LEUKEMIA & LYMPHOMA SOCIETY®

SPOTLIGHT ON HODGKIN LYMPHOMA (HL)

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Associate Professor of Medicine
Harvard Medical School
Boston, MA

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WELCOMING REMARKS

SPOTLIGHT ON HODGKIN LYMPHOMA (HL)

Lizette Figueroa-Rivera, MA
Sr. Director, Education & Support
The Leukemia & Lymphoma Society

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WELCOMING REMARKS

SPOTLIGHT ON HODGKIN LYMPHOMA (HL)

Erin Cummings, MSA, LCSW
Co-Founder & Executive Director, Hodgkin's International Inc.
Hodgkin Lymphoma Survivor

Be sure to visit Hodgkin's International website to learn more about their upcoming symposium June 7-9, 2024:

Hodgkin's International Symposium on Long-Term Survivorship: Instilling Hope and Advocating for Change!

HodgkinsInternational.org

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DISCLOSURES

SPOTLIGHT ON HODGKIN LYMPHOMA (HL)

Dr. Jeremy Abramson

Honoraria/Consultation:

AbbVie, Astra-Zeneca, BeiGene, BMS, Caribou Biosciences, Cellectar Biosciences, Genentech, Gilead, Interius, Janssen, Lilly, Seagen,Takeda

Grant Support:

BMS, Cellectis, Merck, Mustang Bio

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Mass General Brigham
Mass General Cancer Center

Hodgkin Lymphoma

Jeremy S. Abramson, MD

HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

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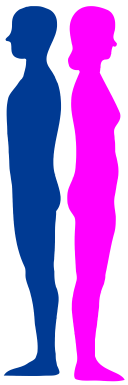
2024 Estimated US New Cancer Cases



Breast	313,510	16%
Prostate	299,010	15%
Lung & bronchus	234,580	12%
Colon & rectum	152,810	8%
Melanoma of skin	100,640	5%
Lymphoma	89,190	4%
Non-Hodgkin	80,620	
Hodgkin	8,570	
Urinary bladder	83,190	4%
Kidney	81,610	4%
Uterus	67,880	3%
Pancreas	66,440	3%
Leukemia	62,770	3%
Oral cavity & pharynx	58,450	3%
Liver and bile duct	41,630	2%
Multiple myeloma	35,780	2%
Central nervous system	25,400	1%
Ovary	19,680	1%
ALL SITES	2,001,140	

CA: A Cancer Journal for Clinicians, January/February 2024

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Ancient History

Thomas Hodgkin: "*On some morbid appearances of the absorbent glands and spleen." Medico-Chirurgical Transactions, London, 1832, 17: 68-114.*

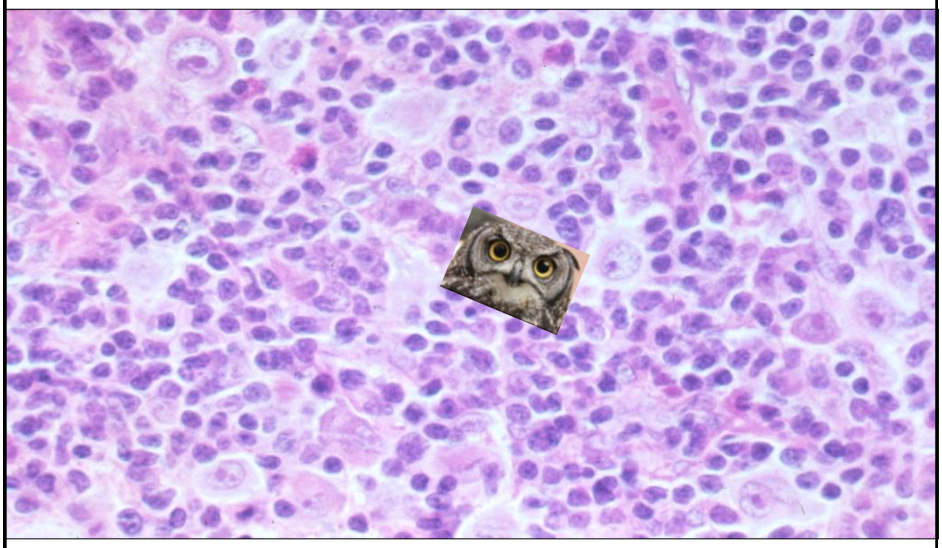
Dubbed "Hodgkin's Disease" in 1865 by Samuel Wilks. "*Cases of enlargement of the lymphatic glands and spleen*."

Dorothy Reed: "On the pathological changes in Hodgkin's disease, with special reference to its relation to tuberculosis." Johns Hopkins Hosp Rep 1902;10:133-96.

Karl Sternberg: "Uber eine eigenartige unter dem Bilde der Pseudoleukamie verlaufende Tuberculose des lymphatischen Apparates." Ztschr Heilk 1898;19:21-90.

In 1994 Kuppers and Rajevsky find clonal IgV gene rearrangements and somatic hypermutation in microdissected R-S cells

7



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Hodgkin Lymphoma Classification

- Neoplastic tissues usually contain few neoplastic cells in an inflammatory cell rich background
- Subtypes differ in terms of clinical features, how they appear under the microscope, and frequency of EBV infection

- *Classical Hodgkin lymphoma*
  - *Nodular sclerosis*
  - Mixed cellularity
  - Lymphocyte rich
  - Lymphocyte depleted

- *Nodular lymphocyte predominant Hodgkin lymphoma*

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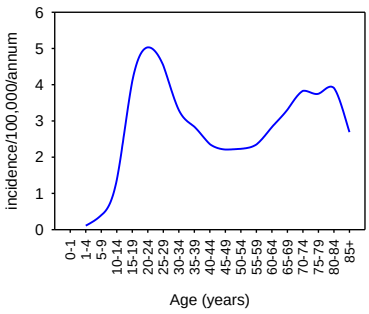
Epidemiology

- Incidence 8500 cases per year, 900 deaths
- Median age 35
  - Bimodal distribution
- Slight male predominance
- Incidence is stable
- Risk factors
  - Most cases are sporadic
  - 2-4 fold increased risk after mono
  - 3-5 fold increased risk among 1st degree relatives
  - 100-fold increased risk in identical twins
  - 10-fold increased risk in HIV infection



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Clinical Presentation

- 70% present with painless lymph node enlargement
- Limited in 55%, Advanced in 45%
- 30% will have "B" symptoms
  - Fever, drenching night sweats, >10% weight loss in prior 6 months
- Diffuse itching
- Hypercalcemia (increased 1,25 (OH)2 Vit D production)
- Very rare- pain with alcohol

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Involved sites at Presentation

Nodal regions
- Cervical/Supraclavicular (L>R) 60-70%
- Mediastinal 60%
- Axillary 25-35%
- Hilar nodes 15-35%
- Para-aortic 30-40%
- Iliac 15-20%
- Inguinal 8-15%
- Mesenteric 1-4%

Other lymphoid organs
- Spleen 30-35%
- Waldeyer's ring 1-2%

Extranodal sites (10-15%)
- Liver 2-6%
- Bone marrow 2-8%
- Other organs (lung, bone) 10%

From Mauch, PM, ed. 1999

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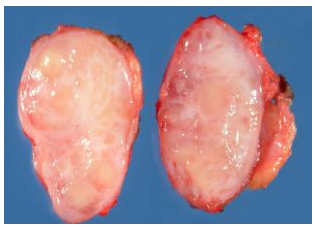
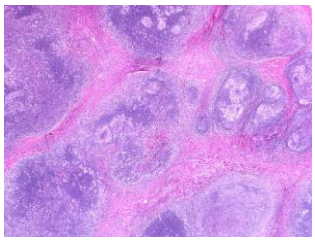
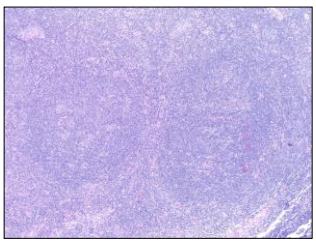
Diagnosis

- Fine Needle Aspiration (FNA) insufficient
- Not detected by flow cytometry
- Core needle or excisional biopsy required







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Initial Evaluation and Workup

History
- "B" symptoms, functional status, pulmonary and cardiac history

Physical exam

Staging studies
- PET/CT scan
- Bone marrow usually not required

Fertility counseling

Labs
- CBC with differential
- Erythrocyte Sedimentation Rate
- Albumin, LFTs, Ca++
- HIV and hepatitis serologies

Preparation for chemotherapy
- Echocardiogram
- Pulmonary Function Tests, with DLCO (if bleomycin is planned)
- Consider port-a-cath

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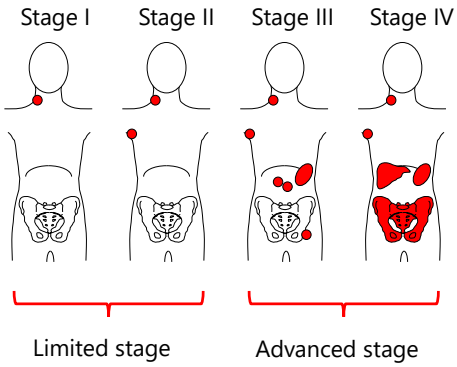
Ann Arbor / Lugano Staging System



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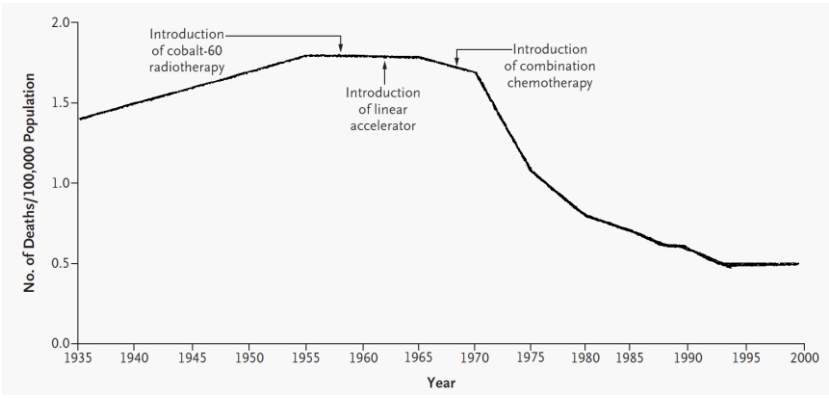
Therapy and Incidence of Death from Hodgkin Lymphoma



DeVita NEJM 2003

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Treatment of NLPHL

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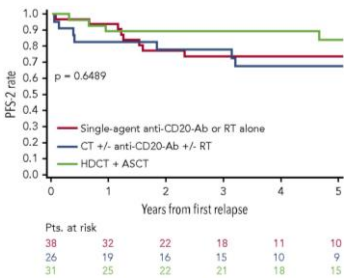
Nodular Lymphocyte Predominant Hodgkin Lymphoma (NLPHL)

- Indolent natural history, risk of late relapse or transformation
- Radiation or surgical excision alone for localized cases
- Advanced stage disease often treated with R-CHOP
- Treatment at relapse is often extrapolated from NHL

Progression-free survival after 2nd line therapy for NLPHL



Eichenauer et al. Blood 2018

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Treatment of Classic Hodgkin Lymphoma

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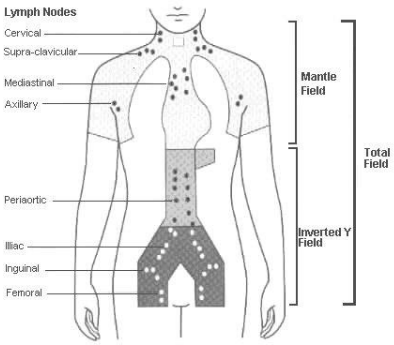
Radiation Therapy for Hodgkin Lymphoma



1901: Crude x-irradiation noted active against lymphoid disease

1931: Gilbert and Babaiantz report remission in 7/15 patients by treating involved and adjacent nodal regions

1950: Peters reports 10 year OS of 79% in stage I HD

1956: linear accelerator developed by Henry Kaplan, and others.

For years, represented the standard treatment for limited stage HL

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Chemotherapy for Hodgkin Lymphoma

- 1942: Louis Goodman and Alfred Gilman recruited to US Department of Defense from Yale University to study therapeutic value of chemical warfare toxins
- December 2, 1943: Nazis launch air attack on Allied forces in Bari, Italy, including USS John Harvey, carrying a secret cargo of 2,000 mustard gas bombs, each of which held 60-70 lb of sulfur mustard.
- G&G observed that autopsies of soldiers killed had profound lymphoid hypoplasia and myelosuppression
- Expose mice to mustard gas and document regression of lymphoid xenograft
- They recruit Gustav Lindskog to inject nitrogen mustard into a patient with advanced lymphoma and airway obstruction
- Mediastinal and lymphatic masses regressed… if only fleetingly

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Evolution of Chemotherapy for cHL

MOPP developed at National Cancer Institute in 1964
- 54% freedom from progression at 10 years
- Sterilizing
- Leukemogenic

ABVD developed at Milan Cancer Institute in 1973
- Not sterilizing
- Not associated with MDS or leukemia
- Superior to MOPP in a randomized trial

<u>For a period- drastically different standards of care:</u>
- Radiation for limited stage disease
- Chemotherapy for advanced stage disease

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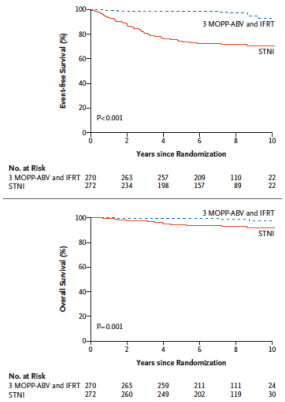
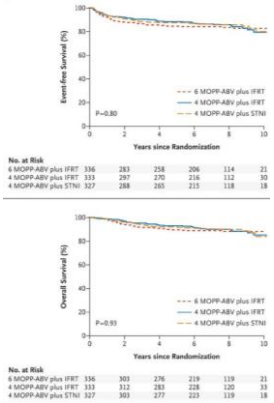
Combined Modality Therapy is Superior to Radiation Alone and allows reduction in both chemotherapy and radiation field





Fermé C et al. *N Engl J Med.* 2007;357:1916-1927.

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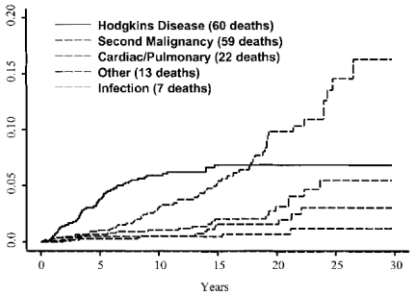
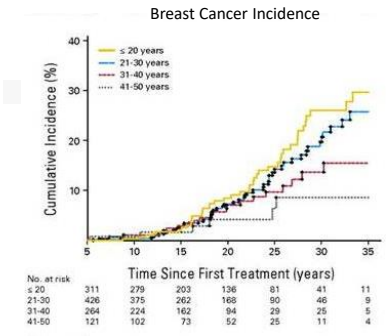
Beware the Late Effects of Therapy





Ng AK et al. *J Clin Oncol.* 2002;20:2101-2108.; De Bruin ML et al. *J Clin Oncol.* 2009;27:4239-4246.

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How low can you go?

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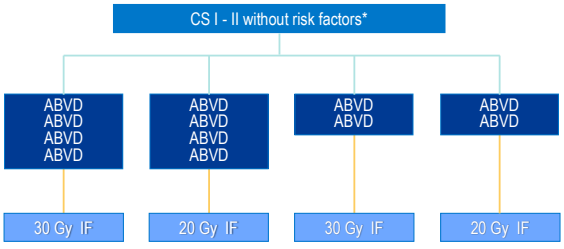
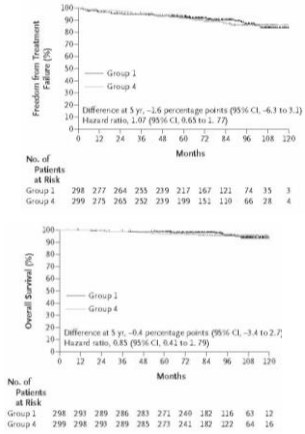
Less is more for chemotherapy and radiation



8Risk factors: Large mediastinal mass, extranodal disease, >3 nodal regions, elevated ESR



Engert A et al. *N Engl J Med.* 2010;363:640-652.

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Omitting radiation entirely based on interim PET scan

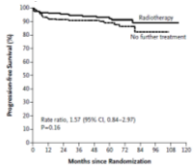
Non-bulky: 3-4 cycles of ABVD

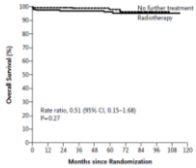
Progression-free survival

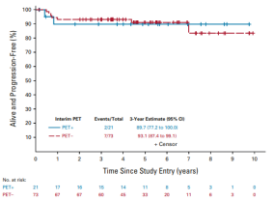
Overall survival

Bulky: 6 cycles of ABVD

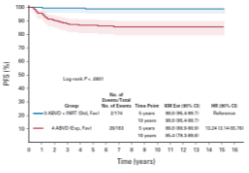
UK Rapid

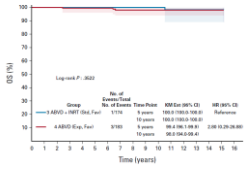






EORTC





Radford J et al. NEJM 2015; Federico, et al. JCO 2023; LaCasce, et al. JCO 2023

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Treatment of limited stage classical HL today

- Goal is for chemotherapy alone for 4-6 cycles of ABVD
- Radiation is reserved for settings of suboptimal response to chemotherapy alone

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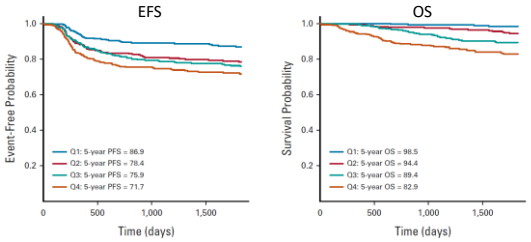
New risk model for advanced stage Hodgkin lymphoma

Advanced stage Hodgkin IPI for patients age 18-65

- Age (continuous)
- Male Gender (yes, no)
- Stage (2B, 3, 4)
- Bulk (yes, no)
- Lymphocyte count (continuous)
- Hemoglobin (continuous)
- Albumin (continuous)



https://holistic-calculator.web.app/

Rodday, et al. JCO 2023

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Treatment of advanced stage disease

- Goal is to maximize cure and reduce treatment-associated toxicity
- ABVD had long been standard of care since vanquishing MOPP
- Randomized trial showed that bleomycin can be discontinued if PET scan after 2 cycles is negative
- Can addition of novel agents improve outcomes further?

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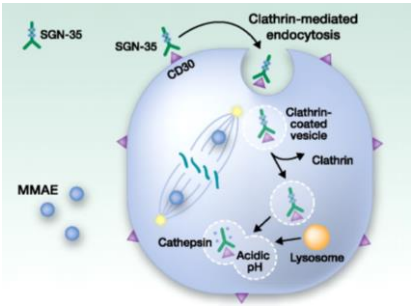
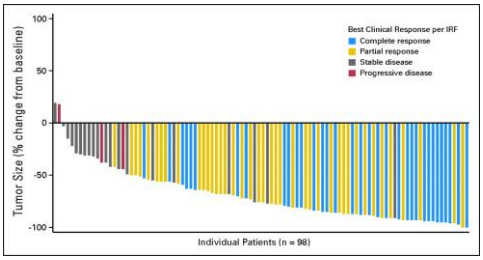
Brentuximab vedotin





Katz J et al. CCR 2011; Younes et al. JCO 2012

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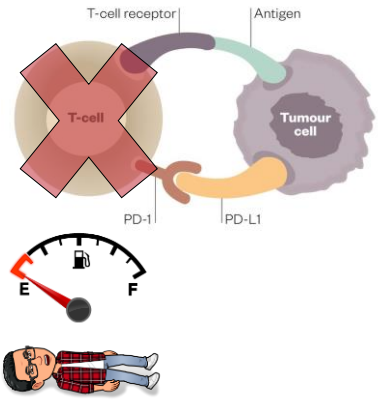
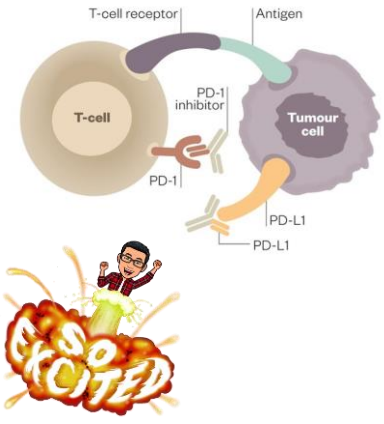
Immune checkpoint inhibitors





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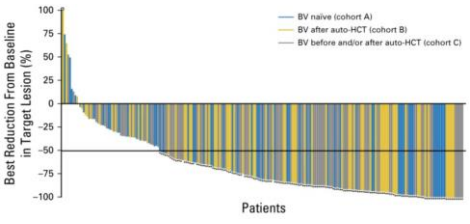
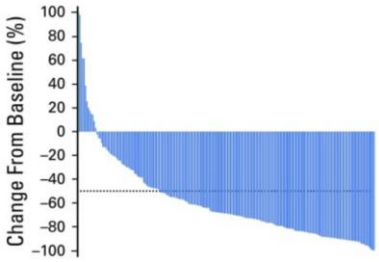
Nivolumab or Pembrolizumab in relapsed Hodgkin lymphoma





Armand, et al. JCO 2018; Chen, et al. JCO 2017

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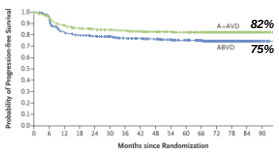
Incorporation of novel targeted therapies for advanced stage disease

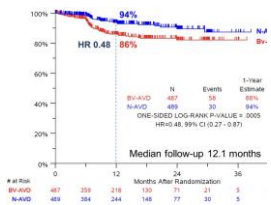
Substitution of Brentuximab vedotin for bleomycin (Bv-AVD) improved progression-free (2018) and overall survival (2022) compared to ABVD

- Eliminated risk of bleomycin lung injury
- Higher risk of peripheral neuropathy and neutropenic fever



Substitution of Nivolumab for Brentuximab vedotin for bleomycin (Nivo-AVD) improved progression-free survival (2023) compared to Bv-AVD

- Less neuropathy with nivolumab
- Low rate of immune related adverse events
- Follow-up is still brief, not yet FDA approved



Ansell, et al. NEJM 2022; Herrera, et al. Proc ASCO 2023

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Relapsed cHL

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Treatment at relapse is personalized to the patient

- Young fit patients receive 2nd line therapy followed by high dose chemotherapy and autologous stem cell transplant if responding to treatment
  - 2nd line therapy options: Pembro-GVD, Pembro-ICE, Nivo-ICE, Bv-nivo
  - BEAM high dose chemotherapy with autologous stem cell transplant
  - Maintenance brentuximab vedotin post transplant may be used in high-risk patients
- Older patients (not eligible for transplant)
  - Single agent therapy: Pembrolizumab, Nivolumab, Brentuximab vedotin
  - Combination: Bv-nivo

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Survivorship

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Considerations during Survivorship

- Risk of relapse
- Ongoing side effects
  - Fatigue, peripheral neuropathy, immune suppression, fatigue, anxiety
- Late risks
  - Radiation: Thyroid dysfunction, secondary malignancies, heart disease, lung disease
  - Chemotherapy: Bleomycin lung injury, neuropathy, cardiomyopathy, late bone marrow injury (myelodysplasia, leukemia)
- Survivorship care is personalized to the patient based on risk factors and treatment received

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The future

- Hodgkin lymphoma remains a highly treatable and highly curable disease
- No cure rate less than 100% is good enough, and there is no such thing as a “good cancer”
- Ongoing research efforts are seeking to incorporate targeted therapies and reduce quantity and intensity of chemotherapy and radiation to improve likelihood of cure with less toxicity
- Novel approaches including CAR T-cells and bispecific antibodies are under investigation

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Thank you for your attention!

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ASK A QUESTION
SPOTLIGHT ON HODGKIN LYMPHOMA (HL)

Ask a question by phone:

Press star (*) then the number 1 on your keypad.

Ask a question by web:

Click “Ask a question”

Type your question

Click “Submit”

Due to time constraints, we can only take one question per person. Once you’ve asked your question, the operator will transfer you back into the audience line.

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LLS EDUCATION & SUPPORT RESOURCES

HOW TO CONTACT US:

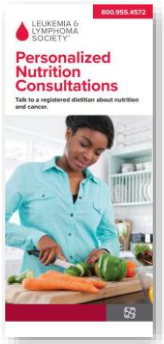
To contact an **Information Specialist** about disease, treatment and support information, resources and clinical trials:

Call: (800) 955-4572
Monday to Friday, 9 a.m. to 9 p.m. ET

Chat live online: www.LLS.org/InformationSpecialists
Monday to Friday, 10 a.m. to 7 p.m. ET

Email: www.LLS.org/ContactUs
All email messages are answered within one business day.

CLINICAL TRIAL SUPPORT CENTER
Work one-on-one with an LLS Clinical Trial Nurse Navigator who will help you find clinical trials and personally assist you throughout the entire clinical-trial process.
www.LLS.org/Navigation



NUTRITION CONSULTATIONS
Our registered dietitian has expertise in oncology nutrition and provides free one-on-one consultations by phone or email.
www.LLSNutrition.org

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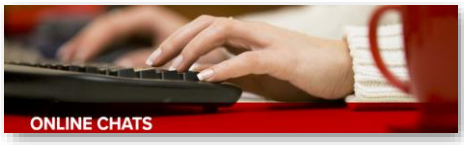
LLS EDUCATION & SUPPORT RESOURCES



Online Chats

Online Chats are free, live sessions, moderated by oncology social workers. To register or for more information, please visit **www.LLS.org/Chat**

Education Videos

View our free education videos on disease, treatment, and survivorship. To view all patient videos, please visit **www.LLS.org/EducationVideos**

Patient Podcast

The Bloodline with LLS is here to remind you that after a diagnosis comes hope. To listen to an episode, please visit **www.TheBloodline.org**

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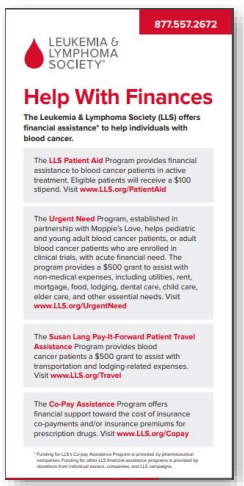
LLS EDUCATION & SUPPORT RESOURCES



The Leukemia & Lymphoma Society (LLS) offers the following financial assistance programs to help individuals with blood cancers: www.LLS.org/Finances

To order free materials: **www.LLS.org/Booklets**

LEUKEMIA & LYMPHOMA SOCIETY

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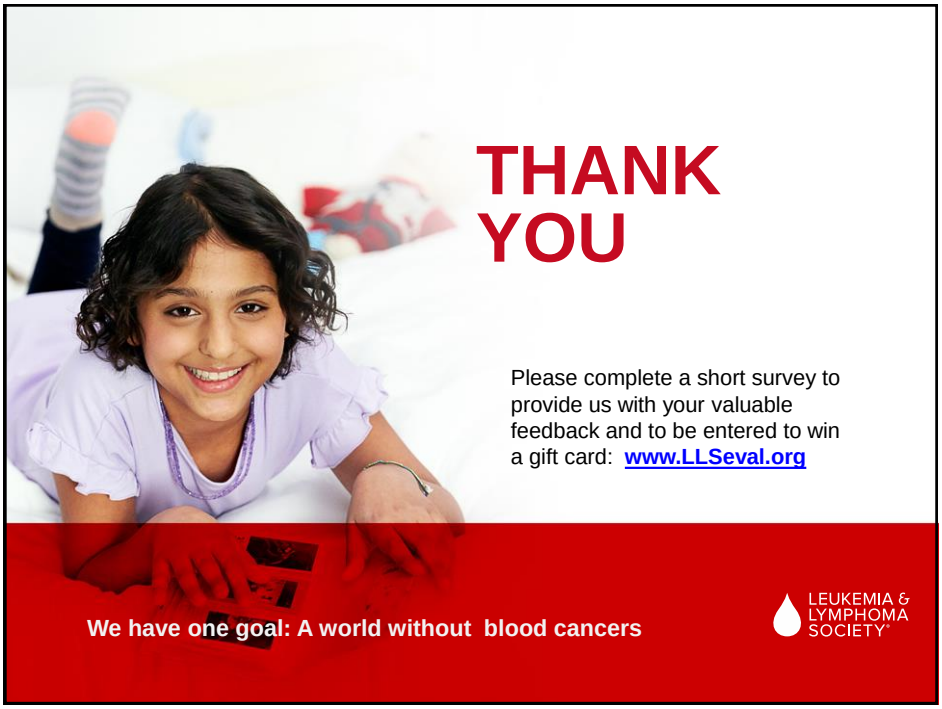
THANK YOU
Please complete a short survey to provide us with your valuable feedback and to be entered to win a gift card: www.LLSeval.org
We have one goal: A world without blood cancers
LEUKEMIA & LYMPHOMA SOCIETY®

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