies
- Most data on systemic therapies originate from small phase 1/2 studies, single-arm, with AIDS-related KS
- No comparative data
- PLD is the recommended L1 therapy
- Several new active drugs available during the last 2 years

SYSTEMIC THERAPY
REFERENCES

Bortezomib

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Etoposide

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Thank you very much for your attention