CORSO EDUCAZIONALE

GRUPPO LINFOMI IN PAZIENTI CON IMMUNODEFICIT

Milano, Starhotels Anderson
24 maggio 2024

Farmaci biologici e immunoterapia nei pazienti HIV positivi con linfoma: DLBCL e non solo..

Emanuele Ravano – ASST Niguarda

Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Takeda						x	
SERT						x	

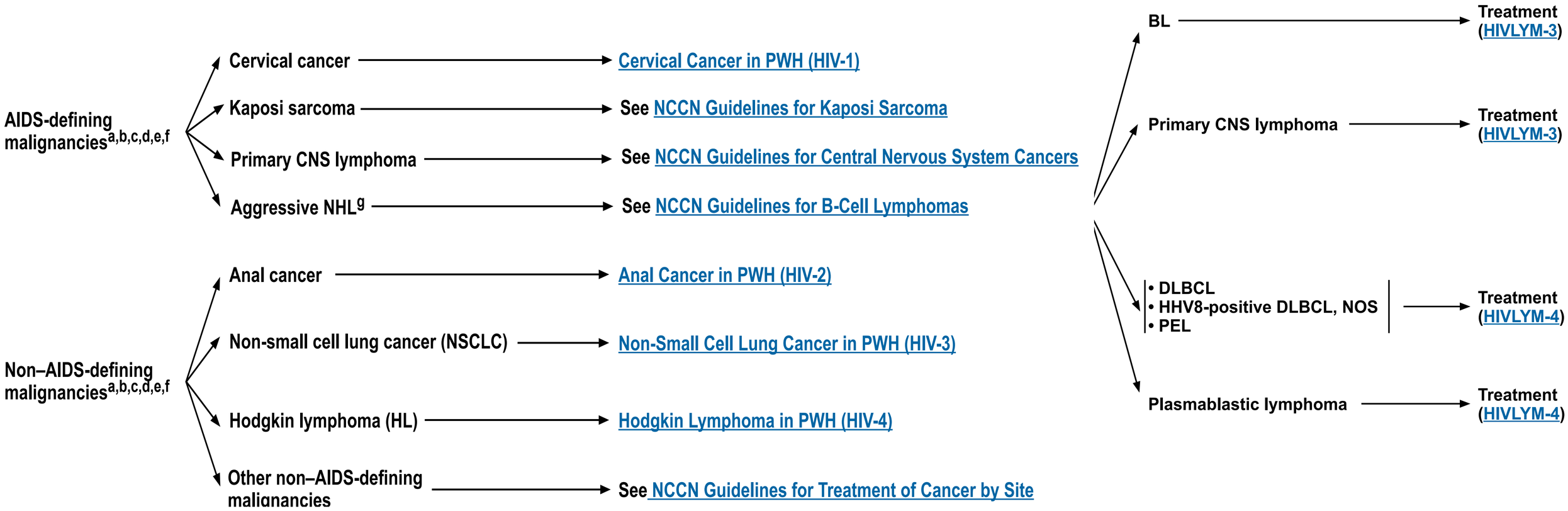

AIDS-defining malignancies[a,b,c,d,e,f]
Cervical cancer
Cervical Cancer in PWH (HIV-1)
Kaposi sarcoma
See NCCN Guidelines for Kaposi Sarcoma
Primary CNS lymphoma
See NCCN Guidelines for Central Nervous System Cancers
Aggressive NHL[g]
See NCCN Guidelines for B-Cell Lymphomas
Non–AIDS-defining malignancies[a,b,c,d,e,f]
Anal cancer
Anal Cancer in PWH (HIV-2)
Non-small cell lung cancer (NSCLC)
Non-Small Cell Lung Cancer in PWH (HIV-3)
Hodgkin lymphoma (HL)
Hodgkin Lymphoma in PWH (HIV-4)
Other non–AIDS-defining malignancies
See NCCN Guidelines for Treatment of Cancer by Site
BL
Treatment (HIVLYM-3)
Primary CNS lymphoma
Treatment (HIVLYM-3)
• DLBCL
• HHV8-positive DLBCL, NOS
• PEL
Treatment (HIVLYM-4)
Plasmablastic lymphoma
Treatment (HIVLYM-4)

Table 1. Distribution of lymphoma histotypes in individuals infected by HIV over 30 years in a European cohort (615 patients) compared with the CNICS USA cohort (476 patients)

Histotype	1986-1995; London (158 patients)	1996-2005; London (200 patients)	2006-2015; London (257 patients)	1996-2000; CNICS (132 patients)	2001-2005; CNICS (201 patients)	2006-2010; CNICS (143 patients)
BL	3%	10%	20% ↑	7.6%	10.9%	16.8% ↑
DLBCL	63%	59%	37% ↓	43.9%	45.8%	35.7% ↓
HL	4%	11%	26% ↑	15.2%	15.4%	19.6% ↑
PCNSL				14.4%	10.4%	9.8% ↓
PBL	0	2%	6% ↑			
PEL	2%	1%	5% ↑			
Other				18.9%	17.4%	18.2%

Since the introduction of cART, the incidence of NHL has decreased by 50% mainly because of decreased PCNSL and the immunoblastic histologic subtype of DLBCL, consistent with CD4 counts. In contrast, the burden of HIV-associated BL and HL has increased[16]: pre-cART decade (1986-1995); early cART decade (1996-2005); late cART decade (2006-2015). European cohort[26]; CNICS USA cohort.[25] ↑, increase of proportion in late cART decade; ↓, decrease of proportion in late cART decade.

Carbone et al Blood 17 FEBRUARY 2022 | VOLUME 139, NUMBER 7

VOLUME 26 · NUMBER 7 · MARCH 1 2008

JOURNAL OF CLINICAL ONCOLOGY | COMMENTS AND CONTROVERSIES

Including Persons With HIV Infection in Cancer Clinical Trials

Govind C. Persad, Richard F. Little, and Christine Grady, *Department of Bioethics, The Clinical Center, and The Clinical Investigations Branch, Cancer Therapy Evaluation Program, Division of Cancer Therapy and Diagnosis, National Cancer Institute, The National Institutes of Health, Bethesda, MD*

Cancer Care Disparities in People with HIV in the United States

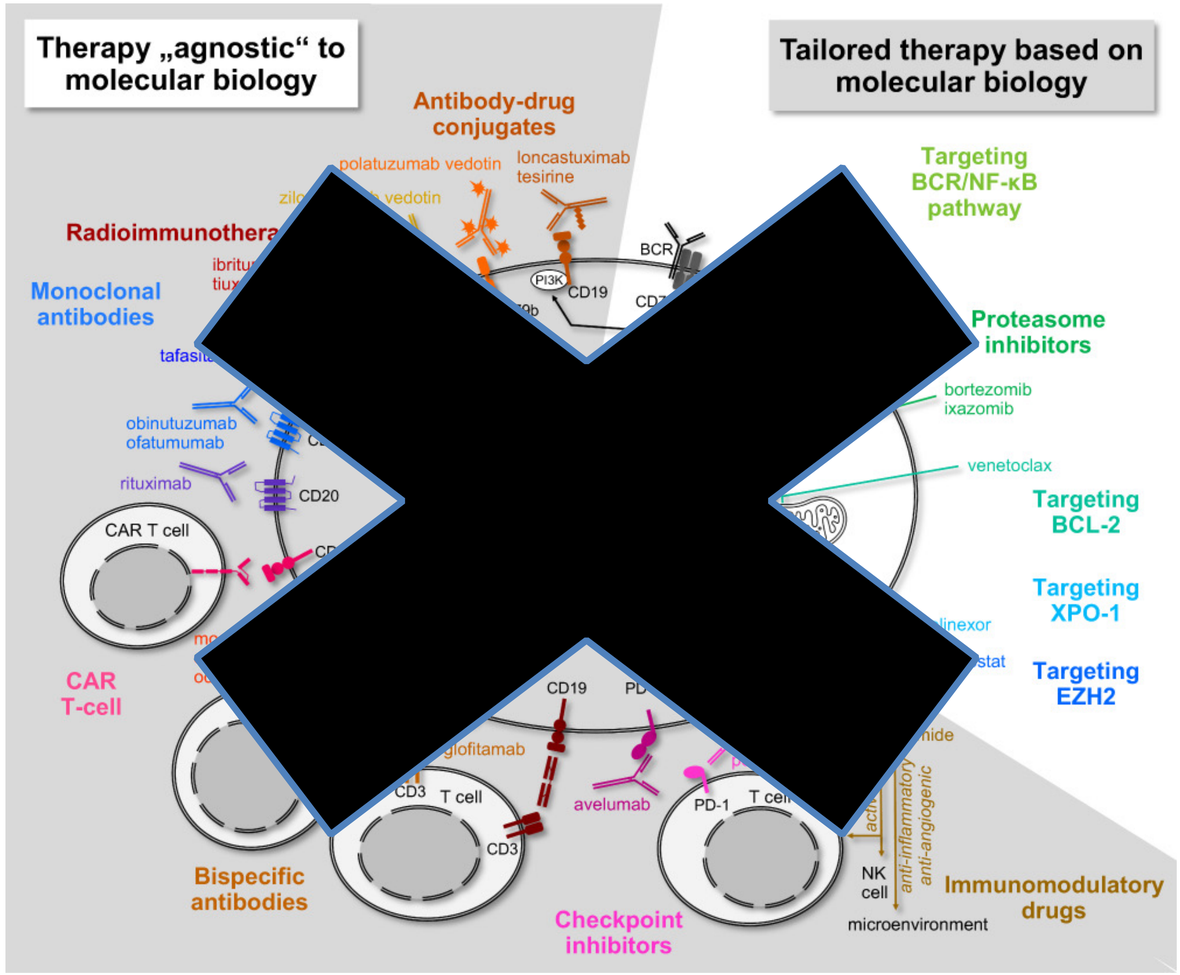
- Higher cancer-specific mortality in HIV-infected people compared with the general population for several cancer types

- Infected cancer patients were less likely to receive cancer treatment compared with uninfected cancer patients for several cancer types (OR 1.39 for diffuse large B-cell lymphoma)

Persad et al. JCO. 2008 March; 26(7).

Anna Coghill, and Gita Suneja, Curr Opin HIV AIDS . 2017 January ; 12(1): 63–68.

New drugs in DLBCL



Criteri di inclusione Zuma: History of human immunodeficiency virus infection or active acute or chronic hepatitis B or hepatitis C infection. Patients with a history of hepatitis infection must have cleared their infection as determined by standard serological and genetic testing per current Infectious Diseases Society of America guidelines or applicable country guidelines

In the ZUMA-1, ZUMA-5, and ZUMA-7 studies, patients with a known history of HIV infection were ineligible for inclusion.[5-7] There are no clinical trial data available on the use of axi-cel in patients with HIV infection.

Studio fase 1/2 Glofitamab: Negative serologic or polymerase chain reaction test results for acute or chronic hepatitis B virus infection, hepatitis C virus, and human immunodeficiency virus

Studio di fase ½ Epcoritamab: Known human immunodeficiency virus (HIV) infection

Studio L-MIND: History of HIV

Thieblemont C. et al Epcoritamab, a Novel, Subcutaneous CD3xCD20 Bispecific T-Cell–Engaging Antibody, in Relapsed or Refractory Large B-Cell Lymphoma: Dose Expansion in a Phase I/II Trial JCOVolume 41, Number 12

M J. Dickinson et al. Glofitamab for Relapsed or Refractory Diffuse Large B-Cell Lymphoma n engl j med 387;24 December 15, 2022

Locke FL, Miklos DB, Jacobson CA, et al. Axicabtagene Ciloleucel as Second-Line Therapy for Large B-Cell Lymphoma. *N Engl J Med*. 2022;386(7):640-654.

Neelapu SS, Locke FL, Bartlett NL, et al. Axicabtagene ciloleucel CAR T-cell therapy in refractory large B-cell lymphoma. *N Engl J Med*. 2017.

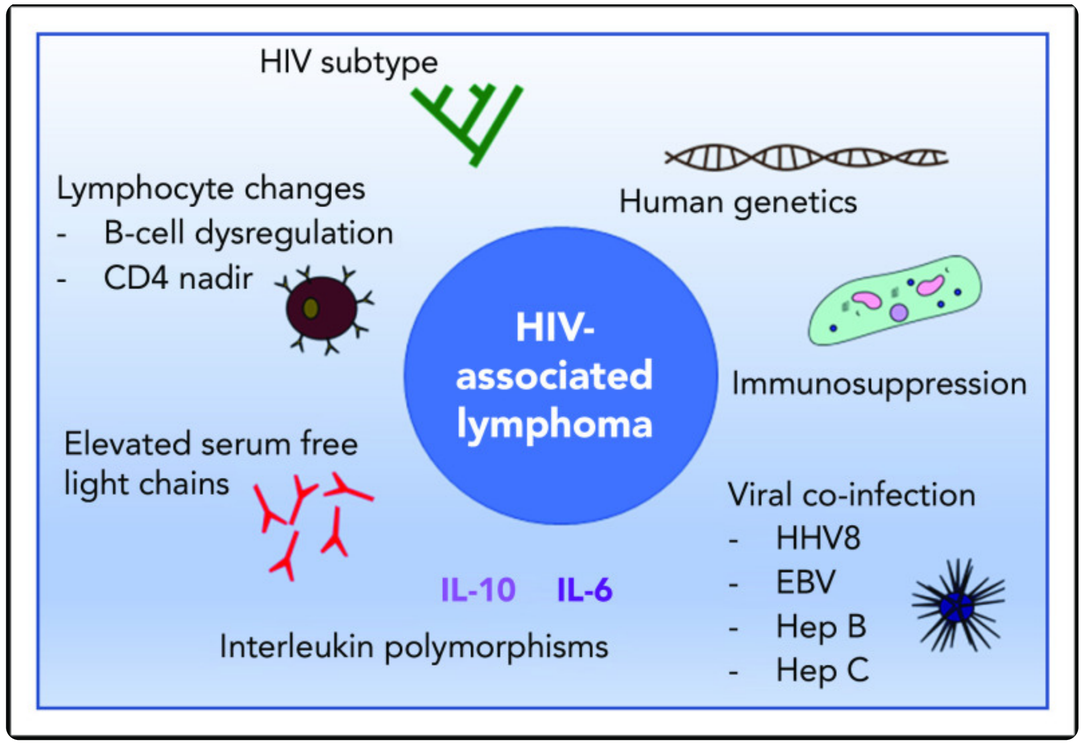
Salles et el. Tafasitamab plus lenalidomide in relapsed or refractory diffuse large B-cell lymphoma (L-MIND): a multicentre, prospective, single-arm.

Yescarta
Popolazioni speciali : *Pazienti con infezione da virus dell'immunodeficienza umana (HIV), virus dell'epatite B (HBV) e virus dell'epatite C (HCV)*
L'esperienza clinica in pazienti con infezione attiva da HIV, HBV o HCV è limitata.

Kymriah
Popolazioni speciali: pazienti sieropositivi per il virus dell'epatite B (HBV), il virus dell'epatite C (HCV) o il virus dell'immunodeficienza umana (HIV). Non vi è esperienza in merito alla produzione di Kymriah per i pazienti con un test positivo per HBV, HCV o HIV attivi. Pertanto il materiale di leucoaferesi raccolto da questi pazienti non sarà accettato per a produzione di Kymriah.

Tecartus
Pazienti sieropositivi per il virus dell'epatite B (HBV), il virus dell'epatite C (HCV) o il virus dell'immunodeficienza umana (HIV)
Non esiste alcuna esperienza sulla produzione di Tecartus per i pazienti con infezione attiva da HBV, con infezione attiva da HCV o positivi al test per l'HIV. Pertanto, il rapporto beneficio/rischio in questa popolazione non è stato ancora stabilito.

Lymphoma in PLWH



- More frequent stage III and IV
- Rapidly growing masses and B symptoms
- Extranodal involvement includes the bone marrow in 25% to 40%, the gastrointestinal tract in 26%, and the CNS in 17% to 32% of cases
- Is more commonly associated with the *MYC* and *BCL6* translocations and with proliferation

Ariela Noy. Optimizing treatment of HIV-associated lymphoma Blood. 2019 Oct 24; 134(17): 1385–1394.

Pagani C. MYC rearrangements in HIV-associated large B-cell lymphomas: EUROMYC, a European retrospective study

Kaplan LD, Ai W. HIV-related lymphomas: clinical manifestations and diagnosis.

ORIGINAL ARTICLE

Brentuximab Vedotin with Chemotherapy for Stage III or IV Hodgkin's Lymphoma

J.M. Connors, W. Jurczak, D.J. Straus, S.M. Ansell, W.S. Kim, A. Gallamini, A. Younes, S. Alekseev, Á. Illés, M. Picardi, E. Lech-Maranda, Y. Oki, T. Feldman, P. Smolewski, K.J. Savage, N.L. Bartlett, J. Walewski, R. Chen, R. Ramchandren, P.L. Zinzani, D. Cunningham, A. Rosta, N.C. Josephson, E. Song, J. Sachs, R. Liu, H.A. Jolin, D. Huebner, and J. Radford, for the ECHELON-1 Study Group*

ABSTRACT

BACKGROUND

Brentuximab vedotin is an anti-CD30 antibody–drug conjugate that has been approved for relapsed and refractory Hodgkin's lymphoma.

METHODS

We conducted an open-label, multicenter, randomized phase 3 trial involving patients with previously untreated stage III or IV classic Hodgkin's lymphoma, in which 664 were assigned to receive brentuximab vedotin, doxorubicin, vinblastine, and dacarbazine (A+AVD) and 670 w
dacarbazine (ABVD). Th
time to progression, dea
therapy) as adjudicated
point was overall survival.

Gennaio 2018

RESULTS

At a median follow-up of 24.6 months, 2-year modified progression-free survival rates in the A+AVD and ABVD groups were 82.1% (95% confidence interval [CI], 78.8 to 85.0) and 77.2% (95% CI, 73.7 to 80.4), respectively, a difference of 4.9 percentage points (hazard ratio for an event of progression, death, or modified progression, 0.77; 95% CI, 0.60 to 0.98; P=0.04). There were 28 deaths with A+AVD and 39 with ABVD (hazard ratio for interim overall survival, 0.73 [95% CI, 0.45 to 1.18]; P=0.20). All secondary efficacy end points trended in favor of A+AVD. Neutropenia occurred in 58% of the patients receiving A+AVD and in 45% of those receiving ABVD; in the A+AVD group, the rate of febrile neutropenia was lower among the 83 patients who received primary prophylaxis with granulocyte colony-stimulating factor than among those who did not (11% vs. 21%). Peripheral neuropathy occurred in 67% of patients in the A+AVD group and in 43% of patients in the ABVD group; 67% of patients in the A+AVD group who had peripheral neuropathy had resolution or improvement at the last follow-up visit. Pulmonary toxicity of grade 3 or higher was reported in less than 1% of patients receiving A+AVD and in 3% of those receiving ABVD. Among the deaths that occurred during treatment, 7 of 9 in the A+AVD group were associated with neutropenia and 11 of 13 in the ABVD group were associated with pulmonary-related toxicity.

CONCLUSIONS

A+AVD had superior efficacy to ABVD in the treatment of patients with advanced-stage Hodgkin's lymphoma, with a 4.9 percentage-point lower combined risk of progression, death, or noncomplete response and use of subsequent anticancer therapy at 2 years. (Funded by Millennium Pharmaceuticals and Seattle Genetics; ECHELON-1 ClinicalTrials.gov number, NCT01712490; EudraCT number, 2011-005450-60.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Connors at the Department of Medical Oncology, British Columbia Cancer Agency, Vancouver, BC V5Z 4E6, Canada, or at jconnors@bccancer.bc.ca.

*All ECHELON-1 investigators are listed in the Supplementary Appendix, available at NEJM.org.

This article was published on December 10, 2017, and last updated on January 26, 2018, at NEJM.org.

N Engl J Med 2018;378:331-44.
DOI: 10.1056/NEJMoa1708984

Brentuximab vedotin with AVD for stage II–IV HIV-related Hodgkin lymphoma (AMC 085): phase 2 results from an open-label, single arm, multicentre phase 1/2 trial

*Paul G Rubinstein, Page C Moore, Milan Bimali, Jeanette Y Lee, Michelle A Rudek, Amy Chadburn, Lee Ratner, David H Henry, Ethel Cesarman, Camille E DeMarco, Dominique Costagliola, Yassine Taoufik, Juan Carlos Ramos, Elad Sharon, Erin G Reid, Richard F Ambinder, Ronald Mitsuyasu, Nicolas Mounier, Caroline Besson, Ariela Noy for the AIDS Malignancy Consortium and the Lymphoma Study Association**

Summary

Background Brentuximab vedotin in combination with doxorubicin, vinblastine, and dacarbazine (AVD) is approved in the upfront setting for advanced stage classical Hodgkin lymphoma (cHL). People living with HIV have been excluded from these studies. We aimed to understand the activity and safety of brentuximab vedotin–AVD in people living with HIV diagnosed with Hodgkin lymphoma, while focusing on HIV disease parameters and antiretroviral therapy (ART) interactions.

Methods We present the phase 2 portion of a multicentre phase 1/2 study. Eligible patients were 18 years or older, had untreated stage II–IV HIV-associated cHL (HIV-cHL), a Karnofsky performance status of more than 30%, a $CD4^+$ T-cell count of 50 cells per µL or more, were required to take ART, and were not on strong CYP3A4 or P-glycoprotein inhibitors. Patients were treated intravenously with 1·2 mg/kg of brentuximab vedotin (recommended phase 2 dose) with standard doses of AVD for six cycles on days 1 and 15 of a 28-day cycle. The primary endpoint of the phase 2 portion was 2-year progression-free survival (PFS), assessed in all eligible participants who began treatment. Accrual has been completed. This trial is registered at ClinicalTrials.gov, NCT017711

Agosto 2024

Findings Be
with a median follow up of 29 months (
) with stage II unfavourable HIV-cHL. 3
sponse. The 2-year PFS was 87% (95% CI 71–94) and the overall survival was 92% (78–97). The most common grade 3 or worse adverse events were peripheral sensory neuropathy (four [10%] of 41 patients), neutropenia (18 [44%]), and febrile neutropenia (five [12%]). One treatment-related death was reported, due to infection.

Interpretation Brentuximab vedotin–AVD was highly active and had a tolerable adverse event rate in HIV-cHL and is an important therapeutic option for people with HIV-cHL. The complete reponse rate is encouraging and is possibly related to a unique aspect of HIV-cHL biology. Upcoming 5-year data will evaluate the sustainability of the outcomes obtained.

Funding National Institutes of Health and National Cancer Institute.

Lancet Haematol 2023; 10: e624–32

See Comment page e563

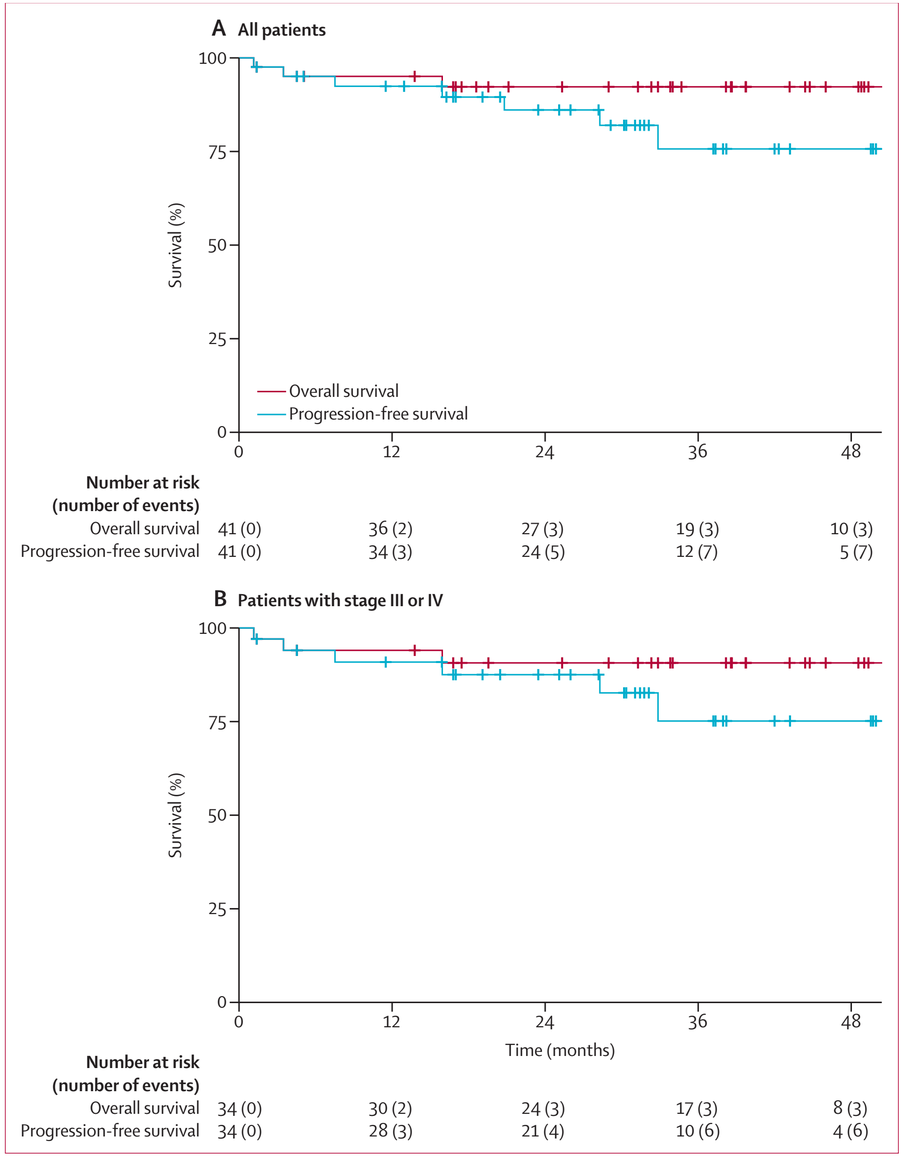
*Members of the AIDS Malignancy Consortium and the Lymphoma Study Association are listed in the appendix

John H Stroger Jr Hospital of Cook County (Cook County Hospital), Section of Hematology/Oncology, Department of Medicine, Chicago, IL, USA (P G Rubinstein MD); **Ruth M Rothstein CORE Center, Chicago, IL, USA** (P G Rubinstein, C E DeMarco MPH); **University of Illinois, Chicago, Section of Hematology/Oncology, Department of Medicine, Chicago, IL, USA** (P G Rubinstein); **University of Arkansas for Medical Sciences, Little Rock, AR, USA** (P C Moore PhD, M Bimali PhD, J Y Lee PhD); **Johns Hopkins University School of Medicine, Baltimore, MD, USA** (M A Rudek PhD, R F Ambinder MD); **Weill Cornell Medical College, Cornell University, New York, NY, USA** (A Chadburn MD, E Cesarman MD, A Noy MD); **Washington University School of Medicine, St Louis, MO, USA** (L Ratner MD); **Abramson Cancer Center, Pennsylvania Hospital, Philadelphia, PA, USA** (D H Henry MD); **INSERM, Institut Pierre Louis d'épidémiologie et de Santé Publique, UPMC Univ Paris 06, Sorbonne Universités, Paris, France** (D Costagliola PhD); **Faculte´ de médecine Paris Sud, Universite´ Paris Sud, Le Kremlin-Bicêtre, France** (Y Taoufik PhD); **Service d'imunologie biologique, Hôpitaux Paris Sud, AP-HP, Le Kremlin-Bicêtre, France** (Y Taoufik); **University of Miami School of Medicine,Sylvester Comprehensive Cancer Center,**

Introduction

People living with HIV have a 6–15-times increased risk of being diagnosed with classical Hodgkin lymphoma, more so than the general population.[1,2] HIV-associated classical Hodgkin lymphoma (HIV-cHL) remains one of the most common non-AIDS defining malignancies, most often presenting with $CD4^+$ T-cell counts above 200 cells per µL, advanced stage, and higher international prognostic index scores than the non-HIV population.[3,4] Outcomes have improved since the introduction of combined antiretroviral therapy (ART) in the mid 1990s, elevating the overall survival using doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) from 48% at 2 years to 75–85% at 5 years for advanced stage disease, similar to patients with Hodgkin lymphoma who do not have HIV.[5–8] Although outcomes have improved with the addition of ART to HIV-cHL therapy, advanced stage disease continues to have a rate of relapse of 30%, necessitating the need for new therapies.[9]

Brentuximab vedotin is an anti-CD30 antibody drug conjugate coupled to monomethyl auristatin E. It is approved for two indications in relapsed Hodgkin lymphoma, as a single agent and in consolidation post autologous haematopoietic stem-cell transplantation. In the frontline setting it has received two additional indications: first, in the paediatric population in combination with AVEPC (doxorubicin, vincristine, etoposide, prednisone, and cyclophosphamide) for high risk cHL and, second, in adults with advanced stage cHL, in combination with doxorubicin, bleomycin, and



- AMC 085 is an open-label phase 2 trial for the upfront treatment of stage II–IV cHL with brentuximab vedotin– AVD

- ORR 100%, 92% OS, and an 87% PFS with a median follow-up of 29 months for all patients.

- Results compare favourably with the brentuximab vedotin–AVD group of the ECHELON-1 study, which had a complete remission rate of 73%.

- Comparisons with the **ECHELON-1** study and AMC-085, are made with the caveat that the former study was a **large phase 3 study.**

- PET/CT scans can be used effectively in patients with HIV-cHL, as all patients who completed therapy had negative scans. Whether chemotherapy escalation based on a **positive cycle 2 PET/CT** could be indicated is **unclear.**

- **Peripheral neuropathy** occurred 20% more often compared with the non-HIV population;

- Infectious complications, hospitalisations, deaths during therapy, febrile neutropenia, **were all similar**.

Rubinestein et al. Lancet Haematol 2023; 10: e624–32

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2024
Cancer in People with HIV

NCCN Guidelines Index
Table of Contents
Discussion

INTRODUCTION

- People with human immunodeficiency virus (HIV) (PWH) and AIDS have a higher incidence of many common cancers compared with the general population. AIDS-defining cancers include aggressive non-Hodgkin lymphoma (NHL), Kaposi sarcoma, and invasive cervical cancer. Dramatically improved treatment of HIV over the last two decades has led to a decrease in the risk of AIDS development, an increase in immune function and survival, and a decline in AIDS-defining cancers in this population; however, the incidence of non-AIDS defining cancers has increased because of longer life expectancies due to antiretroviral therapy (ART), accelerated aging as a consequence of HIV, a higher likelihood of co-infection with oncogenic infections, and a higher prevalence of carcinogen exposure.
- Cancer in PWH should be co-managed by an oncologist, and HIV specialist, and PWH should receive cancer treatment as per standard guidelines. Although modifications to ART may be needed, HIV therapy should be continued during cancer therapy. Multidisciplinary decision-making, involving HIV specialists, is critical.

AIDS-defining malignancies[a,b,c,d,e,f]

- Cervical cancer → Cervical Cancer in PWH (HIV-1)
- Kaposi sarcoma → See NCCN Guidelines for Kaposi Sarcoma
- Primary CNS lymphoma → See NCCN Guidelines for Central Nervous System Cancers
- Aggressive NHL[g] → See NCCN Guidelines for B-Cell Lymphomas

Non–AIDS-defining malignancies[a,b,c,d,e,f]

- Anal cancer → Anal Cancer in PWH (HIV-2)
- Non-small cell lung cancer (NSCLC) → Non-Small Cell Lung Cancer in PWH (HIV-3)
- Hodgkin lymphoma (HL) → Hodgkin Lymphoma in PWH (HIV-4)
- Other non–AIDS-defining malignancies → See NCCN Guidelines for Treatment of Cancer by Site

[a] Principles of HIV Management While Undergoing Cancer Therapy (HIV-A).
[b] Principles of Systemic Therapy and Drug-Drug Interactions (HIV-B).
[c] Principles of Radiation Therapy (HIV-C).
[d] Principles of Surgery (HIV-D).
[e] Principles of Supportive Care (HIV-E).
[f] Principles of Imaging (HIV-F).
[g] Burkitt lymphoma; diffuse large B-cell lymphoma (DLBCL); Kaposi sarcoma associated herpesvirus (KSHV)-positive DLBCL, not otherwise specified (NOS); primary effusion lymphoma; and plasmablastic lymphoma.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2024
HIV-Related B-Cell Lymphomas

NCCN Guidelines Index
Table of Contents
Discussion

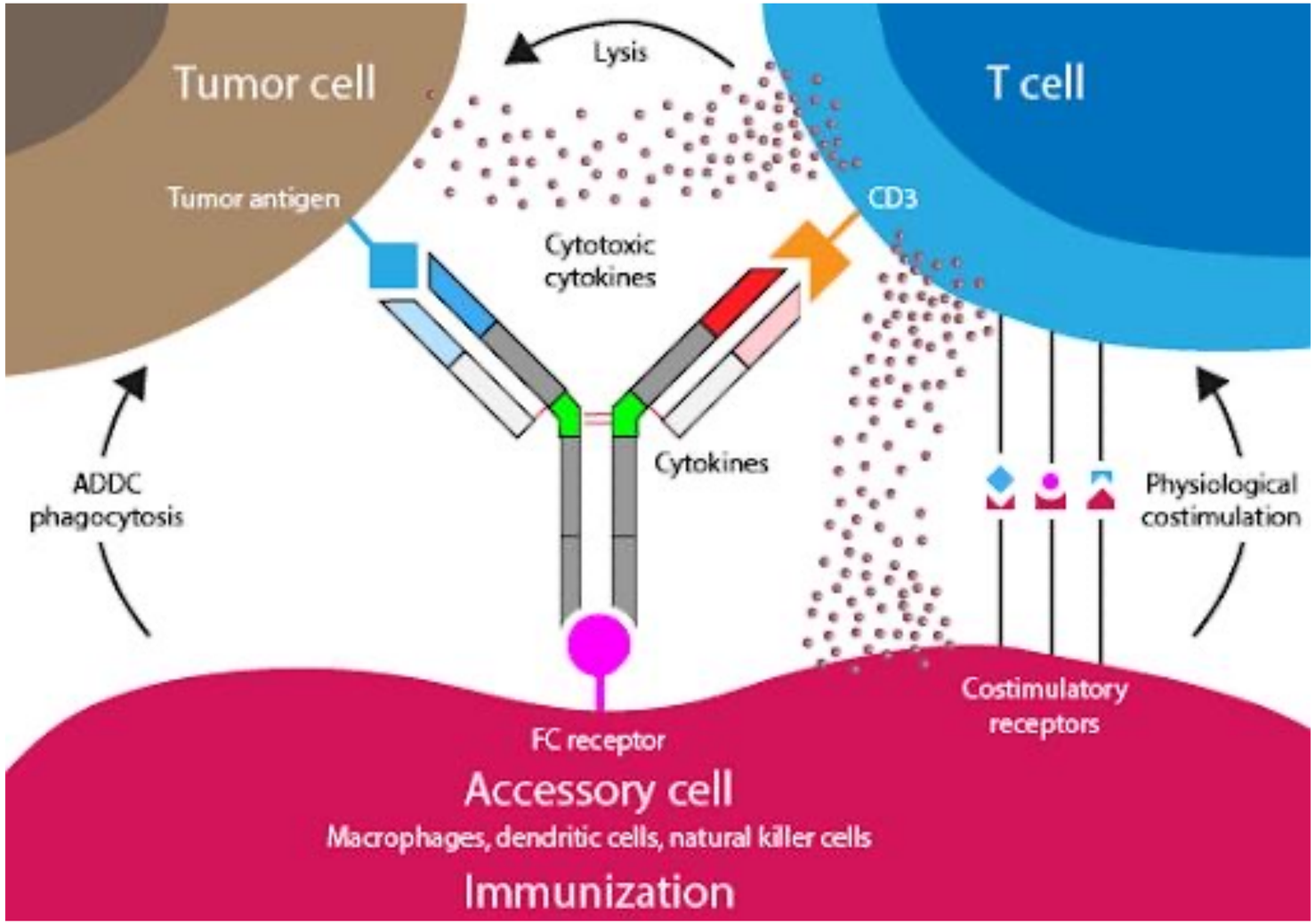
WORKUP

ESSENTIAL
- Physical exam: attention to node-bearing areas, including Waldeyer's ring, and to size of liver and spleen
- Performance status
- B symptoms
- CBC with differential
- LDH
- Comprehensive metabolic panel
- Uric acid, phosphate
- PET/CT scan (preferred) or C/A/P CT with contrast of diagnostic quality
- CD4 count
- Lumbar puncture, except for PEL
- HIV viral load
- Hepatitis B testing[b]
- Hepatitis C testing[c]
- Echocardiogram or MUGA scan if anthracycline or anthracenedione-based regimen is indicated
- Pregnancy testing in patients of childbearing age (if chemotherapy or RT planned)

USEFUL IN SELECTED CASES:
- Upper GI/barium enema/endoscopy
- Adequate bone marrow biopsy (>1.6 cm) ± aspirate; bone marrow biopsy is not necessary if PET/CT scan demonstrates bone disease
- Neck CT with contrast
- Plain bone radiographs and bone scan
- Brain MRI with and without contrast, or head CT with contrast
- Beta-2-microglobulin
- EBV PCR
- Quantitative Ig
- Discuss fertility preservation[d]

- BL → Treatment (HIVLYM-3)
- Primary CNS lymphoma → Treatment (HIVLYM-3)
- DLBCL
  - HHV8-positive DLBCL, NOS
  - PEL
  → Treatment (HIVLYM-4)
- Plasmablastic lymphoma → Treatment (HIVLYM-4)

Bispecific Antibodies



Glofitamab

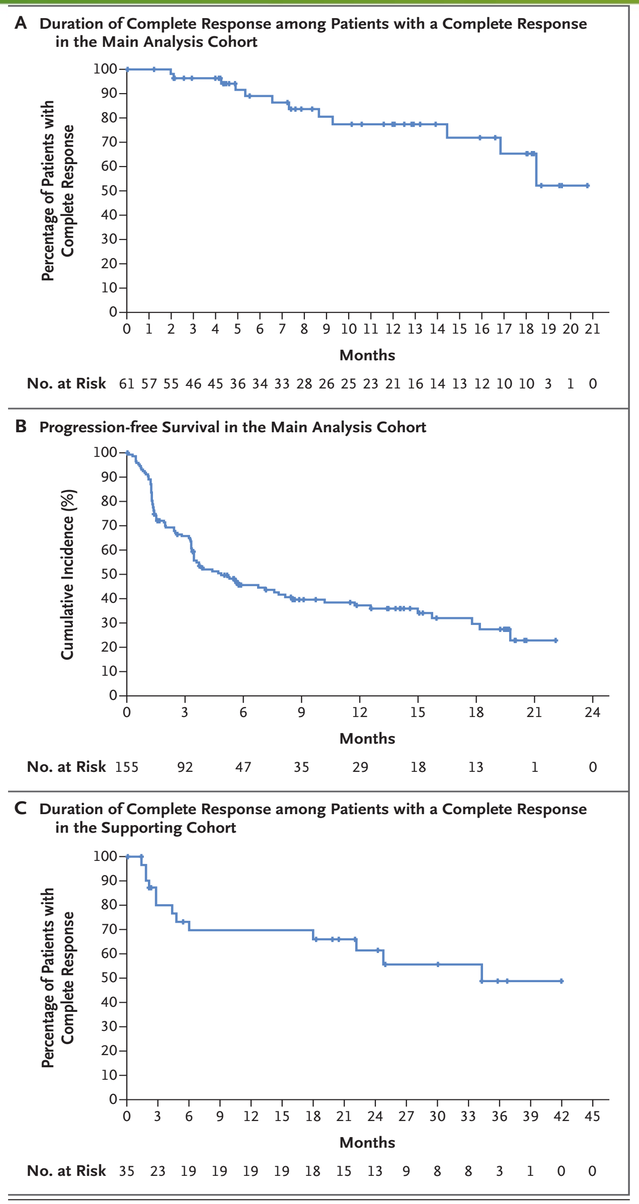
Epcoritamab

Odronextamab
Mosunetuzumab

ORIGINAL ARTICLE

Glofitamab for Relapsed or Refractory Diffuse Large B-Cell Lymphoma

Michael J. Dickinson, M.B., B.S., D.Med.Sc., Carmelo Carlo-Stella, M.D., Franck Morschhauser, M.D., Ph.D., Emmanuel Bachy, M.D., Ph.D., Paolo Corradini, M.D., Gloria Iacoboni, M.D., Cyrus Khan, M.D., Tomasz Wróbel, M.D., Fritz Offner, M.D., Ph.D., Marek Trněný, M.D., Shang-Ju Wu, M.D., Ph.D., Guillaume Cartron, M.D., Ph.D., Mark Hertzberg, M.B., B.S., Ph.D., Anna Sureda, M.D., Ph.D., David Perez-Callejo, Ph.D., Linda Lundberg, Ph.D., James Relf, M.D., Mark Dixon, M.Sc., Emma Clark, M.Sc., Kathryn Humphrey, B.Sc., and Martin Hutchings, M.D., Ph.D.



Subgroup	No. of Patients	Complete Response (95% CI) *percent*
Overall	155	39 (32–48)
Sex		
Female	54	52 (38–66)
Male	101	33 (24–43)
Age		
<65 yr	71	41 (29–53)
≥65 yr	84	38 (28–49)
Previous CAR T-cell therapy		
Yes	52	35 (22–49)
No	103	42 (32–52)
Non-Hodgkin's lymphoma subtype at study entry		
DLBCL	110	40 (31–50)
HGBCL	11	0 (NC–NC)
PMBCL	6	50 (12–88)
Transformed follicular lymphoma	28	50 (31–69)
Relapsed or refractory to last previous therapy		
Refractory	132	34 (26–43)
Nonrefractory	23	70 (47–87)
Disease status after ASCT		
Refractory	7	71 (29–96)
Nonrefractory	21	67 (43–85)
Cell of origin		
Germinal-center B cell	66	36 (25–49)
Activated B cell	17	59 (33–82)
Non–germinal-center B cell	34	32 (17–51)
Missing or unclassified	38	42 (26–59)
No. of previous lines of therapies		
2	62	32 (21–45)
≥3	92	44 (34–55)
Double-hit lymphoma		
Yes	20	25 (9–49)
No	134	41 (33–50)
Unknown or missing data	1	100
Double-expressor lymphoma		
Yes	15	20 (4–48)
No	139	41 (33–50)
Unknown or missing data	1	100
Bulky disease >6 cm		
Yes	64	33 (22–46)
No	90	44 (34–55)
Unknown or missing data	1	0
LDH >250 U/liter		
Yes	96	33 (24–44)
No	49	59 (44–73)
Unknown or missing data	10	0 (NC–NC)
Extranodal involvement		
Yes	95	36 (26–46)
No	60	45 (32–58)

n engl j med 387;24 nejm.org December 15, 2022

ORIGINAL ARTICLE

Glofitamab as a salvage treatment for B-cell lymphomas in the real world: A multicenter study in Taiwan

Ya-Ting Hsu MD[1] | Shang-Ju Wu MD, PhD[2] | Hsiao-Wen Kao MD[3] | Sheng-Yen Hsiao MD, PhD[4] | Chun-Kai Liao MD[5] | Tsai-Yun Chen MD[1] | Ming-Chung Wang MD[6]

Real world ORR 56%

TABLE 1 Demographics and baseline disease characteristics of patients with relapsed/refractory B-cell lymphoma treated with glofitamab ($N = 34$).

Characteristic	
Age, median (range), years	58 (26–79)
Age >65 years, No. (%)	9 (26)
Male, No. (%)	19 (56)
ECOG PS score, No. (%)	
0–1	26 (76)
2	6 (18)
3	2 (6)
Disease type, No. (%)	
Large B-cell lymphoma	31 (91)
De novo DLBCL	24 (71)
Transformed from FL	4 (12)
Transformed from MZL	1 (2)
CLL with RT	2 (6)
Cell of origin of DLBCL	
GCB	5 (15)
Non-GCB	13 (38)
Unknown	6 (18)
Double- or triple-hit phenotype	
Yes	8 (24)
No	2 (6)
Unknown	14 (41)
MCL	1 (3)
BL	1 (3)
B-cell lymphoma, unclassifiable	1 (3)
Prior treatment lines, median (range)	3 (1–10)
HBV infection status, No. (%)	
HBV carrier	7 (20)
Remote HBV infection	14 (38)
HBV naive	15 (42)
HCV infection status, No. (%)	
Anti-HCV(+)	2 (6)
Anti-HCV(–)	29 (85)
Unknown	3 (9)
HIV, No. (%)	
Yes	2 (6)
No	17 (50)
Unknown	15 (44)
Extranodal involvement, No. (%)	23 (68)
CNS	4 (12)
Bone marrow	10 (29)

(Continues)

HbsAg pos → 6/7 prophylaxis
HbcAb pos → 4/14 prophylaxis
No HBV reactivation

International single-arm phase 2 trial addressing feasibility and efficacy of epcoritamab in HIV-positive patients with relapsed/refractory large B-cell lymphoma (EPICO trial)

Inclusion criteria:

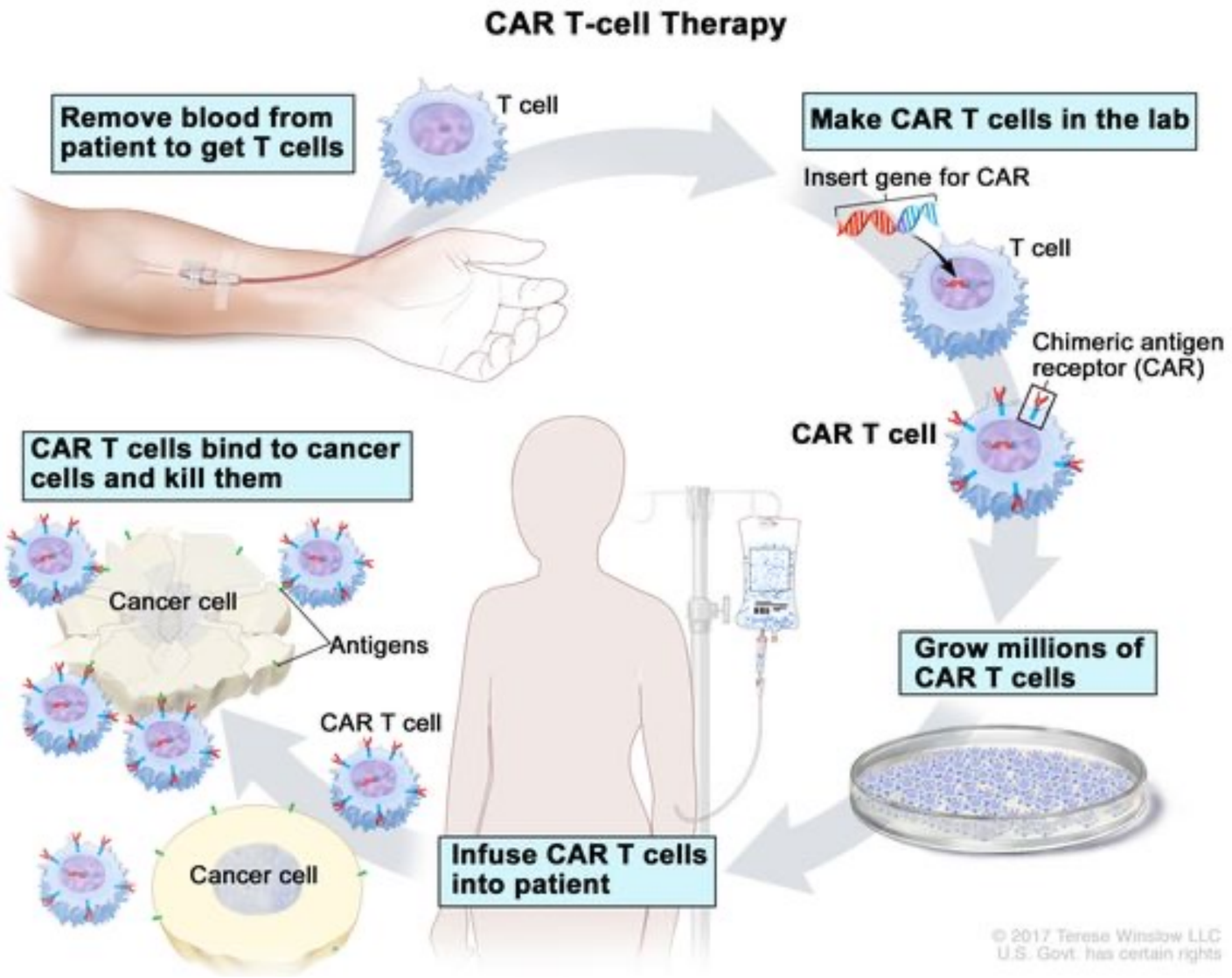
- Adult (≥ 18 yo) HIV+ pts with CD20+ ***RR LBCL****
- ECOG PS score of 0-2
- Prior lines ≥ 2 (anti-CD20)
- CD4 >50 cell/mcL
- Failed or not eligible for HDT-ASCT

*
DLBCL, NOS
HGBCL, NOS
DHL/THL
tFL
FL G3B
PMBCL
EBV-positive DLBCL

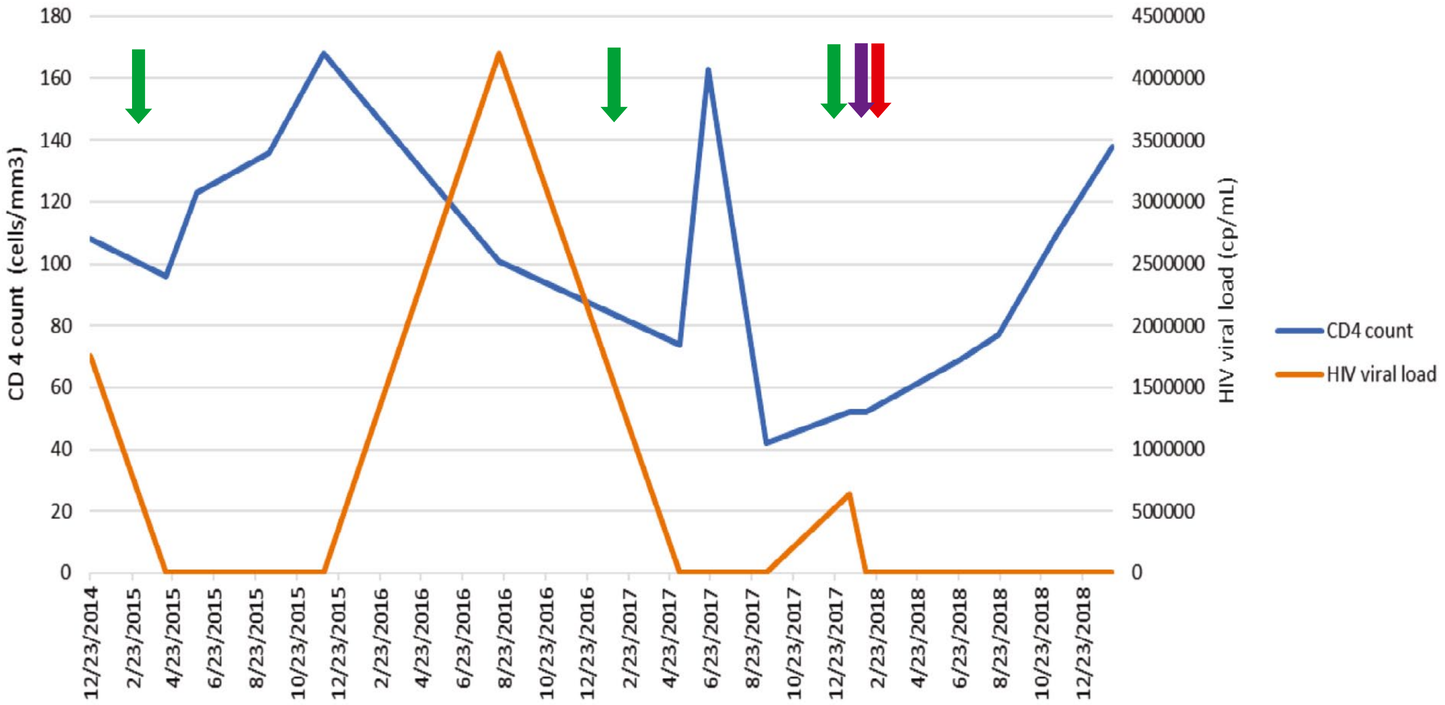
Exclusion criteria:

- ***Burkitt Lymphoma***
- CNS involvement
- Previous CD20xCD3 therapy
- Seizure disorder requiring anti-epileptic therapy
- Active infection
- **Uncontrolled HIV/HCV/HBV infection****

**
HIV resistant to cART (HIV RNA > 500 cp/ml)
Patient ineligible for potentially effective cART
Inadequate compliance to cART
Active HBV or HCV


CAR T-cell Therapy
Remove blood from patient to get T cells
T cell
Make CAR T cells in the lab
Insert gene for CAR
T cell
Chimeric antigen receptor (CAR)
CAR T cell
CAR T cells bind to cancer cells and kill them
Cancer cell
Antigens
CAR T cell
Cancer cell
Infuse CAR T cells into patient
Grow millions of CAR T cells
© 2017 Terese Winslow LLC
U.S. Govt. has certain rights

Successful Anti-CD19 CAR T-Cell Therapy in HIV-Infected Patients With Refractory High-Grade B-Cell Lymphoma



1) Esordio: DLBCL, non GC, stadio IVB (linfonodi sopra e sotto, parotid, tonsilla, milza, scheletro con BOM positive e citogenetica complessa
2) APR schizofrenico, syndrome da stress post-traumatico, plurimi ricoveri per scompensi psichiatrici
3) Status HIV: non assume terapia ART, CD4 100, Viral Load 1760000/mcl
4) R-EPOCH x 2 → RC: rifiuta le cure, ma avvia ART
5) Stop ART → recidiva (accesso in TI per massa polmonare) e incremento viral load HIV. Bx:DHL
6) R-ICE x 2 → RC → recidiva
7) CART → CRS grado 2 and ICANS grado 3
8) RC e assume terapia ART

Abramson JS, et al. Successful anti-CD19 CAR T-cell therapy in HIV-infected patients with refractory high- grade B-cell lymphoma. Cancer. 2019;125:3692–3698.

LETTER TO THE EDITOR Open Access

Axicabtagene ciloleucel CD19 CAR-T cell therapy results in high rates of systemic and neurologic remissions in ten patients with refractory large B cell lymphoma including two with HIV and viral hepatitis

Ahmed Abbasi[1†], Stephen Peeke[1†], Nishi Shah[1†], Jennat Mustafa[1], Fariha Khatun[1], Amanda Lombardo[1], Michelly Abreu[1], Richard Elkind[1], Karen Fehn[1], Alyssa de Castro[2], Yanhua Wang[3], Olga Derman[1], Randin Nelson[3], Joan Uehlinger[3], Kira Gritsman[1], R. Alejandro Sica[1], Noah Kornblum[1], Ioannis Mantzaris[1], Aditi Shastri[1], Murali Janakiram[1], Mendel Goldfinger[1], Amit Verma[1], Ira Braunschweig[1] and Lizamarie Bachier-Rodriguez[1*]

Supplementary Table 1. Viral load and other lab parameters for three patients (1 HIV, 2 patients with HBV)						
		21/12/18	26/02/19	10/06/19	13/09/19	14/10/19
HIV Patient CAR-T infusion on 4/29/2019	HIV-1 Viral RNA Load (copies/ml)	0	0	0	116	683817
	CD4 count (cells/μl)	148	120	62	46	not tested
		13/11/18	04/01/19	05/03/19	07/05/19	13/08/19
Hepatitis B Patient 1 CAR-T infusion 11/28/2018	Hepatitis B viral load IU/ml	68998	not tested	not tested	not tested	not tested
	LFTs (AST, ALT, Alkaline phosphatase, Total bilirubin, direct bilirubin)	normal	normal	normal	normal	normal
		21/12/18	08/04/19	26/07/19		
Hepatitis B Patient 2 CAR-T infusion 3/18/2019	Hepatitis B viral load IU/ml	60	not tested	not tested		
	LFTs (AST, ALT, Alkaline phosphatase, Total bilirubin, direct bilirubin)	normal	Grade I Alkaline phosphatase elevation	Grade I Alkaline phosphatase elevation		

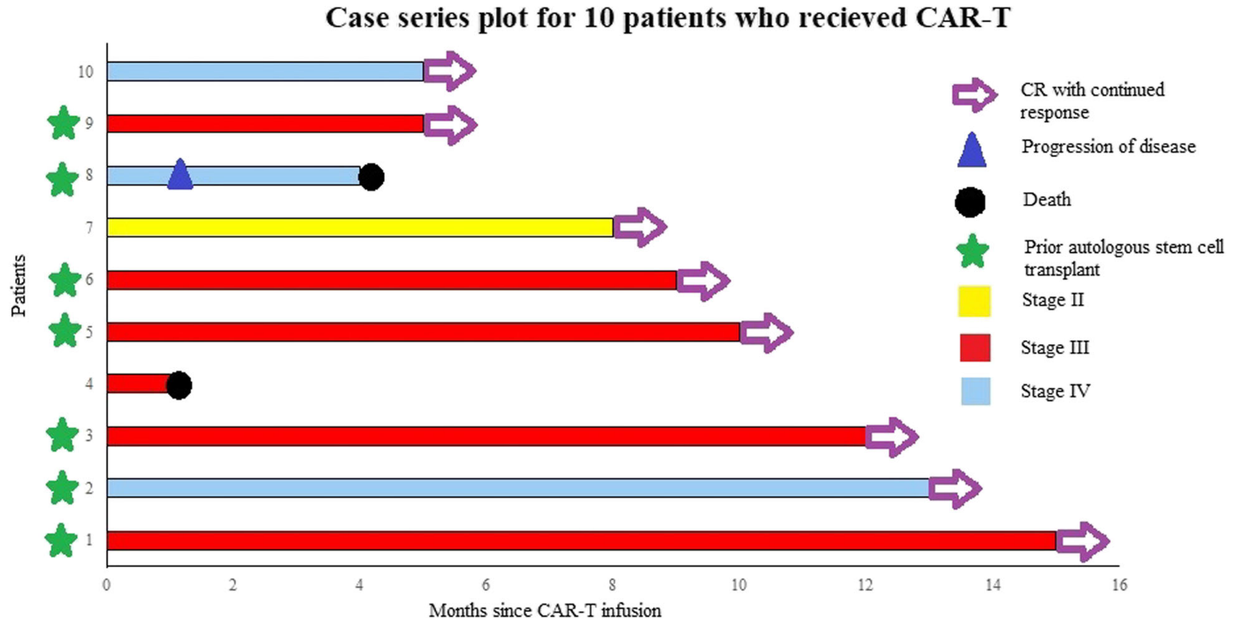
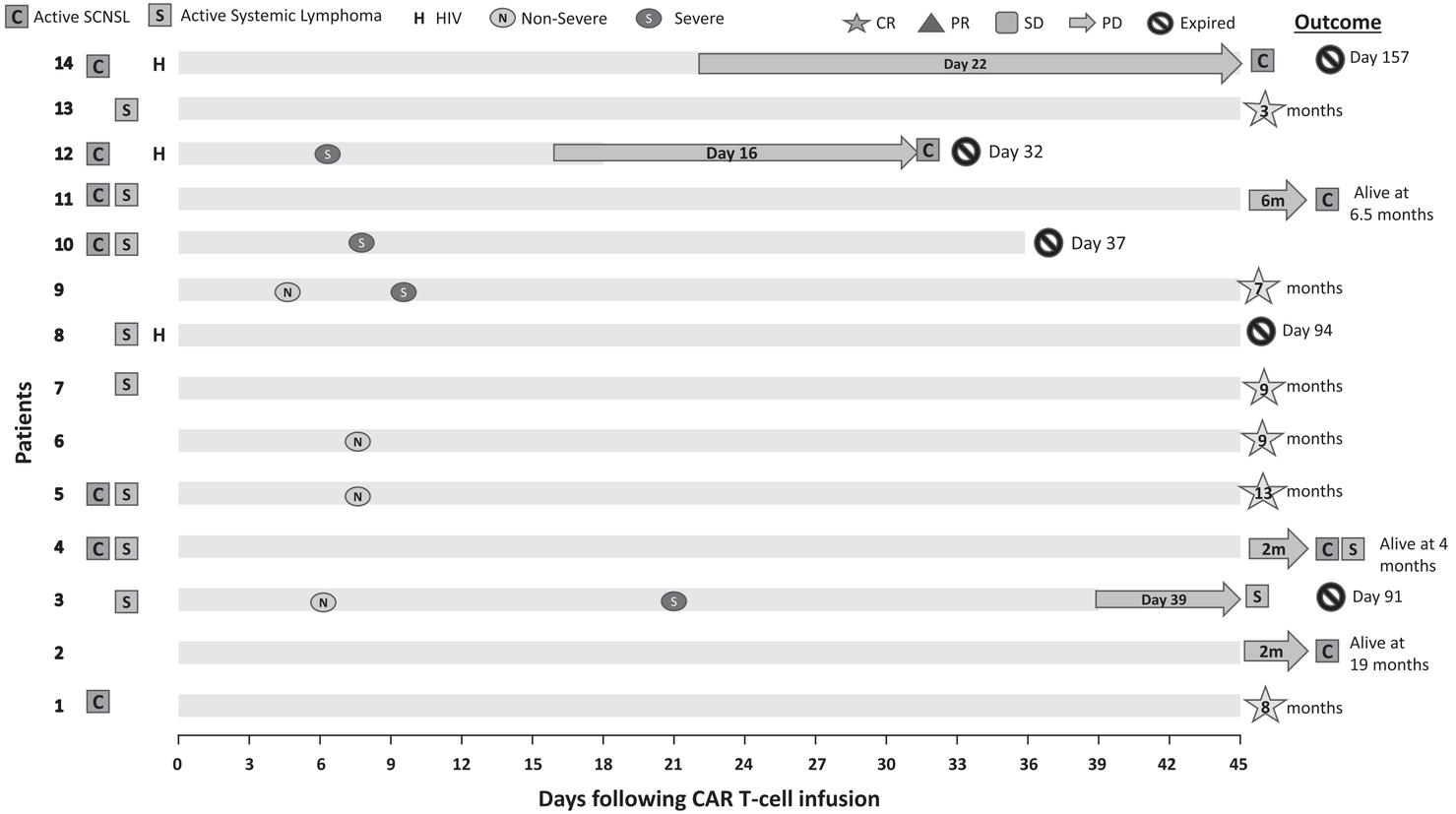


Fig. 1 Response to treatment after axicabtagene ciloleucel. Swimmer's plot showing response to treatment after Axi-cel infusion in patients with DLBCL receiving CD19-directed CAR-T

Axicabtagene Ciloleucel in Patients Ineligible for ZUMA-1 Because of CNS Involvement and/or HIV: A Multicenter Experience

Carlen A. Yuen, Jing-Mei Hsu,† Koen Van Besien,† Ran Reshef,‡ Fabio M. Iwamoto,* Aya Haggiagi,* Benjamin Liechty,§ Cenai Zhang,‖ Sarah F. Wesley,¶ and Rajiv Magge#*



- All patient have controlled HIV
- 3 months of Median Follow up
- 30% severe neurotoxicity
- Death in PD

J Immunother • Volume 00, Number 00, ■■ 2022

Bone Marrow Transplantation (2021) 56:679–682
https://doi.org/10.1038/s41409-020-01018-7

CORRESPONDENCE

Chimeric antigen receptor T-cell therapy for HIV-associated diffuse large B-cell lymphoma: case report and management recommendations

Jeremy Allred[1] · Kharmen Bharucha[2] · Can Özütemiz[3] · Fiona He[1] · Murali Janakiram[1] · Joseph Maakaron[1] · Claire Carrier[1] · Bartosz Grzywacz[4] · Veronika Bachanova[1]

Received: 10 April 2020 / Revised: 31 May 2020 / Accepted: 24 July 2020 / Published online: 6 August 2020

Table 1 Steps to optimize success of CAR-T therapy in HIV+ patient.

(A) Pre CAR-T therapy		
1)	Assess HIV control and T-cell repertoire	—Establish management team including medical oncologist, infectious disease physician, pharmacist and cell therapy physician
		—Review cART regimen and check HIV viral load. Establish effective HIV viral control
2)	Infection control	—Obtain peripheral blood T-cell subsets including absolute CD4 count to assess repertoire. ALC > 100 is recommended (but not required) for axicabtagene manufactering
		—Screen for and treat any active immunodeficiency-associated infections
3)	Assess drug–drug interactions	—Initiate appropriate antimicrobial prophylaxis based on CD4 count and current infectous disease guidelines
		—In collaboration with infectious disease and pharmacy, review and adjust cART regimen for interations and potential overlapping toxicities; select cART regimen that acheives effective HIV control while minimizing drug–drug interactions
(B) Post CAR-T therapy		
1)	Monitor HIV control	—Recommend quantitative HIV viral load at least q3 months for 1 year, more frequently with changes in cART regimen
2)	Assess immune reconstitution	—Administer G-CSF for ANC < 1000 cells/μL after 14 days post CAR-T
		—Monitor total B-cell, CD3 and CD4 T-cell counts post CAR-T
3)	Infection prophylaxis	—Inhaled pentamidine (or equivalent) 1 month prior and montly for 6 months post CAR-T or until CD4 count > 200 cells/μL for PJP pneumonia prophylaxis
		—Antifungal agent with mold activity if high dose steroids to be used for more than 7 days, if heavily pre-treated or if prior autologous HCT within 1 year.
		—Acyclovir for HSV and VZV prophylaxis for minimum 6 months.

VOLUME 26 · NUMBER 7 · MARCH 1 2008

JOURNAL OF CLINICAL ONCOLOGY | COMMENTS AND CONTROVERSIES

Including Persons With HIV Infection in Cancer Clinical Trials

Govind C. Persad, Richard F. Little, and Christine Grady, *Department of Bioethics, The Clinical Center, and The Clinical Investigations Branch, Cancer Therapy Evaluation Program, Division of Cancer Therapy and Diagnosis, National Cancer Institute, The National Institutes of Health, Bethesda, MD*

Cancer Care Disparities in People with HIV in the United States

- Higher cancer-specific mortality in HIV-infected people compared with the general population for several cancer types

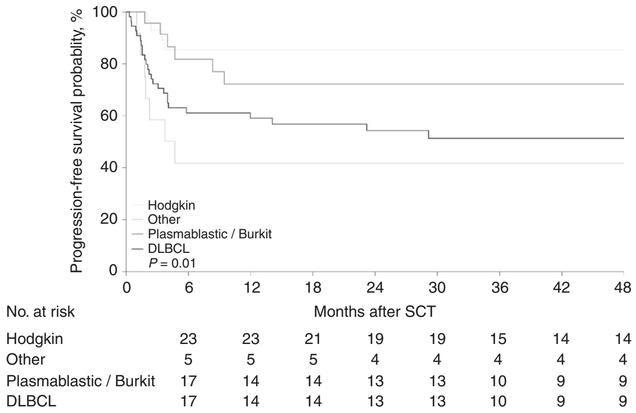
- Infected cancer patients were less likely to receive cancer treatment compared with uninfected cancer patients for several cancer types (OR 1.39 for diffuse large B-cell lymphoma)

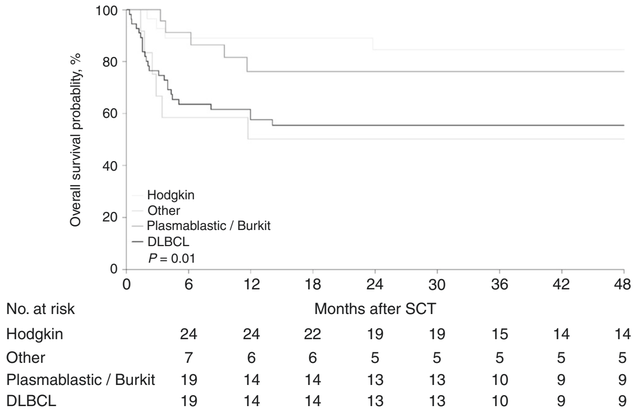
Persad et al. JCO. 2008 March; 26(7).

Anna Coghill, and Gita Suneja, Curr Opin HIV AIDS . 2017 January ; 12(1): 63–68.

Autologous Stem Cell Transplantation in HIV

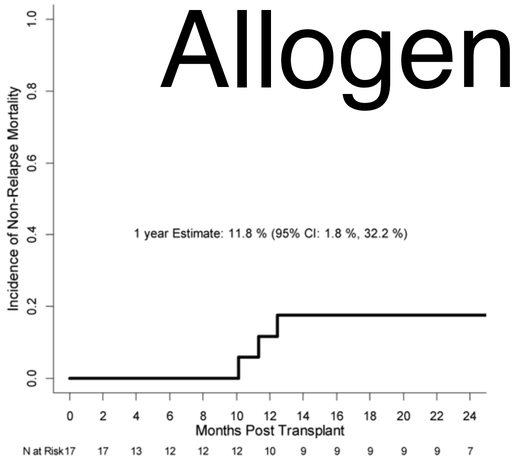
$N = 118$		
Gender	Male	100 (84.7%)
Age at autoHCT, years (median, range)		45 (24–66)
Diagnosis	DLBCL	55 (46.6%)
	Burkitt	15 (12.7%)
	PBL	8 (6.8%)
	HL	28 (23.7%)
	Other	12 (10.2%)
Disease status at autoHCT	CR	52 (44.1%)
	PR	45 (38.1%)
	Less than PR	21 (17.8%)
High-dose regimen	BEAM	86 (72.9%)
	BEAC	10 (8.4%)
	FEAM	4 (3.4%)
	Melphalan	5 (4.2)
	Other	13 (11.0%)
Continuous cART during autoHCT	Yes	118 (100%)
HIV virus load at autoHCT (copies/ml; $n = 108$)	<50	78 (72.7%)
	50–10.000	26 (24.1%)
	10.000–100.000	2 (1.9%)
	>100.000	2 (1.9%)
CD4 cell count at autoHCT, cells/µl (median, range)		194 (0–800)
CD4 cell count at autoHCT < 50 cells/µl		12 (11.1%)

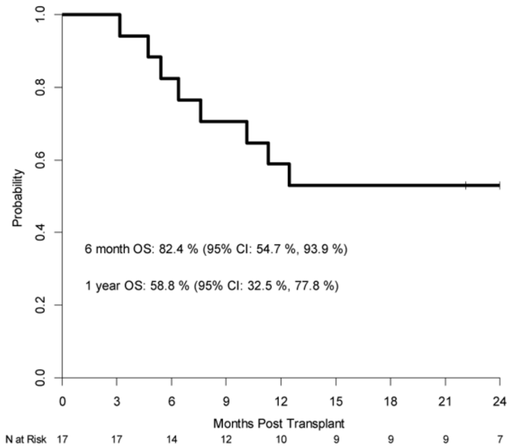




Hubel et al. Bone Marrow Transplantation (2019) 54:1625–1631

Allogeneic Hematopoietic Cell Transplant in HIV





Characteristics	**N (%)**
Total transplanted	17 (100%)
Sex	
Male	17(100%)
Ethnicity	
Hispanic or Latino	1(6%)
Not Hispanic or Latino	15(88%)
Unknown	1(6%)
Race	
American Indian/Alaskan Native	1 (6%)
Black or African American	3 (18%)
White	11 (65%)
Unknown/Other	2 (12%)
Age, years	
Median (range)	47 (25-64)
Performance status	
100	4 (24%)
90	9 (53%)
80	3 (18%)
70	1 (6%)

Patient diagnosis	
Acute Myeloid Leukemia (AML)	9 (53%)
Acute Lymphocytic Leukemia (ALL)	2 (12%)
Myelodysplastic Syndromes (MDS)	2 (12%)
Hodgkin's Lymphoma	1 (6%)
Non-Hodgkin's Lymphoma	3 (18%)
Leukemia Status	
First Complete Remission	8 (73%)
Second Complete Remission	3 (27%)
Lymphoma Status	
Complete Remission	3 (75%)
Partial Remission	1 (25%)
HIV Load	
Undetectable	15 (88%
Detectable	2 (12%)
Mean (copies/mL)	92
Pre-transplant Recipient CMV Serostatus	
Positive	12 (71%
Negative	5 (29%)

Primary causes of death.

Primary cause of death	**N**
Relapse/Progression	5
Acute GVHD	1
Adult Respiratory Distress Syndrome	1
Liver Failure	1
Total	8

Infections

Grade	Site of Infection	Date of Onset (post transplant)	Organism	Treatment	Survival Status (primary Cause of Death)
Grade 2	Blood	39 days	CMV	ganciclovir	Died on Day 308 (ARDS)
Grade 2	Blood	119 days	CMV	foscarnet	Died on Day 194 (relapse)
Grade 2	Blood	124 days, 260 days	CMV	ganciclovir, valacyclovir	Died on Day 379 (acute GVHD)
Grade 2	Blood	36 days	CMV	valganciclovir	Died on Day 143 (relapse)
Grade 2	Tongue, Oral Cavity, and Oro-Pharynx	248 days	Candida	nystatin	Died on 344 (Liver failure)
Grade 2	Upper Airway and Nasopharynx	211 days	Pneumocystis	trimethoprim / sulfamethoxazole	Alive at Day 751
Grade 3	Feces/Stool	35 days	*Candida krusei*	voriconazole	Alive at Day 741

Ambinder et al. Biol Blood Marrow Transplant . 2019 November ; 25(11): 2160–2166

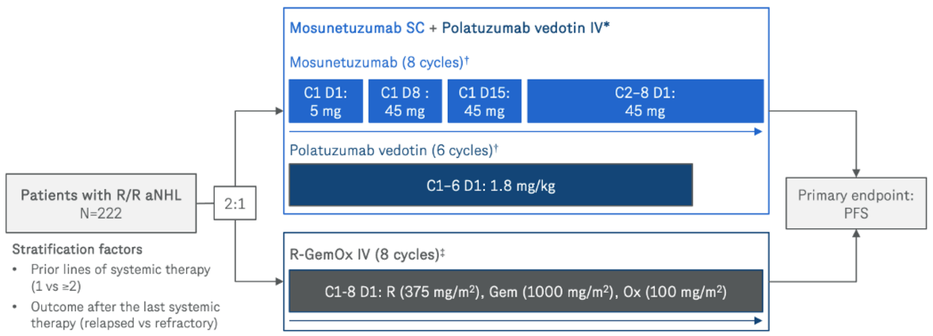
MOSUNETUZUMAB

Mosunetuzumab: sono stati modificati i criteri di inclusione per i pazienti con HIV rispetto allo studio pivotale.

•SUNMO (G043643; NCT05171647) is an ongoing Phase 3 randomized, open-label, multicenter study evaluating the efficacy and safety of SC mosunetuzumab in combination with polatuzumab vedotin IV vs rituximab in combination with gemcitabine plus oxaliplatin IV in patients with R/R aggressive B-cell NHL.
• GO40516 (NCT03671018) is an ongoing Phase 1b/2 open-label, multicenter dose-escalation and expansion study evaluating the safety, tolerability, and efficacy of SQ or IV Lunsumio in combination with polatuzumab vedotin IV in patients with R/R B-cell NHL.

Criteri di inclusione: Test HIV negativo allo screening. I partecipanti con un test HIV positivo allo screening sono eleggibili a condizione che, prima dell'arruolamento, siano stabili in terapia antiretrovirale da almeno 4 settimane, abbiano una conta dei CD4 di almeno 200 microlitri, abbiano una carica virale non rilevabile e non abbiano avuto un'anamnesi di infezione opportunistica attribuibile all'AIDS negli ultimi 12 mesi.

Figure 1. SUNMO Study Schema



GLOFITAMAB

Skyglo
An Open-Label Study Comparing Glofitamab and Polatuzumab Vedotin + Rituximab, Cyclophosphamide, Doxorubicin, and Prednisone Versus Pola-R-CHP in Previously Untreated Patients With Large B-Cell Lymphoma

Nello studio Skyglo i pazienti con HIV possono partecipare nella seguente situazione, criteri di inclusione: Test HIV negativo allo screening, con la seguente eccezione, i soggetti con un test HIV positivo allo screening sono eleggibili a condizione che, prima dell'arruolamento, siano stabili in terapia antiretrovirale, abbiano una conta CD4 >=200/µL e abbiano una carica virale non rilevabile.

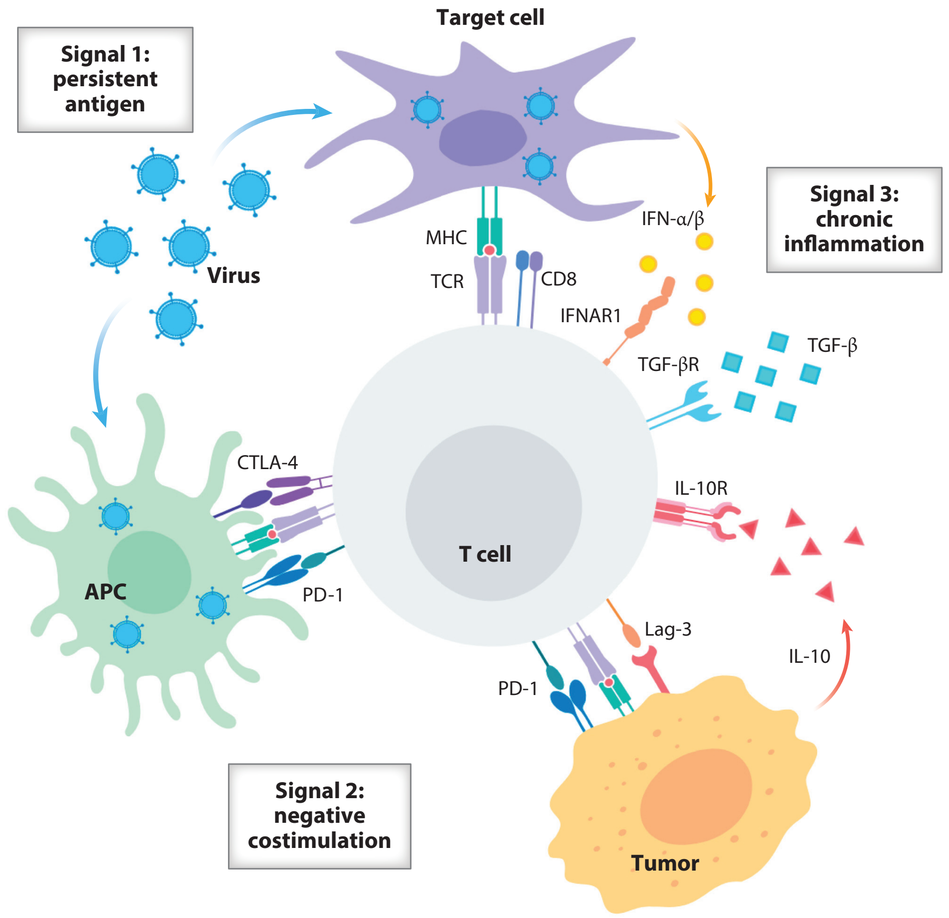
Criteri di inclusione

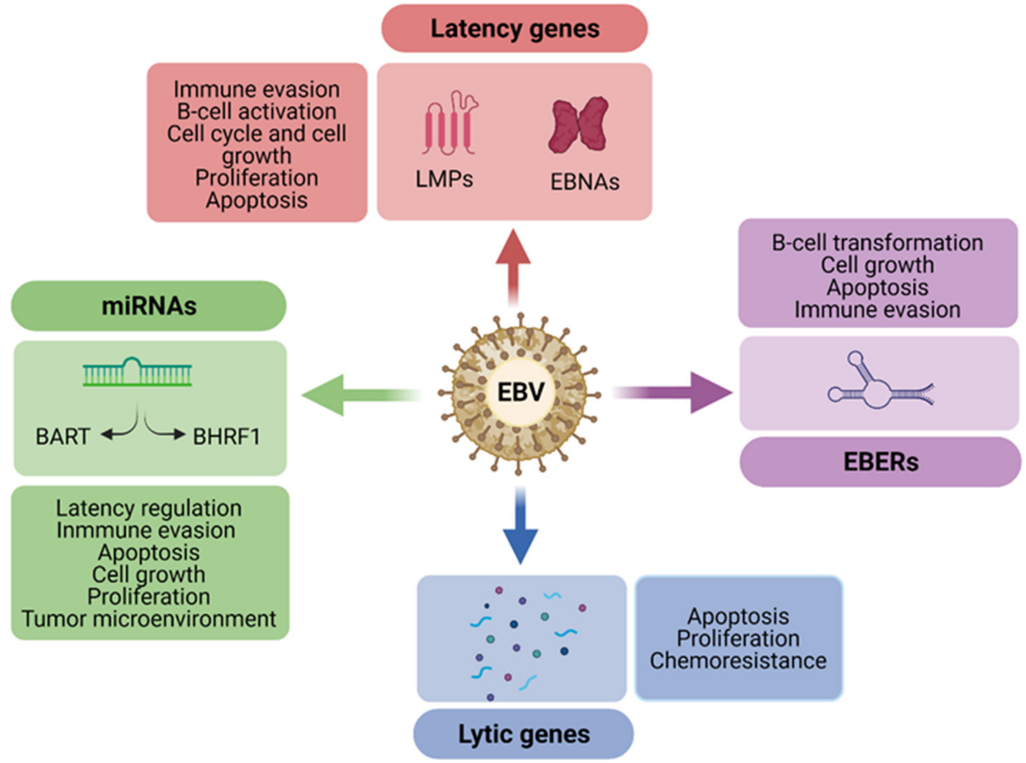
ART da almeno 4 settimane
Conta CD4 > o uguale 200/mcl
Indetectable viral load
No infezioni opportunistiche 12 mesi

Ongoing Trial

Immune Cell Therapy (CAR-T) for the Treatment of Patients With HIV and B-Cell Non-Hodgkin Lymphoma
ClinicalTrials.gov ID NCT05077527
Sponsor AIDS Malignancy Consortium
Information provided by AIDS Malignancy Consortium (Responsible Party)
Start enrollment 14/4/24 → 2026

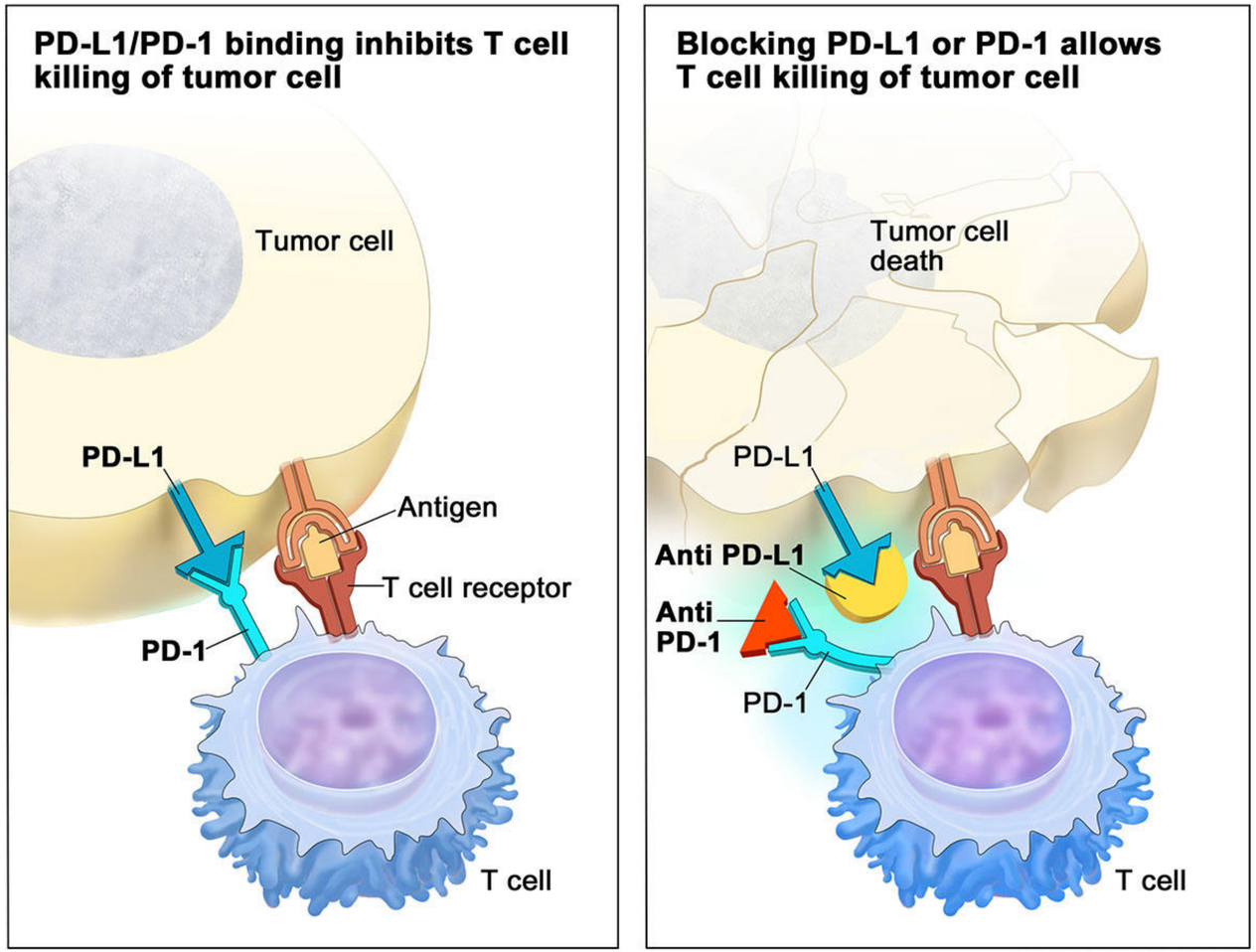
HIV and EBV Lymphoma



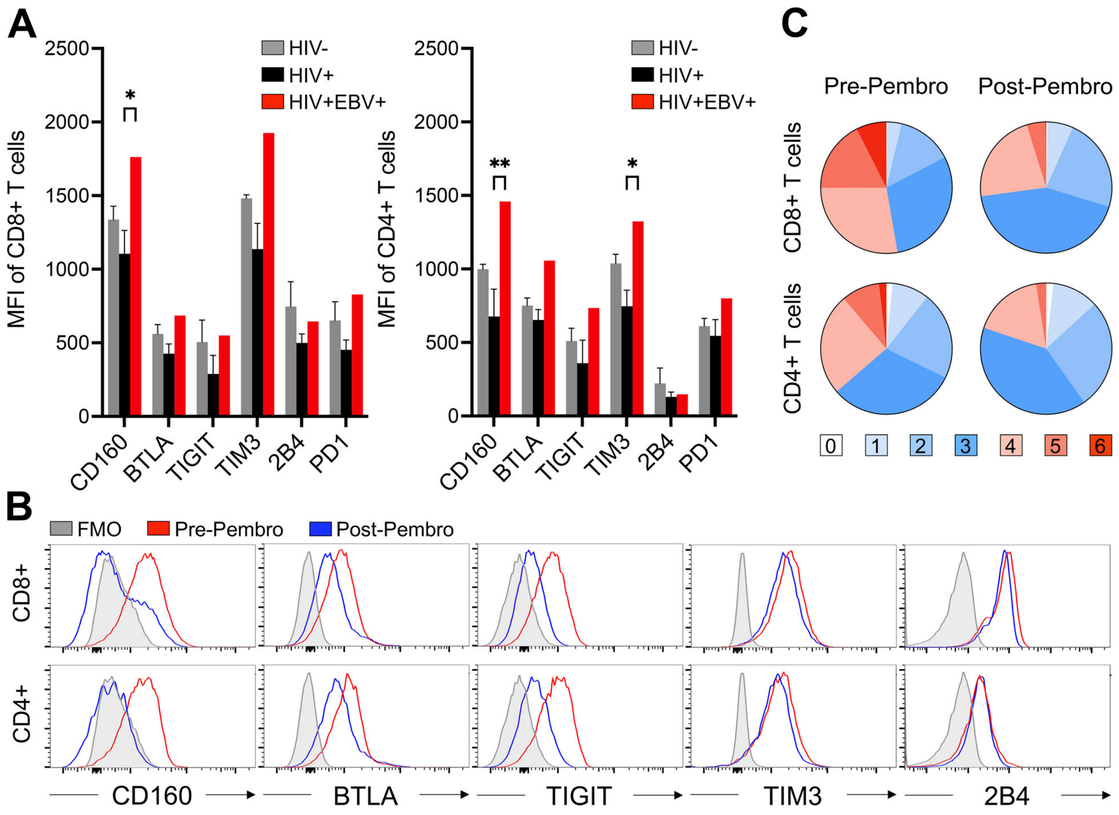


McLane et al, Annu. Rev. Immunol. 2019. 37:457–95
Carbone A. et al Blood 17 FEBRUARY 2022 | VOLUME 139, NUMBER 7
Ling Luo et al *Asia-PacJClinOncol.*2022;18:e17–e22.

Pembrolizumab



Pembrolizumab



1) Treatment with pembrolizumab in HIV pos EBV þos DLBCL patient reduces inhibitory receptor (IRs) expression and T-cell exhaustion.
2) it is possible that the increased expression of these IRs may be related to the EBV infection
3) EBV pos HIV pos higher IRs
4) Riduce t-cell exhaustion
5) PD1 marker CD4 memory

Korsos V. et al. LEUKEMIA & LYMPHOMA 2022, VOL. 63, NO. 5, 1256–1260

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2024
Cancer in People with HIV

NCCN Guidelines Index
Table of Contents
Discussion

INTRODUCTION

- People with human immunodeficiency virus (HIV) (PWH) and AIDS have a higher incidence of many common cancers compared with the general population. AIDS-defining cancers include aggressive non-Hodgkin lymphoma (NHL), Kaposi sarcoma, and invasive cervical cancer. Dramatically improved treatment of HIV over the last two decades has led to a decrease in the risk of AIDS development, an increase in immune function and survival, and a decline in AIDS-defining cancers in this population; however, the incidence of non-AIDS defining cancers has increased because of longer life expectancies due to antiretroviral therapy (ART), accelerated aging as a consequence of HIV, a higher likelihood of co-infection with oncogenic infections, and a higher prevalence of carcinogen exposure.
- Cancer in PWH should be co-managed by an oncologist, and HIV specialist, and PWH should receive cancer treatment as per standard guidelines. Although modifications to ART may be needed, HIV therapy should be continued during cancer therapy. Multidisciplinary decision-making, involving HIV specialists, is critical.

AIDS-defining malignancies[a,b,c,d,e,f]

- Cervical cancer → Cervical Cancer in PWH (HIV-1)
- Kaposi sarcoma → See NCCN Guidelines for Kaposi Sarcoma
- Primary CNS lymphoma → See NCCN Guidelines for Central Nervous System Cancers
- Aggressive NHL[g] → See NCCN Guidelines for B-Cell Lymphomas

Non–AIDS-defining malignancies[a,b,c,d,e,f]

- Anal cancer → Anal Cancer in PWH (HIV-2)
- Non-small cell lung cancer (NSCLC) → Non-Small Cell Lung Cancer in PWH (HIV-3)
- Hodgkin lymphoma (HL) → Hodgkin Lymphoma in PWH (HIV-4)
- Other non–AIDS-defining malignancies → See NCCN Guidelines for Treatment of Cancer by Site

[a] Principles of HIV Management While Undergoing Cancer Therapy (HIV-A).
[b] Principles of Systemic Therapy and Drug-Drug Interactions (HIV-B).
[c] Principles of Radiation Therapy (HIV-C).
[d] Principles of Surgery (HIV-D).
[e] Principles of Supportive Care (HIV-E).
[f] Principles of Imaging (HIV-F).
[g] Burkitt lymphoma; diffuse large B-cell lymphoma (DLBCL); Kaposi sarcoma associated herpesvirus (KSHV)-positive DLBCL, not otherwise specified (NOS); primary effusion lymphoma; and plasmablastic lymphoma.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2024
HIV-Related B-Cell Lymphomas

NCCN Guidelines Index
Table of Contents
Discussion

WORKUP

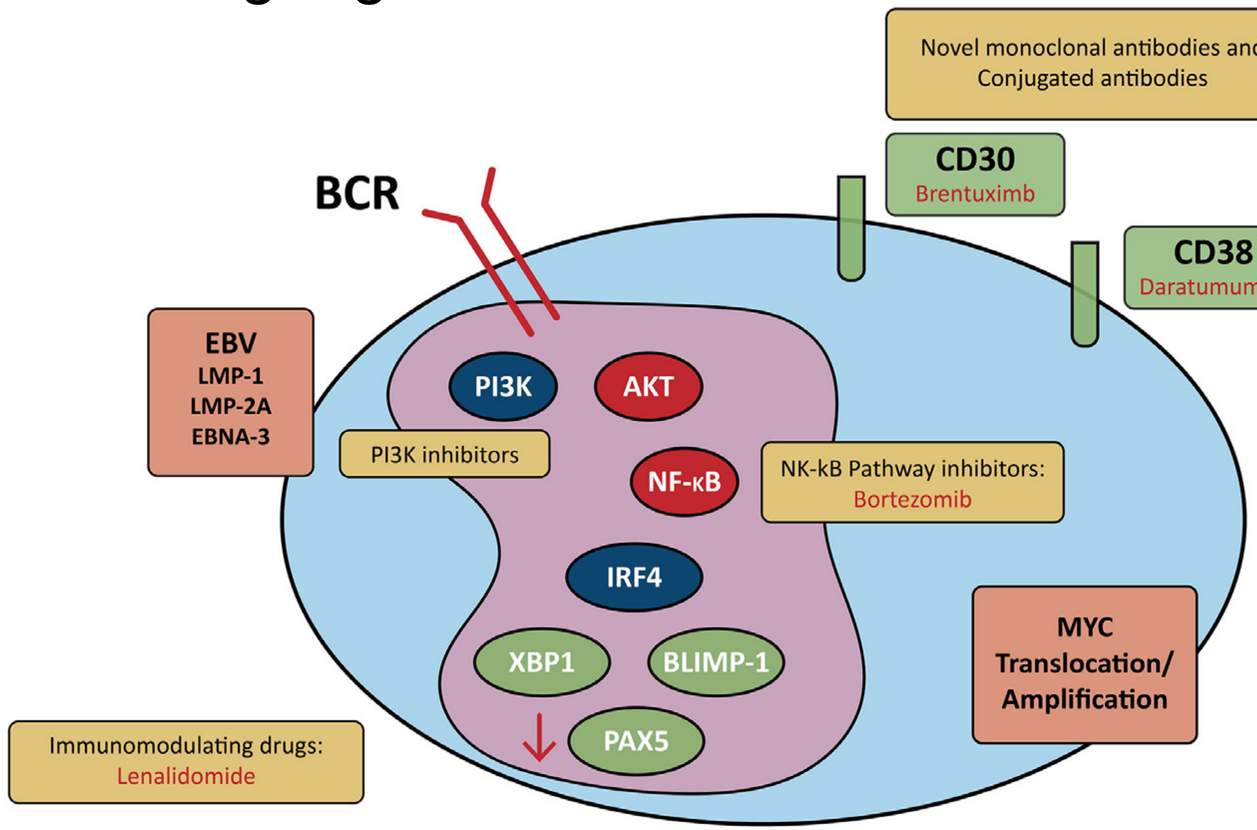
ESSENTIAL
- Physical exam: attention to node-bearing areas, including Waldeyer's ring, and to size of liver and spleen
- Performance status
- B symptoms
- CBC with differential
- LDH
- Comprehensive metabolic panel
- Uric acid, phosphate
- PET/CT scan (preferred) or C/A/P CT with contrast of diagnostic quality
- CD4 count
- Lumbar puncture, except for PEL
- HIV viral load
- Hepatitis B testing[b]
- Hepatitis C testing[c]
- Echocardiogram or MUGA scan if anthracycline or anthracenedione-based regimen is indicated
- Pregnancy testing in patients of childbearing age (if chemotherapy or RT planned)

USEFUL IN SELECTED CASES:
- Upper GI/barium enema/endoscopy
- Adequate bone marrow biopsy (>1.6 cm) ± aspirate; bone marrow biopsy is not necessary if PET/CT scan demonstrates bone disease
- Neck CT with contrast
- Plain bone radiographs and bone scan
- Brain MRI with and without contrast, or head CT with contrast
- Beta-2-microglobulin
- EBV PCR
- Quantitative Ig
- Discuss fertility preservation[d]

- BL → Treatment (HIVLYM-3)
- Primary CNS lymphoma → Treatment (HIVLYM-3)
- DLBCL, HHV8-positive DLBCL, NOS, PEL → Treatment (HIVLYM-4)
- Plasmablastic lymphoma → Treatment (HIVLYM-4)

Linfoma Plasmablastico

1. Median OS 3 months in HIV pos
2. CHOP in inadeguate
3. Bortezomib-conteining regimen are effective



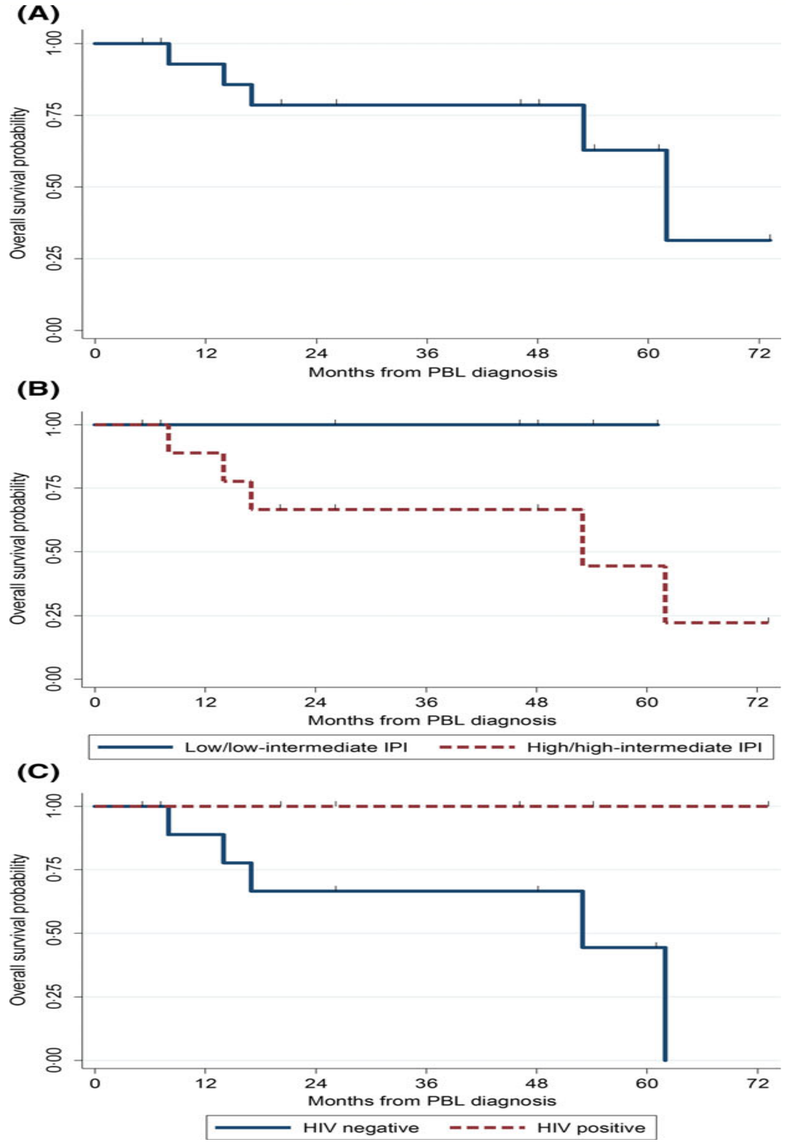
Mediterr J Hematol Infect Dis 2024; 16; e2024015

Bortezomib in PBL HIV positive

Bortezomib alone or with chemotherapy	Cases; age	Outcome	Author, year, ref.
Bortezomib single therapy	1 (55)	P after 4 months.	Jambusaria A. 2008[27]
Bortezomib single therapy	1 (42)	P after 1 months.	Bose P. 2009[28]
Bortezomib + GOVDD	1 (19)	P after 2 months.	Bibas M. 2010[29]
Bortezomib + DRC	1 (68)	PR	Lipstein M. 2010[30]
Bortezomib + Dexamethasone	1(80)	PR	Dasanu CA 2013[31]
Bortezomib + Dexamethasone	1(44)	PR	Saba NS 2013[32]
Bortezomib + Dexamethasone	1(50)	PR	Cao C. 2014[33]
Bortezomib + COMP	1 (66)	CR	Cencini E. 2015[34]
Bortezomib + THP-COP	1 (58)	PR	Hirosawa . 2015[35]
Bortezomib + CHOP	3 (38)	CR 3/3; 3/3ABMT after CR.	Fernandez-Alvarez R. 2015[37]
Bortezomib + EPOCH+ IT MTX	1(50)	CR	Fedele PL 2016[38]
Bortezomib + DA-EPOCH	1(34)	CR	Arora N. 2017[39]
Bortezomib single therapy Bortezomib + chemotherapy	6 (42) 15 (42)	CR 0/6 PR 5/6 CR 9/15 Pr 5/6	Guerrero-Garcia T. 2017[40]
Bortezomib + DA-EPOCH	8 (49)	CR 8/8	Dittus C. 2018[41]
Bortezomib + EPOCH	16 (47)	1/1	Castillo JJ 2019[42]
Bortezomib + oral CTX and DEX	1(64)		Ando K. 2019[43]
Bortezomib single therapy	1(55)	PR	Umeanaeto 2019[44]
Bortezomib + CDOP	1 (63)	PR	Cai J. 2021[45]
Bortezomib +Lenalildomide+ DEX	1 (59)	PR	Sabry W. 2022[46]
Bortezomib + Chemotherapy	31 (55)		Di Ciaccio P.R. 2024 [21]

6 HIV

99 HIV su 200



Castillo et al. BMJ 2019, 184, 634–696

Di Ciaccio et al.. Blood. 2024 Jan 11;143(2):152-165

Bibas et al Mediterr J Hematol Infect Dis 2024

Table 1. Demographic and baseline characteristics

Characteristic	n	%
Sex		
Male	20	91
Female	2	9
Race		
White	15	68
African American	6	27
Other	1	5
Ethnicity		
Hispanic	5	23
Non-Hispanic	17	77
Age, y		
Median	48	
Range	34-66	
CDC risk group		
Homosexual/bisexual contact	15	68
Heterosexual contact	5	23
Homosexual and heterosexual contact	1	5
IV drug use	1	5
Receiving ART at enrollment	20	87
Absolute CD4 count, μL		
Median	315	
Minimum-maximum	45-773	
HIV viral load, copies/mL		
Median	Undetectable	
Minimum-maximum	Undetectable to 241 490	
Ann Arbor stage		
I	3	14
II	3	14
IIE	1	5
III	3	14
IV	12	55
Lymphoma diagnosis		
DLBCL	15	68
PEL	2	9
Plasmablastic lymphoma	3	14
Hodgkin lymphoma	2	9

CDC, Centers for Disease Control and Prevention.

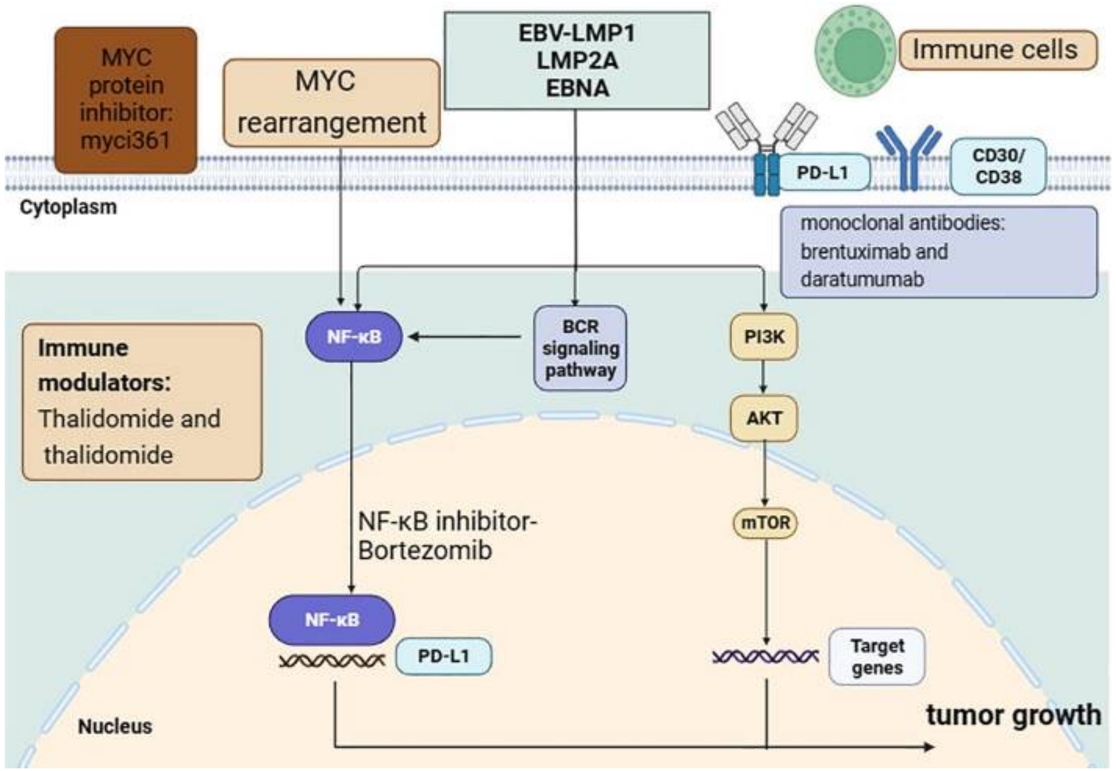
B-ICE +/- R in PBL R/R

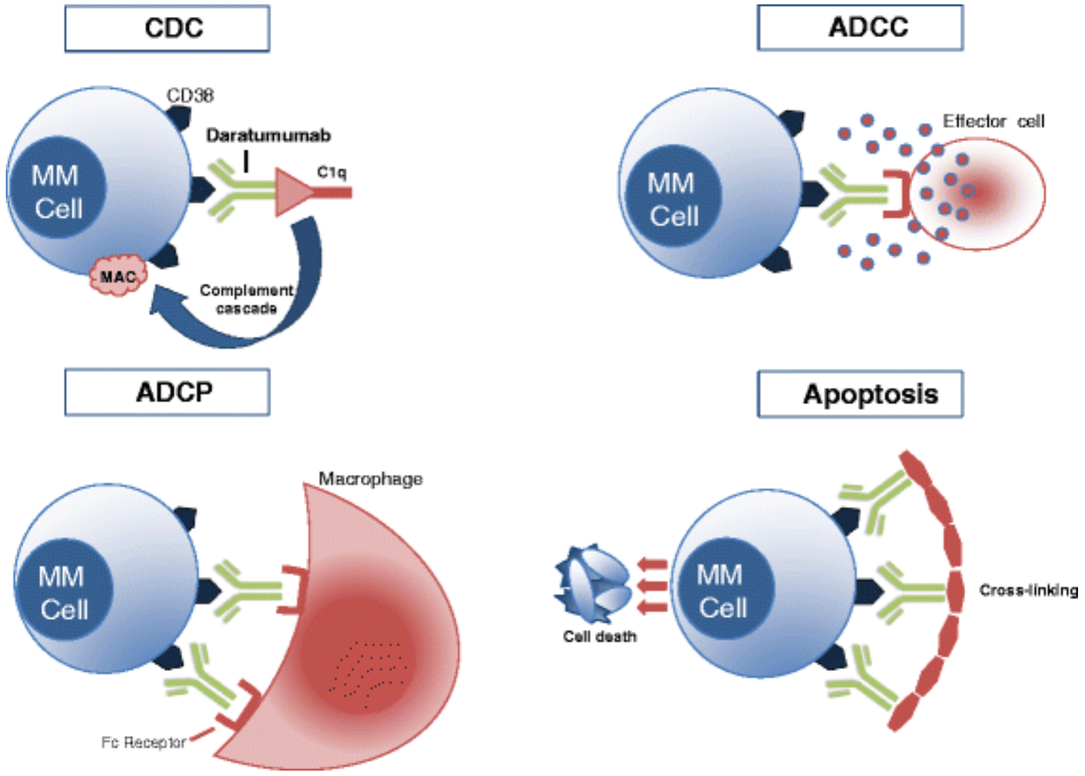
Lymphoma type	Ann Arbor stage	Lymphoma EBV/KSHV status	Baseline CD4, cells/μL	Baseline HIV, copies/mL	Bortezomib dose cohort, mg/m^2	Total no. of cycles completed	Best response	Duration of response, wk	Postprotocol lymphoma therapy	Survival,
DLBCL	IV	EBV positive	294	241 490	0.7	6	CR	>68.5	None	>68
DLBCL	IV	EBV positive	77	85 122	0.7	2	PD*	NA	Radiation	38
DLBCL	IV	EBV positive	402	170	0.7	4	CR*	>55	None	>55
Plasmablastic	IV	EBV positive	169	126	0.7	2	SD	NA	AHSCT	29
PEL	IV	EBV and KSHV positive	570	48	0.7	4	PR	15	AHSCT	24
DLBCL	II	EBV positive	261	—	0.7	2	PD	NA	Radiation	26
DLBCL	IV	EBV positive	336	Undetectable	1.0	3	PR*	4	Not reported	19
Not reported	—	—	—	—	1.0	0	NA	NA	NA	NA
DLBCL	IV	EBV positive	48	8000	1.0	<2	NE	NE	Not reported	9
DLBCL	IV	EBV positive	45	89	1.0	<1	NE	NE	None	3
Hodgkin	III	EBV positive	283	<400	1.0	2	CR*	>55	AHSCT	>55
Plasmablastic	I	EBV positive	476	<20	1.0	4	CR*	>59	AHSCT	>59
DLBCL	IIE	EBV positive	435	Undetectable	1.0	3	PR	>40	AHSCT	>40
DLBCL	IV	EBV negative	334	4.4	1.0	3	PR*	6	Not reported	>13
Hodgkin	III	EBV positive	356	0.7	1.3	3	PR	>60	AHSCT	>60
PEL	II	EBV and KSHV positive	450	1.2	1.3	6	CR*	>58	None	>58
DLBCL	III	EBV negative	237	0.4	1.3	3	PR	>55	AHSCT	>55
Plasmablastic	I	EBV positive	294	0.45	1.5	4	PR	5	Not reported	>14
DLBCL	IV	EBV negative	296	24 817	1.5	3	CR*	>43	None	52
DLBCL	IV	EBV positive	401	24	1.5	5	PR*	>65	Radiation	>65
DLBCL	I	Unknown	241	4.2	1.5	3	PR	2	Not reported	>12
DLBCL	II	Unknown	773	1.3	1.5	4	PR*	>52	R^2-GemOx + AHSCT	>52
DLBCL	IV	EBV negative	339	Undetectable	1.5	3	CR*	6†	AHSCT	16

Bortezomib days 1 and 8 of each cycle, ICE began day 8 of cycle 1 and day 1 of subsequent cycles.

REID et al Blood Advance 26 DECEMBER 2018 x VOLUME 2, NUMBER 24

Daratumumab





Daratumumab alone or with chemotherapy	Cases, age	Outcome	Author, year, ref.
Daratumumab + DHAP after 2 lines of CT + ABMT	1 (47)	CR 46 months	Chikeka I. 2019[80]
Daratumumab + COP after 1 line of CT in Transformed PBL+ABMT	1 (63)	P 2 months.	Marvyi8n K. 2020[81]
Daratumumab after 2 or more lines of CT and ABMT	3 (53)	P 2 months.	Roche P. 2021[82]
Daratumumab+ EPOCH	4(55)	3 CR 20 months PR 4 months	Ricker E. 2021[83]
Daratumumab + CyBorD	1(57)	CR 18 months	Ramadas P. 2021[84]
Daratumumab + Bortezomib and Lenalidomide > 2 lines of CT	1(45)	CR 36 months after AHCT	Kathrotiya M..2021[85]
Daratumumab + EPOCH, or + bortezomib and lenalidomide	7 (76)	6 CR (18-31) months 1 PR	Ryu YK 2021[86]
Daratumumab and Lenalidomide after 1 line of CT	1 (23)	PR >8 months	Lee M. 2022[55]
Daratumumab + ICE	5 (49)	5 CR 8-73 months	Dittus C. 2022[41]
Dartumumab+bortezomib + ABMT after B_EPOCH	1(38)	CR 18 months	Bhat G. 2022[87]
Daratumumab+ EPOCH	1 (66)	P 2 months.	Pinto MP 2023[88]
Active Clinical Trial		Status/sponsor	Clinical trial number
Daratumumab + DA-EPOCH		Recruiting/ AIDS malignancy Consortium	NCT04139304
Daratumumab, bortezomib and Dexamethasone		Recruiting/ Fondazione Italiana Linfomi	NCT04915248

1/4 pts

4/7 pts

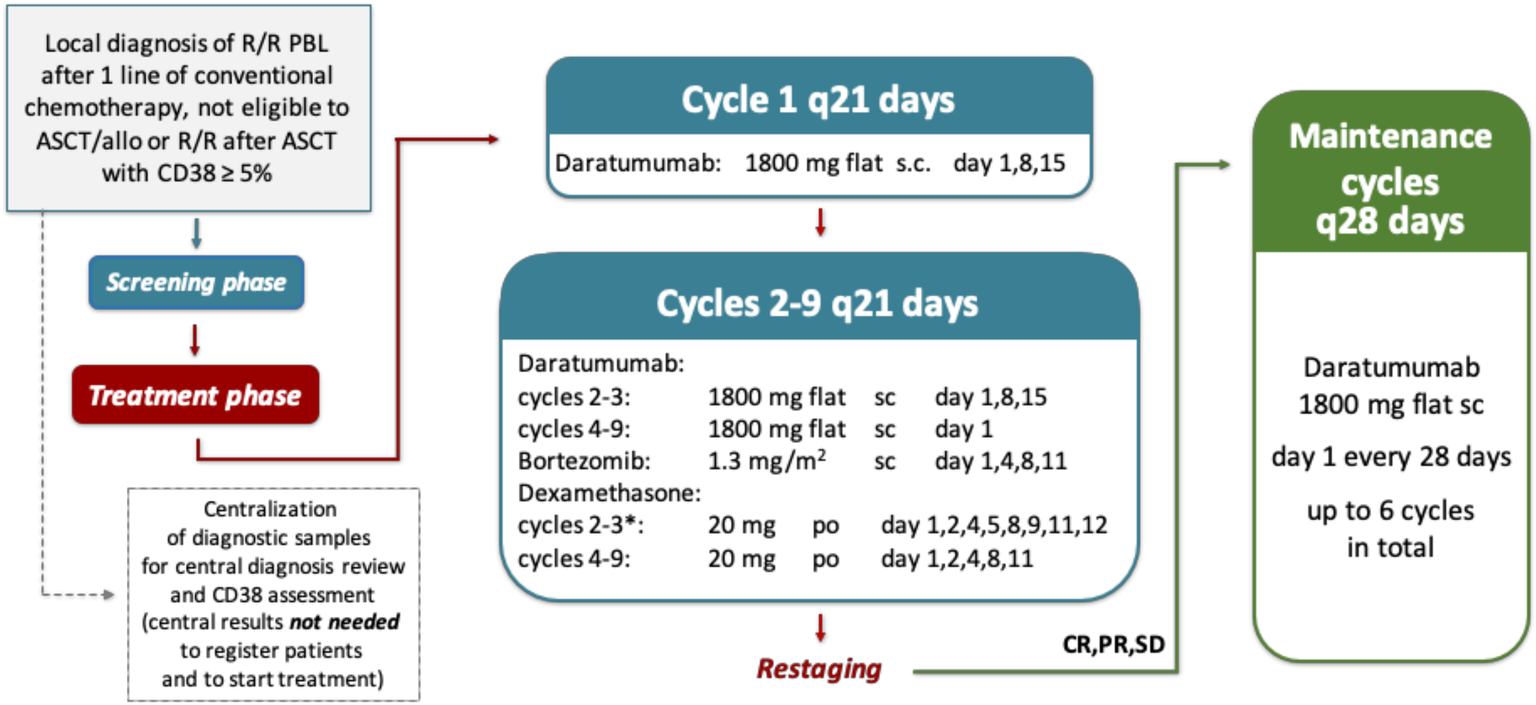
Bibas et al Mediterr J Hematol Infect Dis 2024

PBL Ongoing Trials

Table 1 Ongoing Trials

Regimen	Phase	Line of Therapy	Status	Location	Clinical Trial no
Dara-EPOCH	I	First line	Recruiting	USA	NCT04139304
Belantamab Mafodotin	II	Relapsed and Refractory	Recruiting	USA	NCT04676360
CARCD30	I	First line and relapsed	Active; not recruiting	USA	NCT01192464
Dara, bortezomib and Dexamethasone	II	Relapsed and refractory	Recruiting	Italy	NCT04915248
Allogenic EBV-CTLs targeting CD 19 antigen	I	Relapsed and refractory	Active, not recruiting	USA	NCT01430390
Pomalidomide and Dose-adjusted EPOCH	I	First line	Recruiting	USA	NCT05389423
Nivolumab With or Without Varlilumab	II	Relapsed/Refractory	Active, not recruiting	USA	NCT03038672

Phase 2 Study to Evaluate Activity and Safety of Daratumumab in combination with Bortezomib and Dexamethasone in patients with Relapsed or Refractory PBL (DALYA trial)



* in subjects >75 years, BMI< 18.5, diabetes: 20 mg weekly (day 1, 8, 15)

Treatment stop at any time if PD, unacceptable toxicity, consent withdrawal, investigator decision

CORRESPONDENCE

Daratumumab in Primary Effusion Lymphoma

47 year old, well controlled HIV
PEL: DA-EPOCH, BV, GEM-OX, ICE --> HSCT

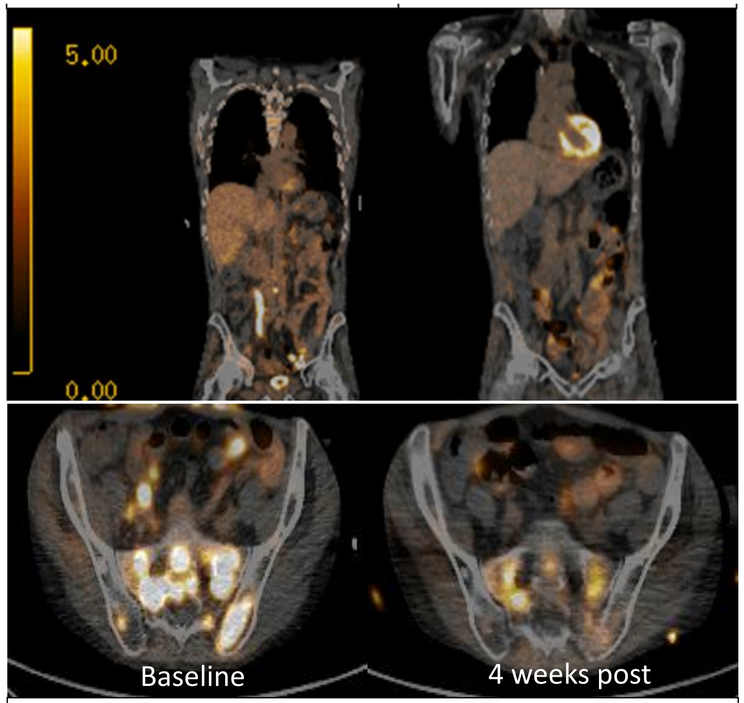


Figure S1. PET imaging prior to daratumumab (left) and response (right) after 4 weekly doses of daratumumab.

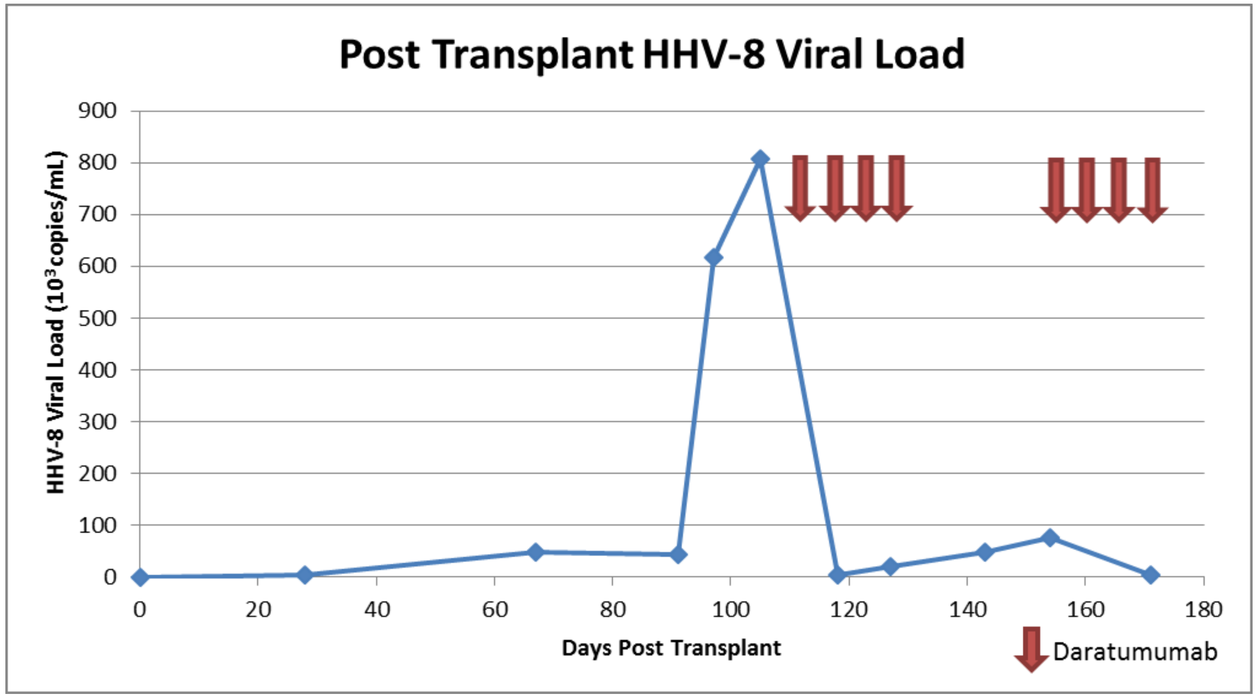


Figure S2. Post-transplant HHV-8 viral load with daratumumab (red arrow) treatment.

N ENGL J MED 379;7 NEJM.ORG AUGUST 16, 2018

Conclusioni

1. Linfomi in PLWH sono una popolazione particolare, che richiede centri attrezzati e collaborazione multidisciplinare.
2. Tale attenzione non dove essere motivo di discriminazione nell'accesso alle cure e ai nuovi farmaci
3. Importanza di includere pazienti HIV nei nuovi trial
4. Arruolare negli studi clinici specifici per pazienti HIV per informazioni sull'outcome
5. Le saltuarie esperienze su farmaci biologici e sull'immunoterapia in pazienti HIV in letteratura sono positive in termini di sicurezza

6. CAR-T nei pazienti HIV che ricevono terapia ART possono essere prodotti
7. Pochi dati a disposizione confermano che i CART nei pazienti HIV positivi possono essere sicuri (No SIRS)
8. Rimane incerta l'efficacia di CAR-T generati da Linfociti T infettati dall'HIV e l'interazione con le frequenti coinfezioni, soprattutto virali (EBV e HHV8).


рахмат
danke
謝謝
ngiyabonga
spas
teşekkür ederim
Баярлалаа
mersi
kia ora
barka
welalin
tack
mahalo
спасибо
faafetai lava
vinaka
dank je
misaotra
paldies
grazzi
tapadh leat
blagodaram
matondo
спасибі
kiitos
dankie
nanni
nandri
thank you
gracias
хвала
dhanyavad
mauruuru
asante
manana
bedankt
hvala
köszönöm
aciu
obrigada
tenki
bayarlalaa
gràçie
dankon
murakoze
enkosi
akun
djiere dieuf
tau
mochchakkeram
дякую
mamnun
dziękuję
chokrane
chnorakaloutioun
gratias ago
gràcies
sulpáy
go raibh maith agat
taiku
sobodi
dėkuji
sagolun
sukriya
kop khun krap
obrigado
arigatô
takk
dakujem
trugarez
mèsi
ありがとう
didi madloba
najis tuke
tanemirt
grazie
rahmet
dhanyavadagalu
shukriya
mercê
мерси
kam sah hamnida
terima kasih
rahmat
ευχαριστώ
diolch
তোমাকে ধন্যবাদ
감사합니다
xièxie
merci