Hodgkin Lymphoma (HL):
Diagnosis, Treatment and Side Effect Management

LEUKEMIA & LYMPHOMA SOCIETY®

1

Learning Objectives

- Describe the various subtypes of Hodgkin lymphoma (HL)
- Identify tests used to diagnose disease and monitor treatment of HL
- Explain the overarching goals of treatment for the subtypes of HL
- Explain approved and emerging treatment options for HL, including stem cell transplantation, and the role of clinical trials
- Describe strategies to manage treatment side effects as well as potential long-term and late effects of treatments for HL
- Describe the roles of the pharmacist, the nurse, and the social worker in treating patients classical HL

LEUKEMIA & LYMPHOMA SOCIETY®

2

Faculty

Matthew Matasar, MD
Chief of Blood Disorders
Rutgers Cancer Institute of New Jersey
New Brunswick, NJ

David Awad, Pharm D, BCOP
Clinical Pharmacist Specialist
Division of Blood Disorders
Rutgers Cancer Institute of New Jersey
New Brunswick, NJ

LEUKEMIA & LYMPHOMA SOCIETY®

3

Disclosures

David Awad, Pharm D, BCOP, has no financial relationships with ineligible companies.

Matthew Matasar, MD, has financial relationships with the following companies:

Advisory Board: Allogene, Epizyme, Genmab, Genentech, Kite, Merck, Regeneron

Consultant: AbbVie, AstraZeneca, Bristol Myers Squib, Epizyme, Novartis, Regeneron, Roche, Pfizer

Research Support: ADC Therapeutics, AstraZeneca, Bristol Myers Squibb, Epizyme, Johnson & Johnson, Kite, Regeneron, Roche, Pfizer

Tara McCabe, APN, AOCNP, MSN, has no financial relationships with ineligible companies.

LEUKEMIA & LYMPHOMA SOCIETY®

4

Roadmap

Overview of Hodgkin lymphoma

Treatment of newly diagnosed Hodgkin lymphoma

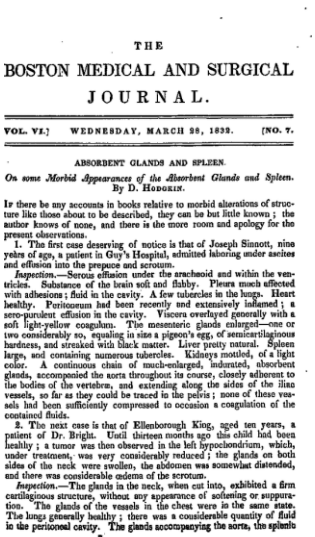
Treatment of relapsed or refractory disease

Emerging and novel therapies

LEUKEMIA & LYMPHOMA SOCIETY

5

In The Beginning…



THE
BOSTON MEDICAL AND SURGICAL
JOURNAL.

VOL. VI.] WEDNESDAY, MARCH 28, 1832. [NO. 7.

ABSORBENT GLANDS AND SPLEEN.

On some Morbid Appearances of the Absorbent Glands and Spleen.
By D. Hodgkin.

In there be any accounts in books relative to morbid alterations of structure like those about to be described, they can be but little known; the author knows of none, and there is the more room and apology for the present observations.

1. The first case deserving of notice is that of Joseph Sinnott, nine years of age, a patient in Guy's Hospital, admitted laboring under ascites and effusion into the prepuce and scrotum.

Inspection.—Serous effusion under the arachnoid and within the ventricles. Substance of the brain soft and flabby. Pleura much affected with adhesions; fluid in the cavity. A few tubercles in the lungs. Heart healthy. Pericardium had been recently and extensively inflamed; a sero-purulent effusion in the cavity. Viscera overlayed generally with a soft light-yellow coagulum. The mesenteric glands enlarged—one or two considerably so, equaling in size a pigeon's egg, of semicartilaginous hardness, and streaked with black matter. Liver pretty natural. Spleen large, and containing numerous tubercles. Kidneys mottled, of a light color. A continuous chain of much-enlarged, indurated, absorbent glands, accompanied the aorta throughout its course, closely adherent to the bodies of the vertebræ, and extending along the sides of the iliac vessels, so far as they could be traced in the pelvis; none of these vessels had been sufficiently compressed to occasion a coagulation of the contained fluids.

2. The next case is that of Ellenborough King, aged ten years, a patient of Dr. Bright. Until thirteen months ago this child had been healthy; a tumor was then observed in the left hypochondrium, which, under treatment, was very considerably reduced; the glands on both sides of the neck were swollen, the abdomen was somewhat distended, and there was considerable edema of the scrotum.

Inspection.—The glands in the neck, when cut into, exhibited a firm cartilaginous structure, without any appearance of softening or suppuration. The glands of the vessels in the chest were in the same state. The lungs generally healthy; there was a considerable quantity of fluid in the pericardial cavity. The glands accompanying the aorta, the spleen

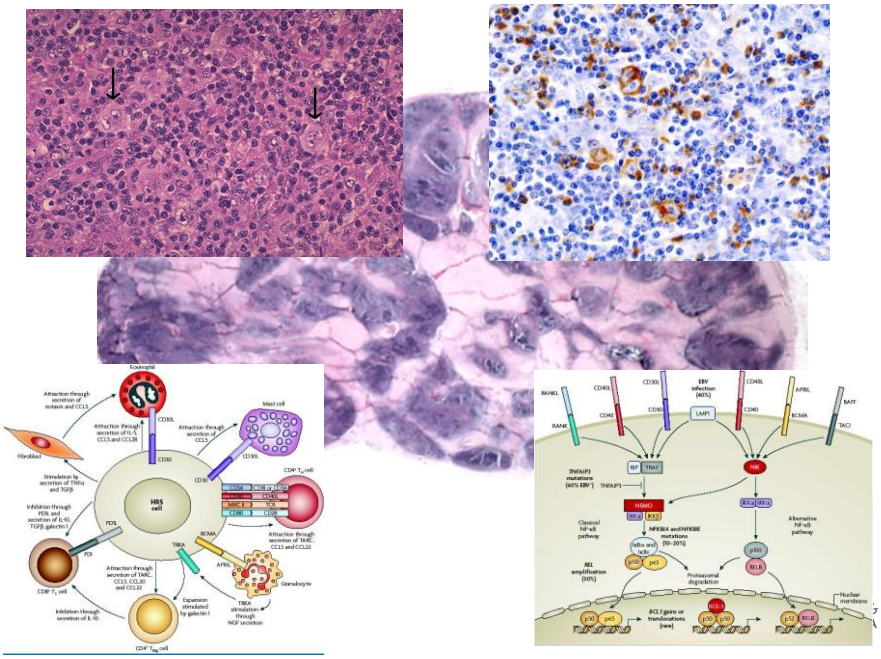
7

(1798-1866)

LEUKEMIA & LYMPHOMA SOCIETY

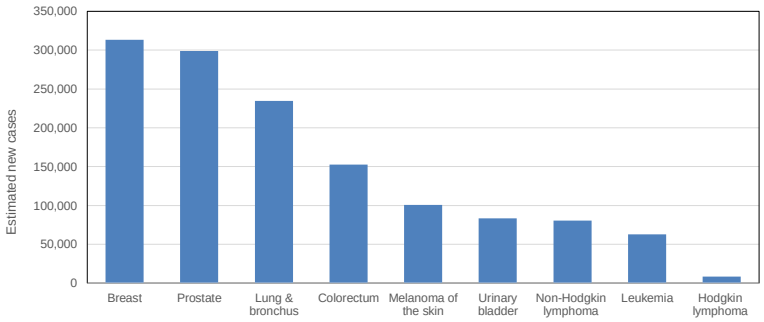
6

Hodgkin Lymphoma Biology

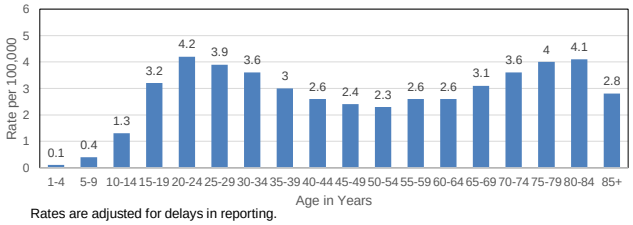


7

Estimated New Cancer Cases, US, 2024



Hodgkin's Lymphoma incidence rate by age, US, 2016-2020



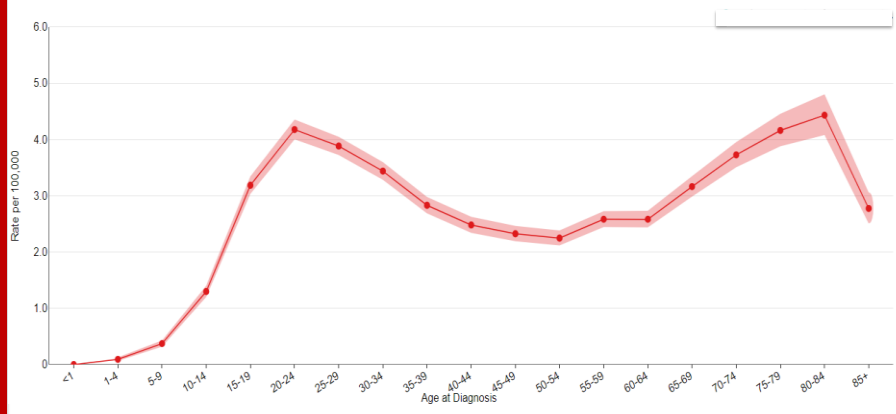
Rates are adjusted for delays in reporting.

LEUKEMIA & LYMPHOMA SOCIETY®

Source: American Cancer Society, 2024.
North American Association of Central Cancer Registries, 2024.

8

Hodgkin Lymphoma
SEER Incidence Rates by Age at Diagnosis, 2016-2020



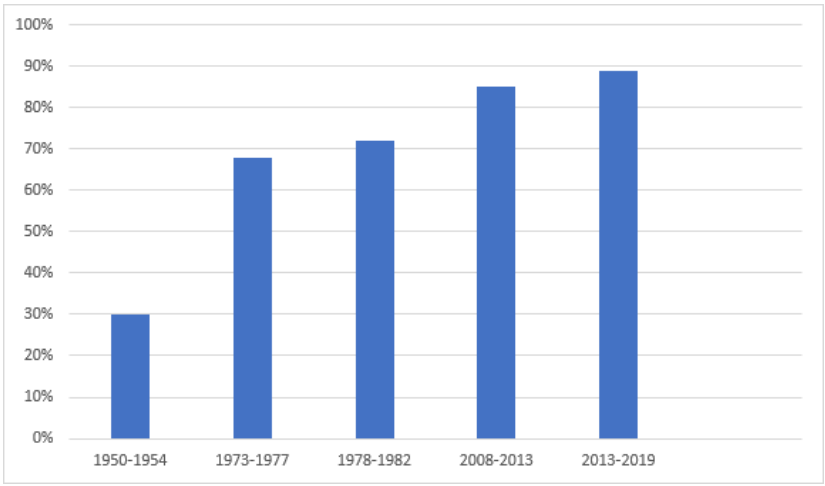
Estimated 2023 US Incidence
~ 8830

SEER*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program, National Cancer Institute; 2023 Apr 19. [updated: 2023 Nov 16; cited 2024 Jan 18]. Available from: https://seer.cancer.gov/statistics-network/explorer/. Data source(s): SEER Incidence Data, November 2022 Submission (1975-2020).

LEUKEMIA & LYMPHOMA SOCIETY®

9

A Cancer Success Story



5-year survival rates 2013-2019 are 88.9%

Mokdad et al. JAMA 2017 317(4):388-406

LEUKEMIA & LYMPHOMA SOCIETY®

10

What Are the Signs of Hodgkin lymphoma?

Non-tender lymph node enlargement (localized)

- Neck, collarbone, armpit most commonly
- Middle of chest (mediastinum) on X-rays or scans
- Groin or pelvis less common

"B symptoms"

- Recurring fevers
- Drenching night sweats
- Unexplained weight loss (10%)

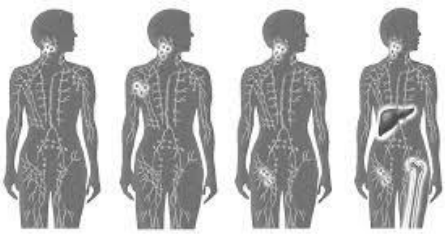
Other symptoms

- Fatigue, itchiness without rash
- Cough, chest pain, or shortness of breath
- Aching pain in chest or areas of swollen nodes after drinking alcohol

LEUKEMIA & LYMPHOMA SOCIETY®

11

"Staging" Hodgkin lymphoma



Stage I	Stage II	Stage III	Stage IV
Early Stage: Favorable		Advanced Stage	
Early Stage: Unfavorable			

LEUKEMIA & LYMPHOMA SOCIETY®

12

Roadmap

Overview of Hodgkin lymphoma

Treatment of newly diagnosed Hodgkin lymphoma

Treatment of relapsed or refractory disease

Emerging and novel therapies

LEUKEMIA & LYMPHOMA SOCIETY

13

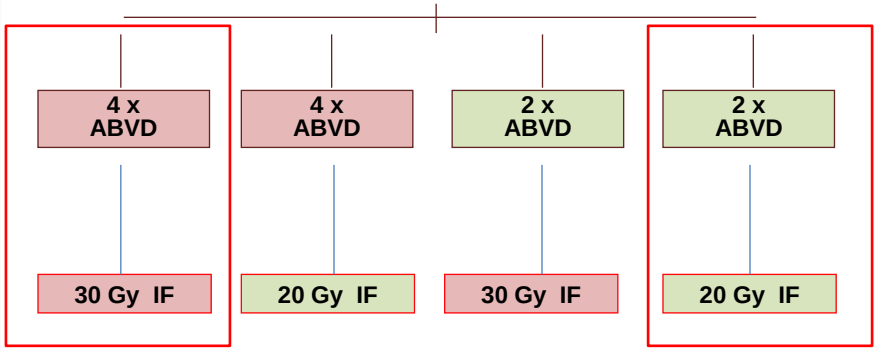
Treatment of Hodgkin lymphoma

LEUKEMIA & LYMPHOMA SOCIETY

14

Early Stage Favorable HL

1,190 patients with early stage (stage I/II), no risk factors



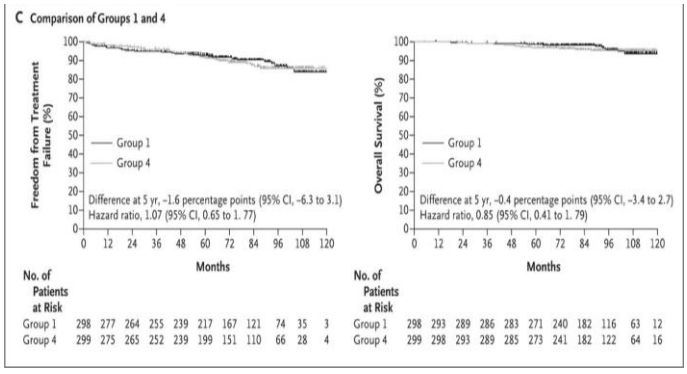
ABVD: doxorubicin hydrochloride (Adriamycin®), bleomycin sulfate (Blenoxane®), vinblastine sulfate (Alkaban-AQ®), and dacarbazine (DTIC-Dome®)
Gy: amount of radiation used in photon radiation therapy is measured in grays; IF: involved-field radiation therapy

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

LEUKEMIA & LYMPHOMA SOCIETY®

15

"Freedom from Treatment Failure" **Overall Survival**



Most vs Least treatment:

ABVD x 4 + 30 Gy
vs
ABVD x 2 + 20 Gy

ABVD: doxorubicin hydrochloride (Adriamycin®) , bleomycin sulfate (Blenoxane®), vinblastine sulfate (Alkaban-AQ®), and dacarbazine (DTIC-Dome®)

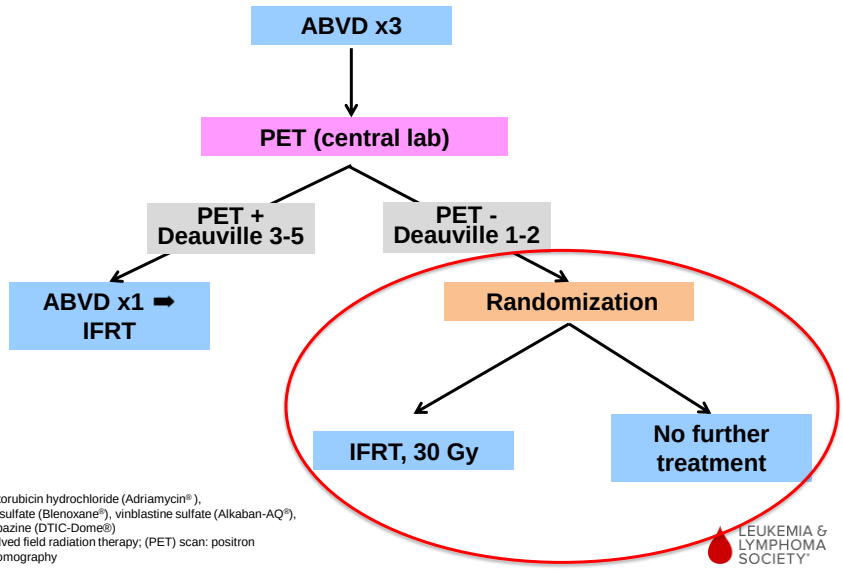
Engert A et al. *N Engl J Med.* 2010;363:640-652.

LEUKEMIA & LYMPHOMA SOCIETY®

16

RAPID Trial

STAGE I/II, NO BULK, NO B SYMPTOMS



ABVD: doxorubicin hydrochloride (Adriamycin®), bleomycin sulfate (Blenoxane®), vinblastine sulfate (Alkaban-AQ®), and dacarbazine (DTIC-Dome®)
IFRT: Involved field radiation therapy; (PET) scan: positron emission tomography

Radford J et al. *N Engl J Med.* 2015;372:1598-1607.

LEUKEMIA & LYMPHOMA SOCIETY®

17

"Deauville" Criteria for PET Scan Results

Score	FDG-PET / CT scan result
1	No uptake above background
2	Uptake ≤ mediastinum
3	Uptake > mediastinum but ≤ liver
4	Uptake moderately more than liver uptake, at any site
5	Markedly increased uptake at any site or new sites of disease

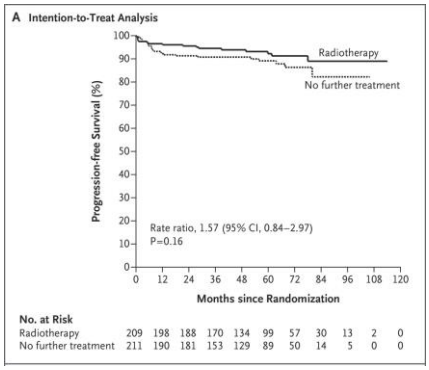
(For RAPID: Only scores of 1 or 2 = PET negative)

LEUKEMIA & LYMPHOMA SOCIETY®

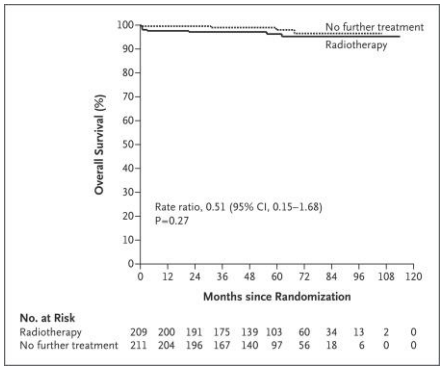
18

RAPID's Results in the PET-Negative Patients

PFS



OS



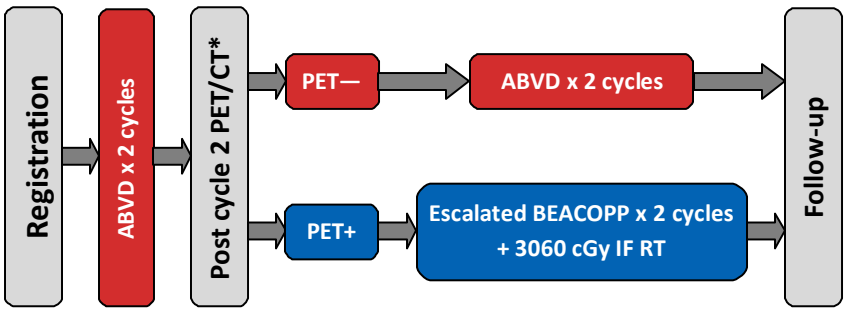
PFS: Progression-Free survival; OS: Overall Survival

Radford J et al. *N Engl J Med.* 2015;372:1598-1607.

LEUKEMIA & LYMPHOMA SOCIETY®

19

CALGB 50604 Design



Phase II trial in newly-diagnosed stages I/II non-bulky HL conducted in Intergroup (CALGB/Alliance, SWOG, ECOG)

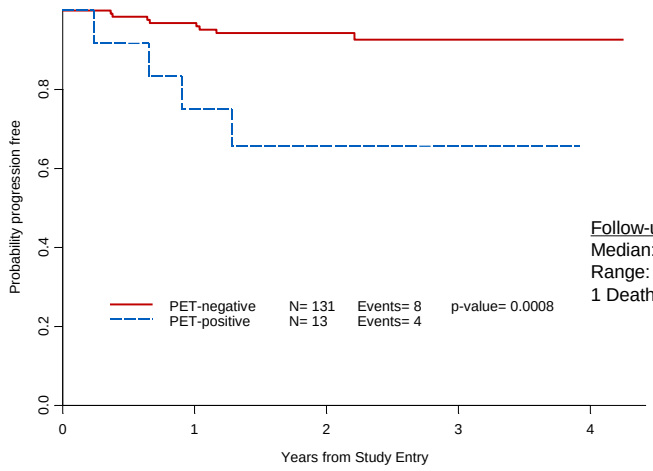
Prophylactic G-CSF only after febrile neutropenia or neutropenia and infection with ABVD. Prophylactic G-CSF with escalated BEACOPP.

G-CSF: prophylactic granulocyte colony-stimulating factor
BEACOPP: A chemotherapy regimen consisting of bleomycin (Blenoxane®), etoposide (Topasar®), doxorubicin hydrochloride (Adriamycin®), cyclophosphamide (Cytoxan®), vincristine (Oncovin®), procarbazine (Matulane®) and prednisone
ECOG: Eastern Cooperative Oncology Group
SWOG: Southwest Oncology Group

LEUKEMIA & LYMPHOMA SOCIETY®

20

CALGB 50604 Progression-Free Survival
Post cycle 2 ABVD PET- and PET+ Patients



Follow-up time
Median: 2.1 years
Range: <1month – 4.3 years
1 Death (Suicide – PET +)

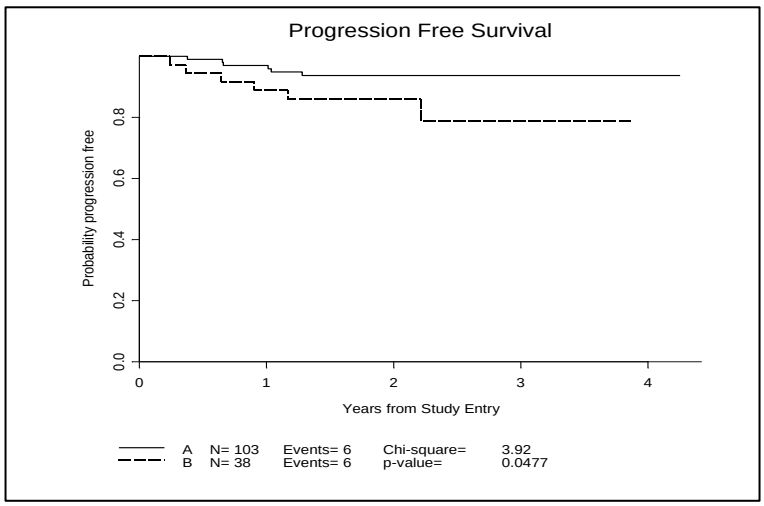
	Est. 3-yr PFS	Hazard Ratio
PET -	92% (84%-96%)	6.04 (1.82-20.08)
PET +	66% (32%-86%)	

Blood. 2015;126:578.

LEUKEMIA & LYMPHOMA SOCIETY®

21

CALGB 50604
PFS for "A" vs. "B" Disease



LEUKEMIA & LYMPHOMA SOCIETY®

22

Breaking Down ABVD

Adriamycin® (doxorubicin)	Bleomycin (Blenoxane®)	Vinblastine (Alkaban-AQ®)	Dacarbazine (DTIC-Dome®)
Mechanism: - Intercalates b/w base pairs, inhibits topo II	**Mechanism**: - Causes single and double strand DNA breaks	**Mechanism**: - Inhibits microtubule formation	**Mechanism**: - Alkylating agent (active metabolite; MTIC)
Admin: Intravenous	**Admin**: Intravenous	**Admin**: Intravenous	**Admin**: Intravenous
AE: - Vesicant - Cardiomyopathy - Nausea (moderate) - Secondary malignancies - Discoloration of urine	**AE**: - Pulmonary fibrosis - Interstitial pneumonitis - Hyperpigmentation - Mucositis - Fever/chills	**AE**: - Vesicant - Myelosuppression - Mucositis - Intrathecal admin → fatal (ISMP 2014) - Peripheral neuropathy	**AE**: - Myelosuppression - Nausea (high) - Flu-like malaise - Photosensitivity
Organ dysfunction: - Renal: none - Hepatic: consider adj for Tbili > 1.2 or AST/ALT > 2X ULN	**Organ dysfunction:** - Renal: consider adj for CrCl < 50 mL/min - Hepatic: none	**Organ dysfunction:** - Renal: none - Hepatic: consider adj for Tbili > 1.5 or AST/ALT > 2X ULN	**Organ dysfunction:** - Renal: consider adj for CrCl < 60 mL/min - Hepatic: none
DDI: - CYP3A4, 2D6 (major) - P-glycoprotein	**DDI**: - None	**DDI**: - CYP3A4 (major) - P-glycoprotein	**DDI**: - CYP1A2 (major)

LEUKEMIA & LYMPHOMA SOCIETY®

23

Supportive Care for ABVD

Bleomycin Pulmonary Toxicity

- Risk Factors
  - >400 units lifetime dose
  - Elderly
  - Prior radiation therapy
  - Renal dysfunction
  - History of lung disease
- Monitoring
  - Baseline PFT's, DLCO – prn during therapy
- Growth factor
  - Safe to treat through neutropenia without dose reduction (requires prophylaxis against fungus and PJP)
  - Concern that growth factor could increase risk of BPT, but recent data question this *(Binder AF et al. Int J Hematol Oncol Stem Cell Res 2017).*

Extravasation

- Vesicants
  - Erythema, blistering, necrosis of tissues
  - "DNA binding vesicant"
    - Doxorubicin, mechlorethamine
  - "Non-DNA binding vesicant"
    - Vinblastine
- Management
  - Stop infusion, aspirate any drug
  - Do not flush line
  - Apply compress
    - Vinblastine – warm
    - Doxorubicin– cold
  - Drug-specific
    - Doxorubicin
      - Dexrazoxane
      - DMSO (dimethyl sulfoxide)
    - Vinblastine
      - Hyaluronidase

LEUKEMIA & LYMPHOMA SOCIETY®

24

Escalated BEACOPP

- **B**leomycin (Blenoxane®) – day 8
- **E**toposide (Toposar®) – days 1-3
- **A**driamycin® (doxorubicin) – day 1
- **C**yclophosphamide (Cytoxan®) – day 1
- **O**ncovin® (vincristine) – day 8
- **P**rednisone – oral, days 1-14
- **P**rocarbazine (Matulane®) – oral, days 1-7

LEUKEMIA & LYMPHOMA SOCIETY®

* Repeat every 21 days with growth factor support.

25

Escalated BEACOPP

- **B**leomycin (Blenoxane®) – day 8
- **E**toposide (Toposar®) – days 1-3
- **A**driamycin® (doxorubicin) – day 1
- **C**yclophosphamide (Cytoxan®) – day 1
- **O**ncovin® (vincristine) – day 8
- **P**rednisone – oral, days 1-14
- **P**rocarbazine (Matulane®) – oral, days 1-7

Every 21 days with growth factor support.

Adverse Effect	COPP-ABVD	Std BEACOPP	**Esc BEACOPP**
Leukopenia (grade 4)	19%	37%	90%
Thrombocytopenia (grade 4)	2%	3%	47%
Anemia (grade 4)	1%	1%	15%
Infection (grade 4)	1%	3%	8%
Mucositis (grade ≥ 3)	1%	2%	8%
Alopecia (grade ≥ 3)	36%	75%	79%

LEUKEMIA & LYMPHOMA SOCIETY®

Diehl V et al. *N Engl J Med.* 2003;348:2386-95.

26

Escalated BEACOPP

- **B**leomycin (Blenoxane®)– IV push, day 8
- **E**toposide (Toposar®)– IV infusion, days 1-3
- **A**driamycin® (doxorubicin) – IV push, day 1
- **C**yclophosphamide (Cytoxan®) – IV infusion, day 1
- **O**ncovin® (vincristine) – IV infusion, day 8
- **P**rednisone – oral, days 1-14
- **P**rocarbazine (Matulane®) – oral, days 1-7
  - Highly emetogenic (>90%)
    - Prophylaxis
    - Consider evening dosing
  - Disulfiram-like reaction (EtOH)
  - MAO* inhibitor
    - Drug interactions
  - Avoid tyramine-containing foods
    - Aged Cheeses, Pepperoni, Pickled Foods
    - Wine
  - CNS depression
  - Typically restricted to a specialty pharmacy, requiring prior authorization

LEUKEMIA & LYMPHOMA SOCIETY®

*MAO: monoamine oxidase

27

Appropriate Chemotherapy Dosing for Obese Adult Patients with Cancer

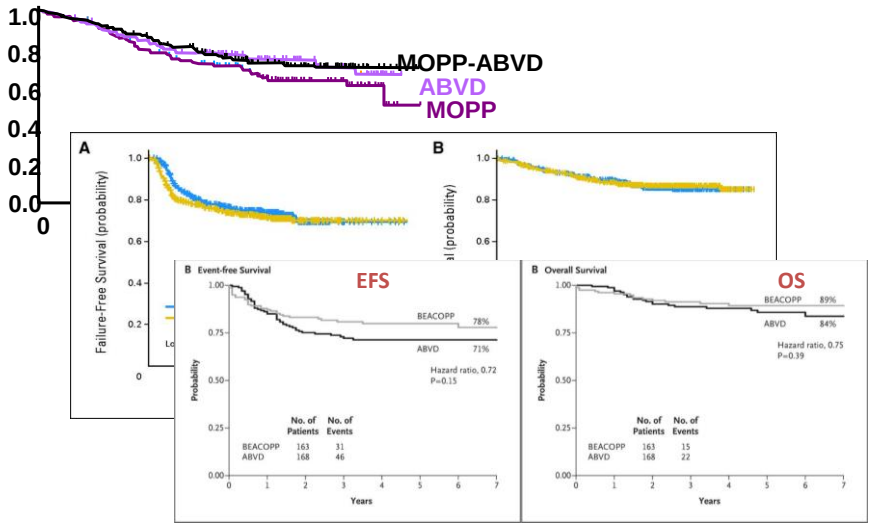
- Use **full weight-based** chemotherapy doses (unless specifically noted) when therapeutic goal is cure
- **Toxicity not shown to be increased** for obese patients receiving full weight-based doses
  - Obese patients receiving full doses of chemotherapy experience similar or less myelosuppression
- Concern regarding **under-dosing** and inferior outcomes if dose-capping were to be utilized

LEUKEMIA & LYMPHOMA SOCIETY®

Griggs JJ et al. *Journ Clin Oncol.* 2012;30(13):1553-1561.

28

Treatment of Advanced Stage HL

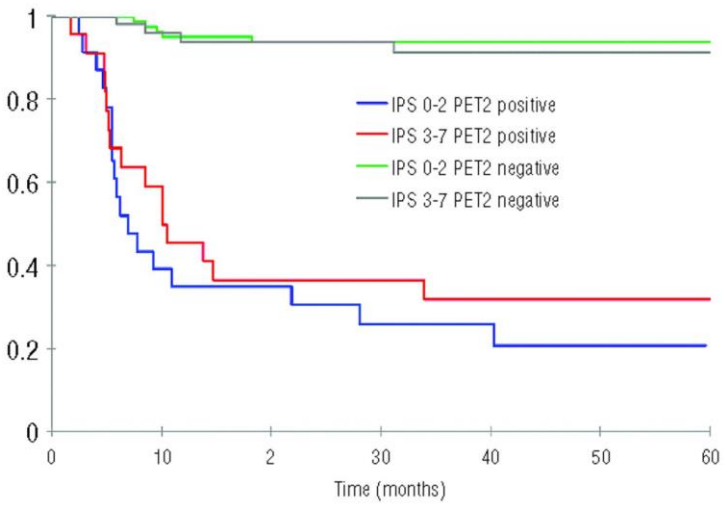


Stanford V treatment (doxorubicin [Adriamycin®], vinblastine [Alkaban-AQ®], mechlorethamine [Mustargen®], etoposide, vincristine [Oncovin®], bleomycin [Blenoxane®], prednisone)

LEUKEMIA & LYMPHOMA SOCIETY®

29

What About "Interim PET"?

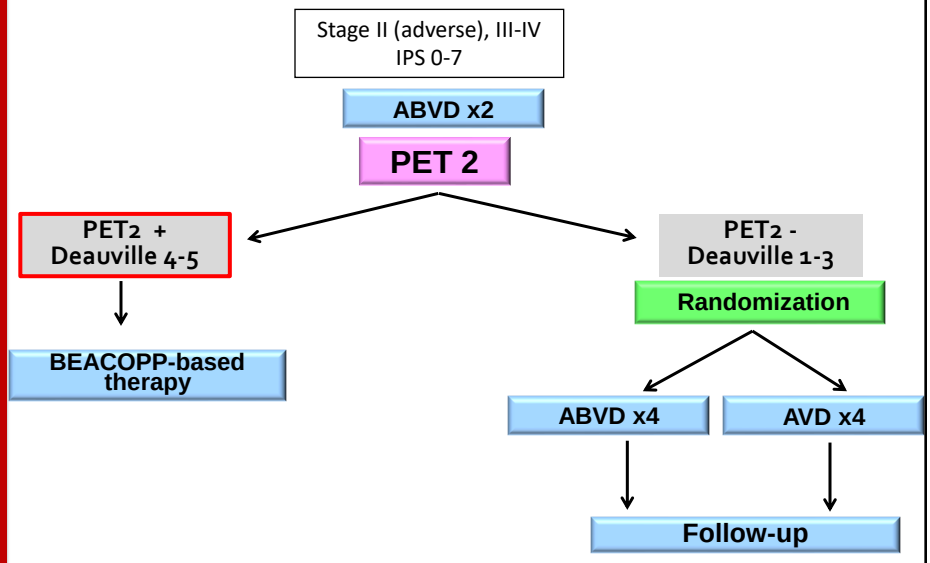


Andrea Gallamini et al. *Haematologica.* 2014;99:1107-1113.

LEUKEMIA & LYMPHOMA SOCIETY®

30

RATHL Trial



ABVD: doxorubicin hydrochloride (Adriamycin®), bleomycin sulfate (Blenoxane®), vinblastine sulfate (Alkaban-AQ®), and dacarbazine (DTIC-Dome®)

Johnson PW, et al. *13th ICML*; 2015; Abst 008.

LEUKEMIA & LYMPHOMA SOCIETY®

31

How'd the PET2 Negative Patients do?

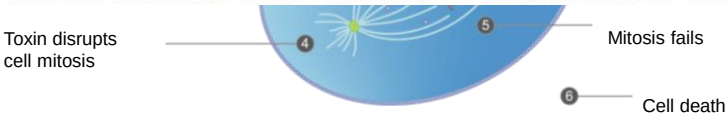
	ABVD N=469	AVD N=466
Complete remission	65%	69%
Deaths (N)	14	14
3-yr PFS	85.4%	84.4%
3-yr OS	97.1%	97.4%
Severe lung disease	3.6%	0.6% (P=.002)

ABVD: doxorubicin hydrochloride (Adriamycin®), bleomycin sulfate (Blenoxane®), vinblastine sulfate (Alkaban-AQ®), and dacarbazine (DTIC-Dome®)

LEUKEMIA & LYMPHOMA SOCIETY®

32

Brentuximab vedotin (Adcetris®): ADC (Antibody-Drug Conjugate)

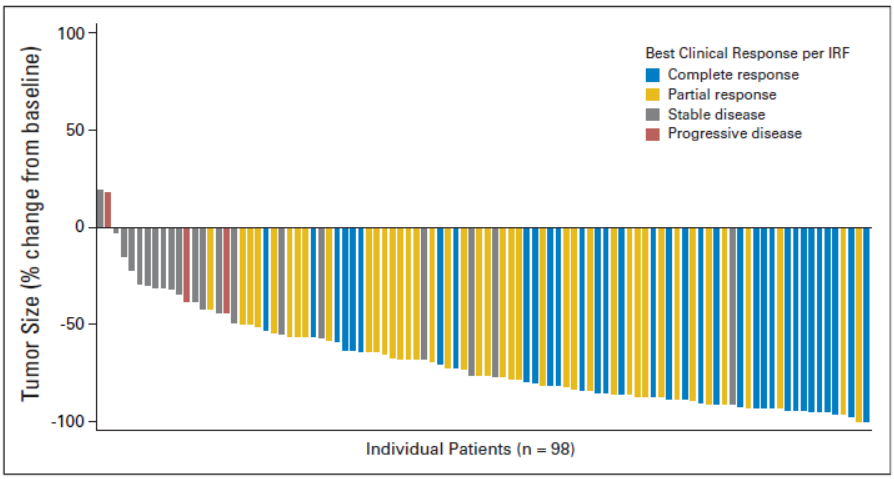


LEUKEMIA & LYMPHOMA SOCIETY®

Younes A et al. *N Engl J Med.* 2010; 363:1812-21 (appendix).

33

Brentuximab (Adcetris®) in Multiply Relapsed HL

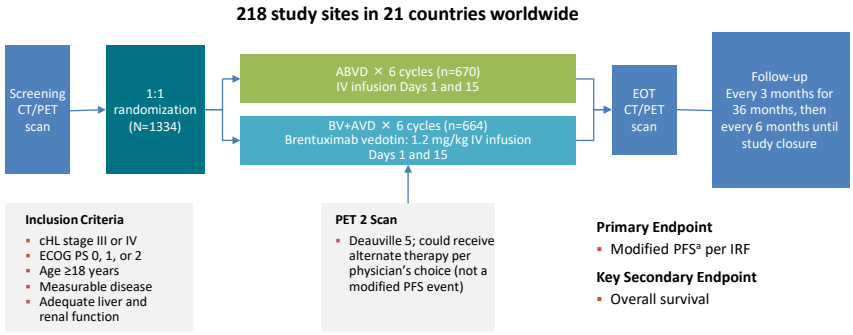


IRF: independent review facility

Younes A et al. *J Clin Oncol.* 2012;30: 2183-9.

34

ECHELON-1: BV+AVD vs ABVD in Advanced cHL



Inclusion Criteria
- cHL stage III or IV
- ECOG PS 0, 1, or 2
- Age ≥18 years
- Measurable disease
- Adequate liver and renal function

PET 2 Scan
- Deauville 5; could receive alternate therapy per physician's choice (not a modified PFS event)

Primary Endpoint
- Modified PFS[a] per IRF

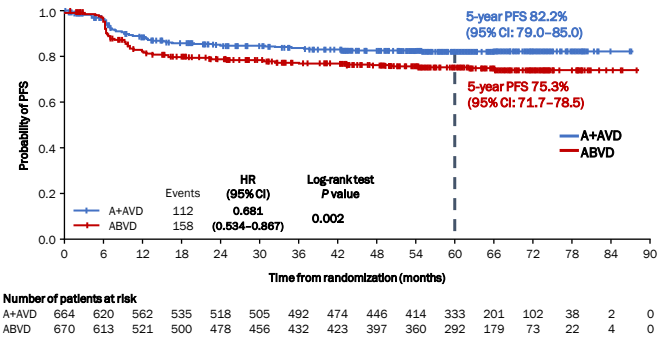
Key Secondary Endpoint
- Overall survival

[a] Modified PFS: Progression, death from any cause, or receipt of additional anticancer therapy for patients not in CR after completion of frontline therapy.
Ansell SM, et al. *N Engl J Med*. 2022;387(4):310-320.

LEUKEMIA & LYMPHOMA SOCIETY®

35

ECHELON-1: PFS Per Investigator at 5-Year Follow-up



Number of patients at risk

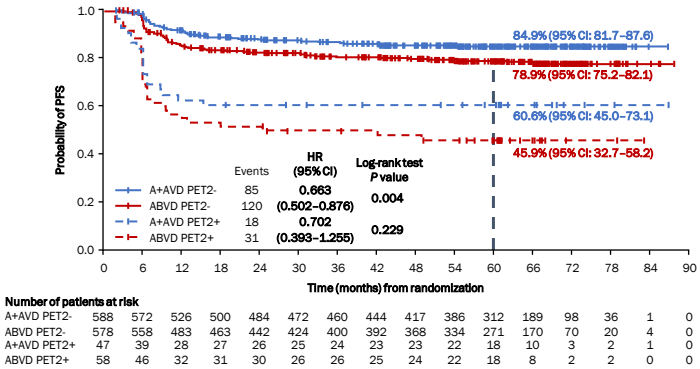
A+AVD	664	620	562	535	518	505	492	474	446	414	333	201	102	38	2	0
ABVD	670	613	521	500	478	456	432	423	397	360	292	179	73	22	4	0

LEUKEMIA & LYMPHOMA SOCIETY® 36

Straus DJ, et al. Presented at: 62nd ASH Annual Meeting. December 5-8, 2020 [Virtual]. Abstract 2973.

36

ECHELON-1: 5-year PFS Rates by PET2 Status



Number of patients at risk

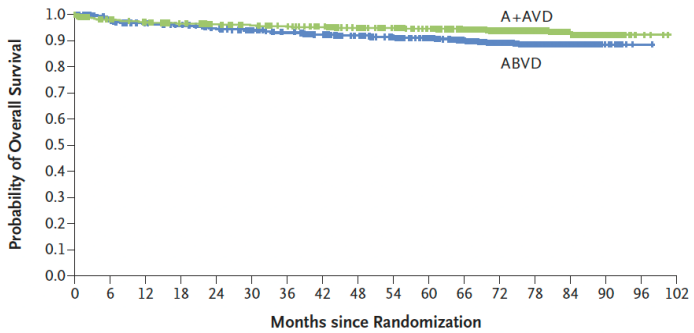
A+AVD PET2-	588	572	526	500	484	472	460	444	417	386	312	189	98	36	1	0
ABVD PET2-	578	558	483	463	442	424	400	392	368	334	271	170	70	20	4	0
A+AVD PET2+	47	39	28	27	26	25	24	23	23	22	18	10	3	2	1	0
ABVD PET2+	58	46	32	31	30	26	26	25	24	22	18	8	2	2	0	0

LEUKEMIA & LYMPHOMA SOCIETY® 37

Straus DJ, et al. Presented at: 62nd ASH Annual Meeting. December 5-8, 2020 [Virtual]. Abstract 2973.

37

ECHELON-1: Overall Survival



6-year OS 93.9% (95% CI: 91.6-95.5)

6-year OS 89.4% (95% CI: 86.6-91.7)

No. at Risk

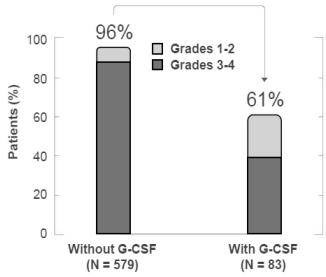
A+AVD	664	638	626	612	598	584	572	557	538	517	494	461	350	209	97	27	4	0
ABVD	670	634	614	604	587	567	545	527	505	479	454	411	308	191	84	11	1	0

LEUKEMIA & LYMPHOMA SOCIETY®

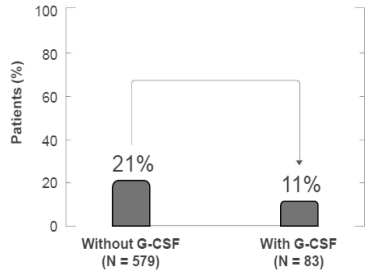
38

ECHELON-1: G-CSF Primary Prophylaxis and Effects on Neutropenia with BV+AVD Treatment

BV+AVD: Neutropenia Rate, by Grade, With and Without G-CSF Primary Prophylaxis



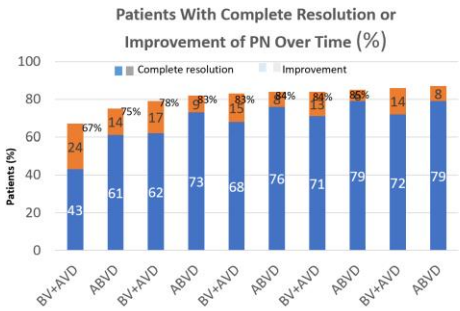
BV+AVD: Febrile Neutropenia Rate, Any Grade, With and Without G-CSF Primary Prophylaxis

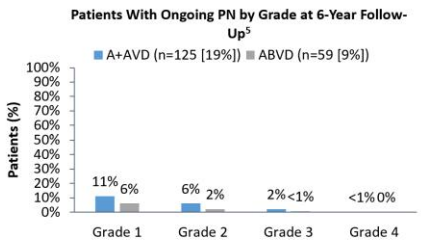


LEUKEMIA & LYMPHOMA SOCIETY®

39

ECHELON-1: Peripheral Neuropathy Resolution and Improvement

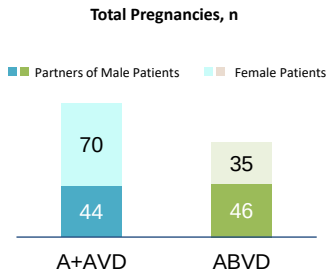


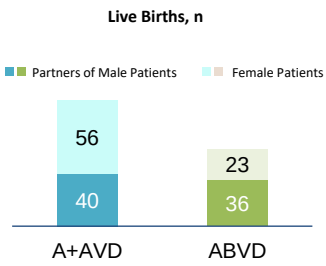


LEUKEMIA & LYMPHOMA SOCIETY®

40

ECHELON-1: Pregnancy Data





- 195 pregnancies were reported among patients and their partners (A+AVD: 114; ABVD: 81)
- No still births were reported in either arm

LEUKEMIA & LYMPHOMA SOCIETY®

41

Brentuximab Vedotin (Adcetris®)

- Indication(s)
  - Previously untreated stage 3-4 cHL (**in combination with AVD**)
  - Relapsed cHL following 2 or more therapies or following ASCT
  - **Consolidation** in cHL patients at high risk of relapse post-ASCT
- Dosing
  - 1.2-1.8 mg/kg (max weight: **100 kg**) every 2-3 weeks (depending on indication)
  - IV infusion over 30 minutes
  - No routine premedications
- Precautions/Warnings
  - BBW: Progressive multifocal leukoencephalopathy (PML)
  - Myelosuppression, infection
  - Dermatologic
  - Renal
    - CrCl < 30 mL/min: contraindicated
    - MMAE excreted renally, inc grade 3/4 toxicities in severe impairment
  - Hepatic
    - CP A: Reduce dose (1.8 → 1.2 mg/kg, 1.2 → 0.9 mg/kg)
    - CP B/C: Avoid use
    - **MMAE** metabolized hepatically, 2.2 fold inc in AUC in hepatic impairment

AVD: Adriamycin® (doxorubicin), vinblastine, dacarbazine; ASCT: autologous stem cell transplant;
CP: Child Pugh; MMAE: monomethyl auristatin E

LEUKEMIA & LYMPHOMA SOCIETY®

42

Roadmap

Overview of Hodgkin lymphoma

Treatment of newly diagnosed Hodgkin lymphoma

Treatment of relapsed or refractory disease

Emerging and novel therapies

LEUKEMIA & LYMPHOMA SOCIETY

43

Treatment of Relapsed / Refractory HL

Three main types of treatments

- **Chemotherapy (ICE⁺, GVD*, bendamustine)**
- **Brentuximab vedotin (if not used yet)**
- **"Checkpoint inhibitors" (nivolumab, pembrolizumab)**

Treatment programs often combine them:

- **Pembrolizumab + GVD**
- **Brentuximab + nivolumab**
- **Brentuximab + bendamustine**

Goal is usually

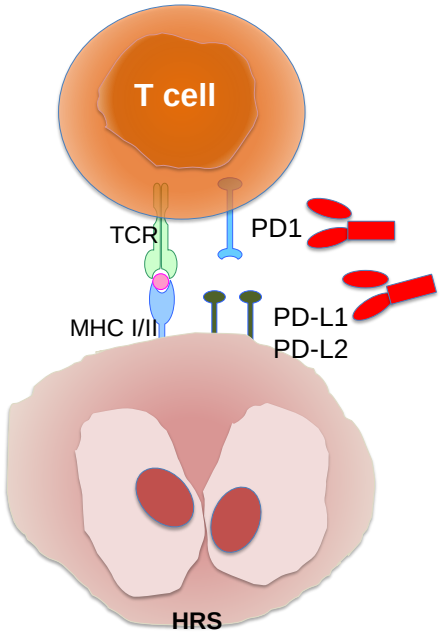
1) **Remission, and then**
2) **Autologous (self) stem cell transplant**

ICE⁺ ifosfamide, carboplatin, and etoposide
GVD: gemcitabine, vinorelbine, doxorubicin

LEUKEMIA & LYMPHOMA SOCIETY

44

Immunotherapy in HL: "Checkpoint Inhibitors"



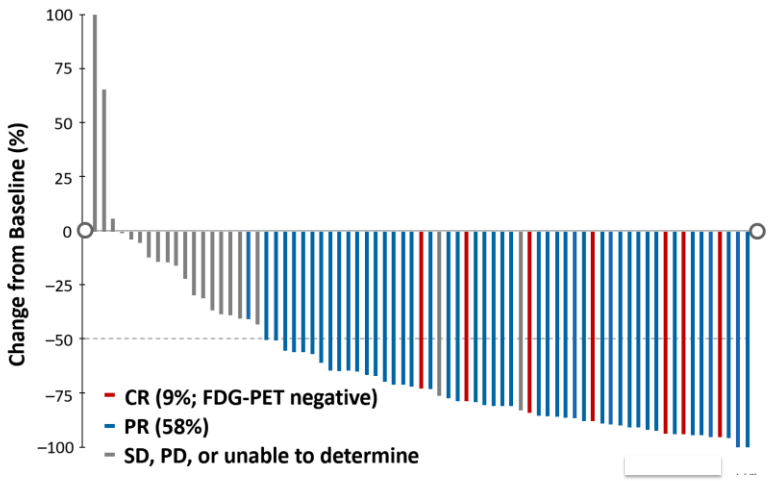
HRS: Hodgkin Reed-Sternberg Cell

Adapted from Stathis & Younes: Ann Oncology 2015.

LEUKEMIA & LYMPHOMA SOCIETY

45

Nivolumab (Opdivo®) in Multiply Relapsed HL



CheckMate 205B

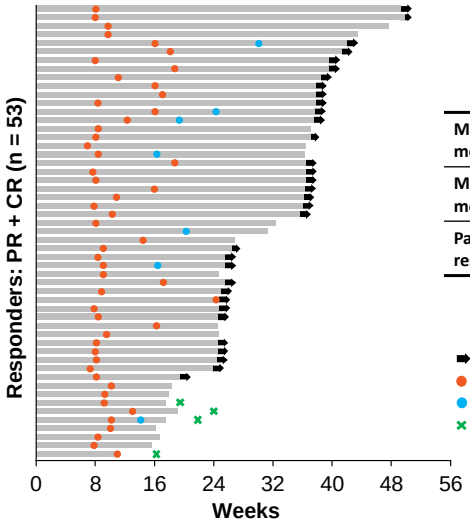
Per IRRC assessment.

46

LEUKEMIA & LYMPHOMA SOCIETY

46

Time to and Durability of Response to nivolumab (Opdivo®)



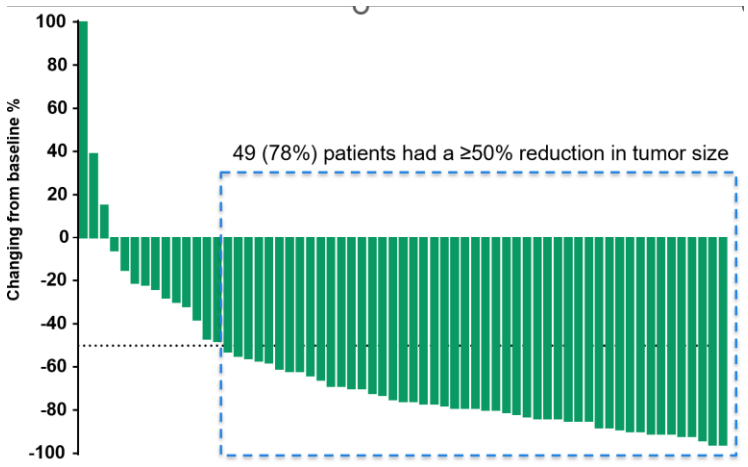
Median time to response, months (range)	2.1 (1.6–5.7)
Median duration of response, months (95% CI)	7.8 (6.6–NE)
Patients with ongoing response, n/N (%)	33/53 (62%)

- Censored with ongoing response
- First partial response
- First complete response
- Transplant

LEUKEMIA & LYMPHOMA SOCIETY®

47

Pembrolizumab (Keytruda®) in Multiply Relapsed HL

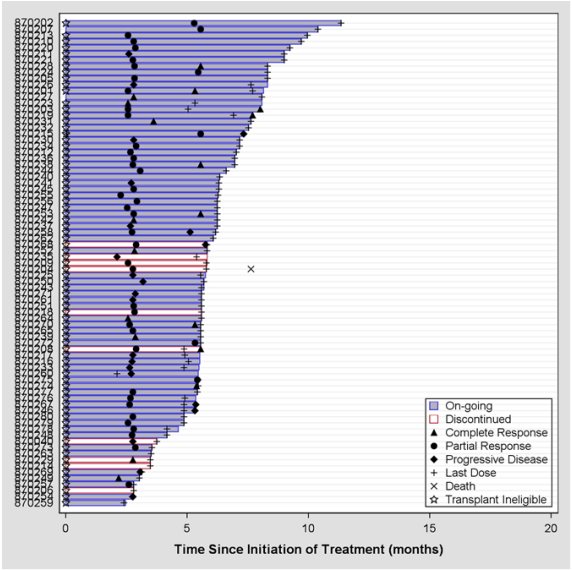


LEUKEMIA & LYMPHOMA SOCIETY®

48

48

Pembrolizumab (Keytruda®) in Multiply Relapsed HL



Median number of treatment cycles: 9 (range, 1-17)

Majority of patients on ongoing treatment at data cutoff

†Data cutoff: June 27, 2016.

LEUKEMIA & LYMPHOMA SOCIETY®

49

Checkpoint Blockade in HL

Nivolumab (Opdivo®)

- Indication(s)
  - Relapse following **ASCT** and **brentuximab vedotin** (Adcetris®)**,** or following **3 or more lines** of therapy including ASCT
  - Continue until disease progression or toxicity
- Dosing/Administration
  - 240 mg q2 weeks or 480 mg q4 weeks
    - FLAT dosing
  - IV infusion over 30 minutes
  - No routine premedications
- Precautions/Warnings
  - Immune-mediated toxicities
  - History of autoimmune disorders
  - Allo-SCT complications

Pembrolizumab (Keytruda®)

- Indication(s)
  - Relapse following **3 or more** lines of therapy (independent of PD-L1 expression)
  - Continue until disease progression, toxicity, or **up to 24 months**
- Dosing/Administration
  - 200 mg q3 weeks
    - FLAT dosing
  - IV infusion over 30 minutes
  - No routine premedications
- Precautions/Warnings
  - Immune-mediated toxicities
  - History of autoimmune disorders
  - Allo-SCT complications

LEUKEMIA & LYMPHOMA SOCIETY®

50

"ITIS"

Hypothyroidism

Hyperthyroidism

Pneumonitis

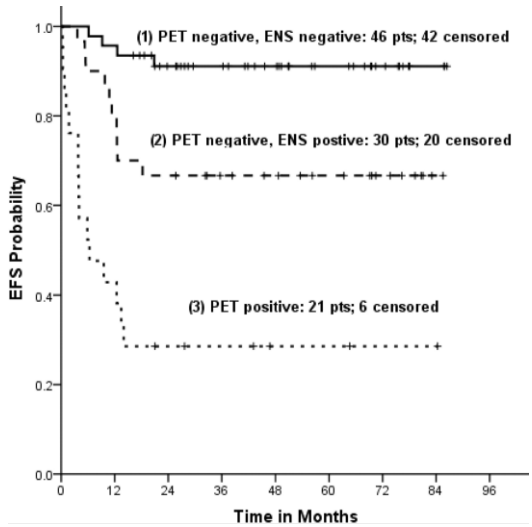
Colitis

Word of Caution: Avoid these agents when there is a history of bleomycin, brentuximab, or gemcitabine-associated pneumonitis that required steroid support

LEUKEMIA & LYMPHOMA SOCIETY®

51

Auto-transplant for Relapsed/Refractory HL



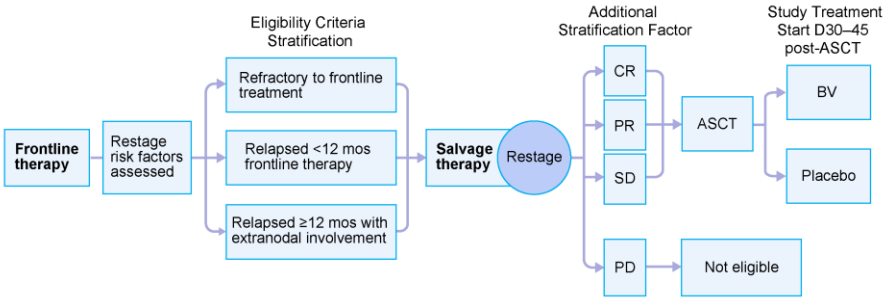
Moskowitz C H et al. *Blood*, 2012.

LEUKEMIA & LYMPHOMA SOCIETY®

52

The AETHERA Study

329 patients were randomized at 78 sites in North America and Europe



CR: Complete Response: PR: Partial Response,: SD: Stable Disease: PD: Primary Disease

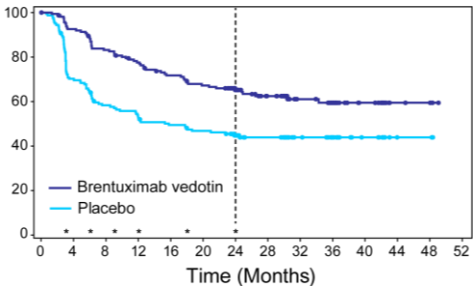
Moskowitz C, et al. *Lancet*, 2015.

LEUKEMIA & LYMPHOMA SOCIETY®

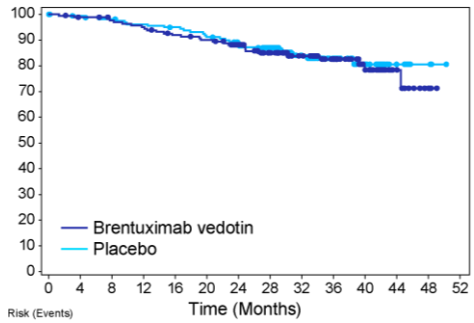
53

AETHERA: Results

Progression-free survival



Overall survival

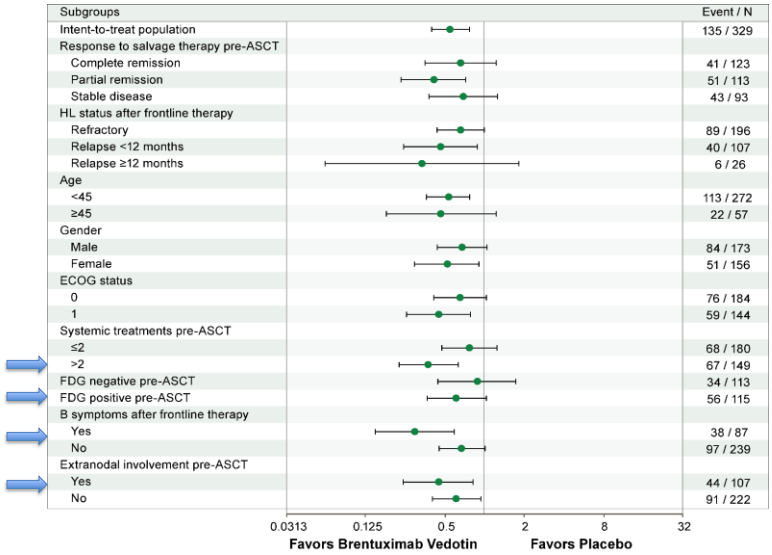


Moskowitz C, et al. *Lancet*, 2015.

LEUKEMIA & LYMPHOMA SOCIETY®

54

Who Benefits the Most?



Moskowitz C, et al. *Lancet*, 2015.

55

Roadmap

Overview of Hodgkin lymphoma

Treatment of newly diagnosed Hodgkin lymphoma

Treatment of relapsed or refractory disease

Emerging approaches

56

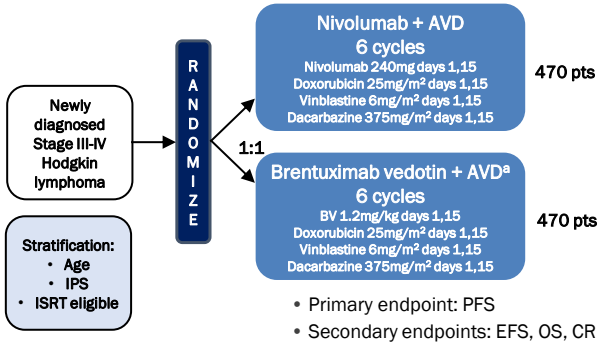
Moving Treatment of Newly Diagnosed HL Forward

Given the success of checkpoint inhibitors in patients with relapsed disease, can they be incorporated into first-treatment to improve outcomes?

LEUKEMIA & LYMPHOMA SOCIETY®

57

S1826 Intergroup Study



- Primary endpoint: PFS
- Secondary endpoints: EFS, OS, CR

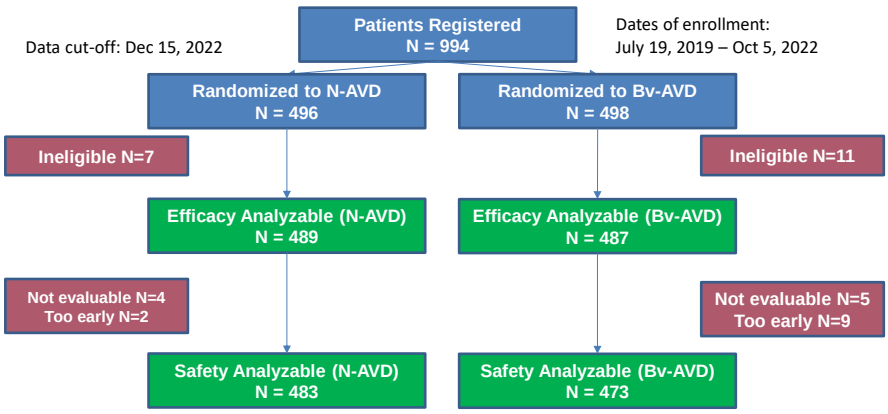
[a]G-CSF is mandatory in BV-AVD arm, optional in N-AVD arm

LEUKEMIA & LYMPHOMA SOCIETY®

Herrera AF, et al. Presented ASH 2020. December 5-8, 2020 (Virtual). Abstract 2969.

58

S1826 CONSORT Diagram



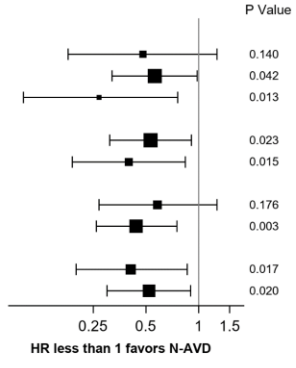
LEUKEMIA & LYMPHOMA SOCIETY®

Presented by: Alex F. Herrera, MD

59

PFS Benefit Consistent Across Subgroups

Subgroup	N + AVD Events/N (%)	BV + AVD Events/N (%)	HR (95% CI)	P Value
Age				
12 - 17 y	6/120 (5.0)	12/117 (10.3)	0.48 (0.18, 1.27)	0.140
18 - 60 y	19/323 (5.9)	32/323 (9.9)	0.56 (0.32, 0.98)	0.042
> 60 y	5/46 (10.9)	14/47 (29.8)	0.27 (0.10, 0.76)	0.013
IPS				
0 - 3	20/331 (6.0)	36/330 (10.9)	0.53 (0.31, 0.91)	0.023
4 - 7	10/158 (6.3)	22/157 (14.0)	0.40 (0.19, 0.84)	0.015
Stage				
III	11/187 (5.9)	15/167 (9.0)	0.58 (0.27, 1.27)	0.176
IV	19/301 (6.3)	43/317 (13.6)	0.44 (0.26, 0.75)	0.003
Symptoms				
A	10/202 (5.0)	24/210 (11.4)	0.41 (0.20, 0.86)	0.017
B	20/286 (7.0)	34/274 (12.4)	0.52 (0.30, 0.90)	0.020

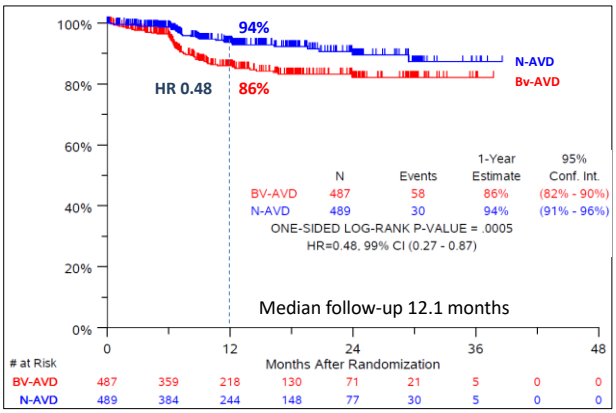


LEUKEMIA & LYMPHOMA SOCIETY®

Presented by: Alex F. Herrera, MD

60

S1826: PFS AT 1 YEAR



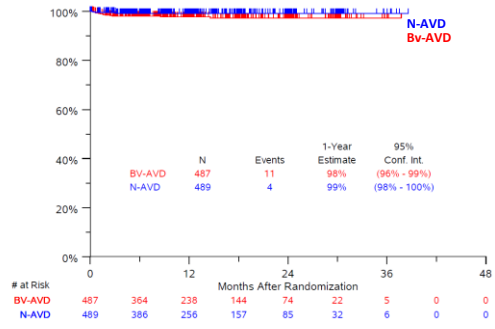
1-year PFS
N-AVD 94%
Bv-AVD 86%

LEUKEMIA & LYMPHOMA SOCIETY®

Presented by: Alex F. Herrera, MD

61

Overall Survival



Median follow-up 12.1 months

Cause of death	N-AVD	Bv-AVD
Infection	2	4
Sepsis	1	2*
Cardiac arrest	0	1
Pneumonitis	0	1
Dehydration, vomiting, cHL	0	1
cHL	1**	0
Unknown	0	2
Total OS events	**4**	**11**

* 1 death from COVID-19/sepsis
** never received treatment, unevaluable for toxicity

LEUKEMIA & LYMPHOMA SOCIETY®

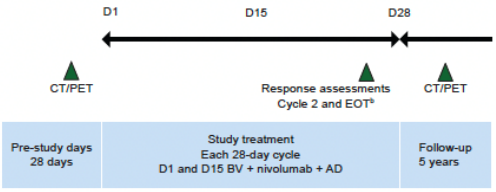
Presented by: Alex F. Herrera, MD

62

Brentuximab Vedotin, Nivolumab, Doxorubicin, and Dacarbazine (AN+AD) for Advanced-Stage Classical Hodgkin Lymphoma: Updated Efficacy and Safety (SGN35-027)

- Open label, multiple part Phase 2 clinical trial
- Part B enrolled patients with Stage II bulky mediastinal, Stage III or Stage IV cHL
- Patients received up to 6 cycles of AN+AD
- Primary endpoint is CR rate at EOT
- Key secondary endpoints include safety, tolerability, ORR, DOR DOCR and PFS

Study Design[a] - Part B



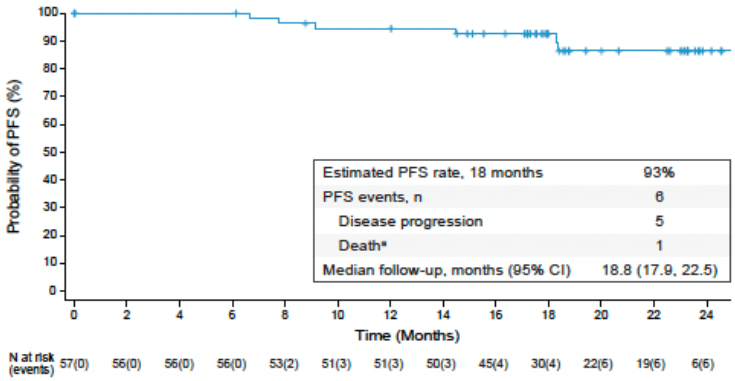
[a]Disease response was assessed by Lugano 2014[9] and LYRIC[10] at Cycle 2 and at EOT.
[b]Response assessments include PET and diagnostic-quality CT scan on Day 25 to 28 of Cycle 2, and at EOT.

LEUKEMIA & LYMPHOMA SOCIETY®

63

SGN35-027 Part B: PFS

Progression-Free Survival



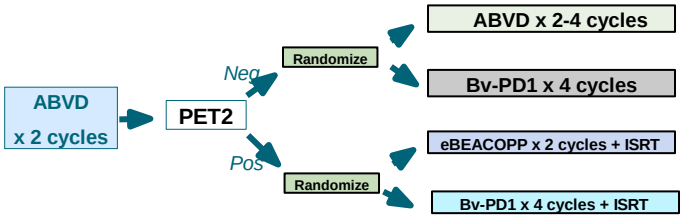
Estimated PFS rate, 18 months	93%
PFS events, n	6
Disease progression	5
Death*	1
Median follow-up, months (95% CI)	18.8 (17.9, 22.5)

*Patient died from sepsis secondary to aspiration pneumonia and bacteremia after safety reporting period.

LEUKEMIA & LYMPHOMA SOCIETY®

64

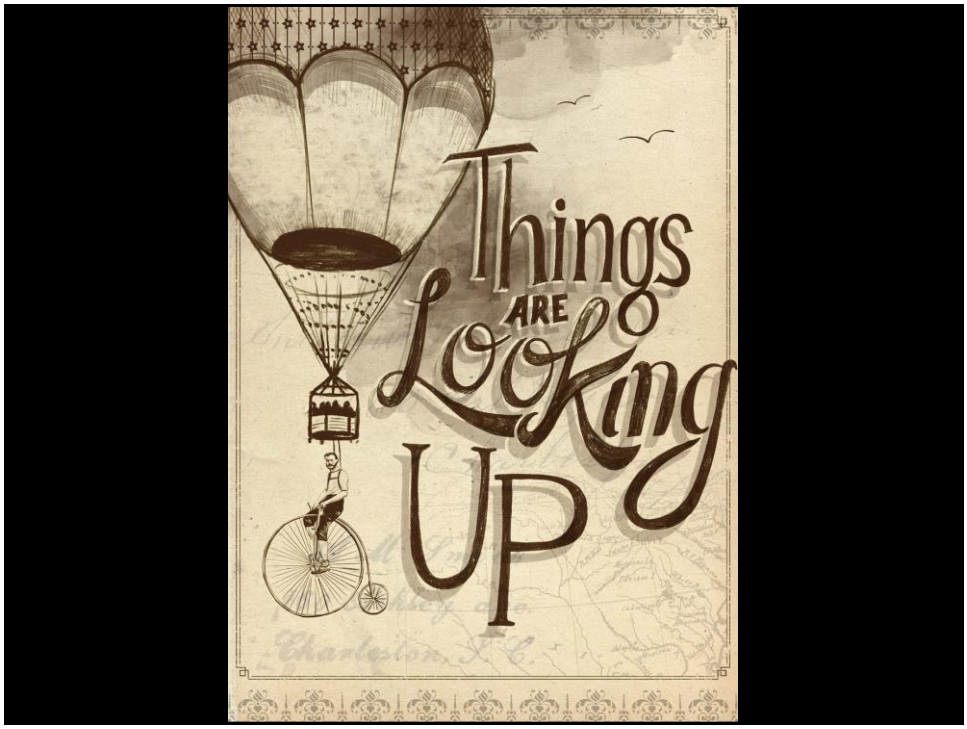
AHOD 2131: Newly Diagnosed Early Stage Hodgkin Lymphoma



Sample Size Projections:
n=1782 over 5 years-
PET neg – 1514
PET pos - 268

LEUKEMIA & LYMPHOMA SOCIETY®

65



66

Thank You

LEUKEMIA & LYMPHOMA SOCIETY®

67

Hodgkin's Lymphoma and Nursing Care

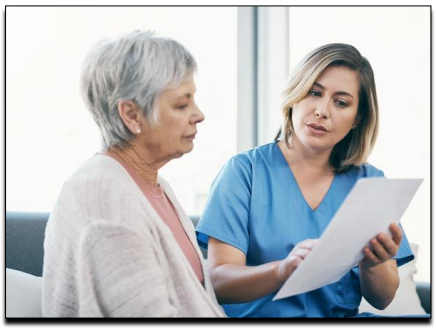
Tara McCabe, APN, AOCNP, MSN
Advanced Practice Nurse
Rutgers Cancer Institute of New Jersey
New Brunswick, NJ

LEUKEMIA & LYMPHOMA SOCIETY®

68

Role of the APP and RN

- Helps to coordinate care
- Addresses any patient concerns/questions
- Medication Compliance
- Symptom Management



LEUKEMIA & LYMPHOMA SOCIETY®

69

Initial Diagnosis

- Review diagnosis
- Discuss treatment plan
- Address any questions
- Review medications and side effect profiles
- Financial/social support

LEUKEMIA & LYMPHOMA SOCIETY®

70

Treatment Planning

- What to expect at each visit
  - Timing, IV access, blood draws
- Cycle calendars
- Chemotherapy teaching
- Medication schedule
- Imaging Schedule

LEUKEMIA & LYMPHOMA SOCIETY

71

Symptom Management

GI Side Effects

- Nausea/Vomiting
  - ❑ Antiemetics
  - ❑ Need for IV hydration
- Diarrhea
  - ❑ Antidiarrheals
- Constipation
  - ❑ Assess nutritional intake
  - ❑ Bowel regimen
  - ❑ Activity status

LEUKEMIA & LYMPHOMA SOCIETY

72

Symptom Management

Pain
- Role of nonopioids vs opioids
- Severity and location

Fatigue
- Activity status
- Sleep hygiene

Peripheral Neuropathy
- Early identification
- Management

LEUKEMIA & LYMPHOMA SOCIETY®

73

Symptom Management

Myelosuppression
- Anemia
- Neutropenia
- Thrombocytopenia

Role of Prophylaxis
- Antiviral
- Antifungal
- Antibiotic

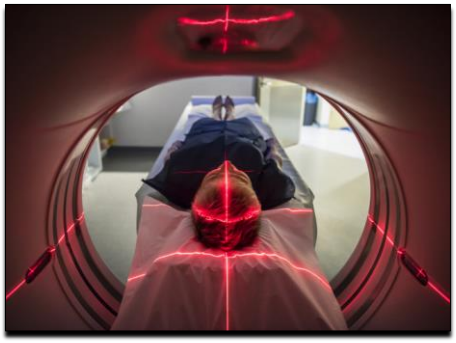
LEUKEMIA & LYMPHOMA SOCIETY®

74

Mid Cycle Treatment and Assessment

End of cycle 2 scan

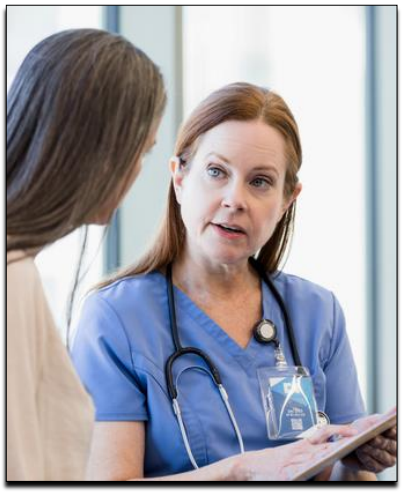
PET response – what this means for further treatment



LEUKEMIA & LYMPHOMA SOCIETY®

75

END OF TREATMENT PLANNING AND ASSESSMENT



- End of treatment PET scan
- Central line removal discussion
- Begin the discussion of active surveillance and survivorship

LEUKEMIA & LYMPHOMA SOCIETY®

76

Active Surveillance and Survivorship

- For first 2 years clinic visit every 3 months
- Scans every 6 months
- After year 2, clinic visits are spaced out to every 6 months and annual scans

LEUKEMIA & LYMPHOMA SOCIETY®

77

Conclusion and Final Thoughts

- The APP and RN are a crucial support network for patients and caregivers.
- Collaborative approach leads to better outcomes
- Autonomy when treating patients

LEUKEMIA & LYMPHOMA SOCIETY®

78

FREE LLS RESOURCES FOR HEALTHCARE PROVIDERS

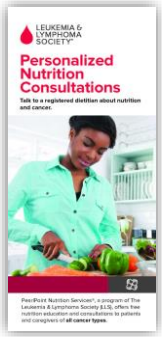
- ❑ CME & CE courses: www.LLS.org/CE
- ❑ Fact Sheets for HCPs: www.LLS.org/HCPbooklets
- ❑ Videos for HCPs: www.LLS.org/HCPvideos
- ❑ Podcast series for HCPs: www.LLS.org/HCPpodcast

LEUKEMIA & LYMPHOMA SOCIETY

79

FREE LLS RESOURCES FOR PATIENTS

- ❑ **Information Specialists** – Personalized assistance for managing treatment decisions, side effects, and dealing with financial and psychosocial challenges (IRC).
  - ➢ www.LLS.org/IRC
- ❑ **Nutrition Education Services Center** – one-on-one consultation with a registered dietician for patients/caregivers of all cancer types (NESC).
  - ➢ www.LLS.org/Nutrition
- ❑ **Clinical Trial Nurse Navigators** – RNs and NPs provide a personalized service for patients seeking treatment in a clinical trial, sift through the information and provide information to bring back to their HC team (CTSC).
  - ➢ www.LLS.org/CTSC
- ❑ **Reach out Monday–Friday, 9 am to 9 pm ET**
  - Phone: (800) 955-4572
  - Live chat: www.LLS.org/IRC
  - Email: infocenter@LLS.org
  - HCP Patient Referral Form: www.LLS.org/HCPreferral



LEUKEMIA & LYMPHOMA SOCIETY

80

HERE TO HELP: LLS COMMITMENT

LLS is committed to providing education and resources to help patients access clinical trials.

CLINICAL TRIAL SUPPORT CENTER

- A team of highly trained nurses and nurse practitioners experienced with hematological malignancies and clinical research.
- Provide education to patients about clinical trials, treatment options, and other disease specific information.
- Provide patients, families, and their caregivers with a professional, detailed, individualized search to discuss with their HCP.
- Provide guidance and serve as advocates throughout the clinical trial process. Help make connections between the patient and the trial site to facilitate enrollment as appropriate.
- Provide a personal connection and develop long term relationships to help better serve our patients.

LEUKEMIA & LYMPHOMA SOCIETY®

81

FREE LLS RESOURCES FOR PATIENTS AND CAREGIVERS

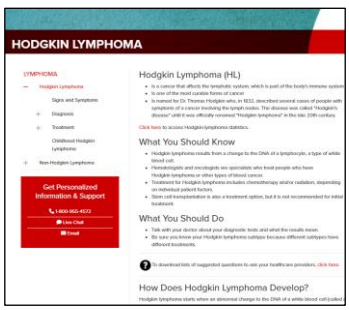
❑ **Webcasts, Videos, Podcasts, booklets**:

- www.LLS.org/Webcasts
- www.LLS.org/EducationVideos
- www.LLS.org/Podcast
- www.LLS.org/Booklets
- **www.LLS.org/Lymphoma**

❑ **Support Resources**

❑ Financial Assistance: www.LLS.org/Finances
- Urgent Need
- Patient Aid
- Travel Assistance

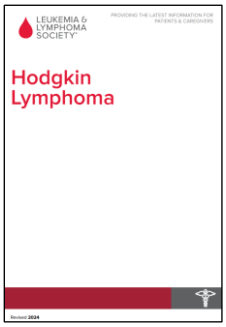
❑ Other Support: www.LLS.org/Support
- LLS Regions
- Online Weekly Chats Facilitated by Oncology SW
- LLS Community Social Media Platform
- First Connection Peer to Peer Program

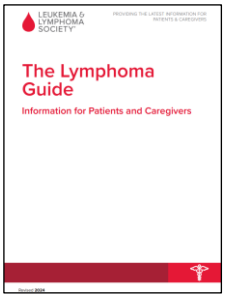


LEUKEMIA & LYMPHOMA SOCIETY®

82

FREE LLS RESOURCES FOR YOUR PATIENTS

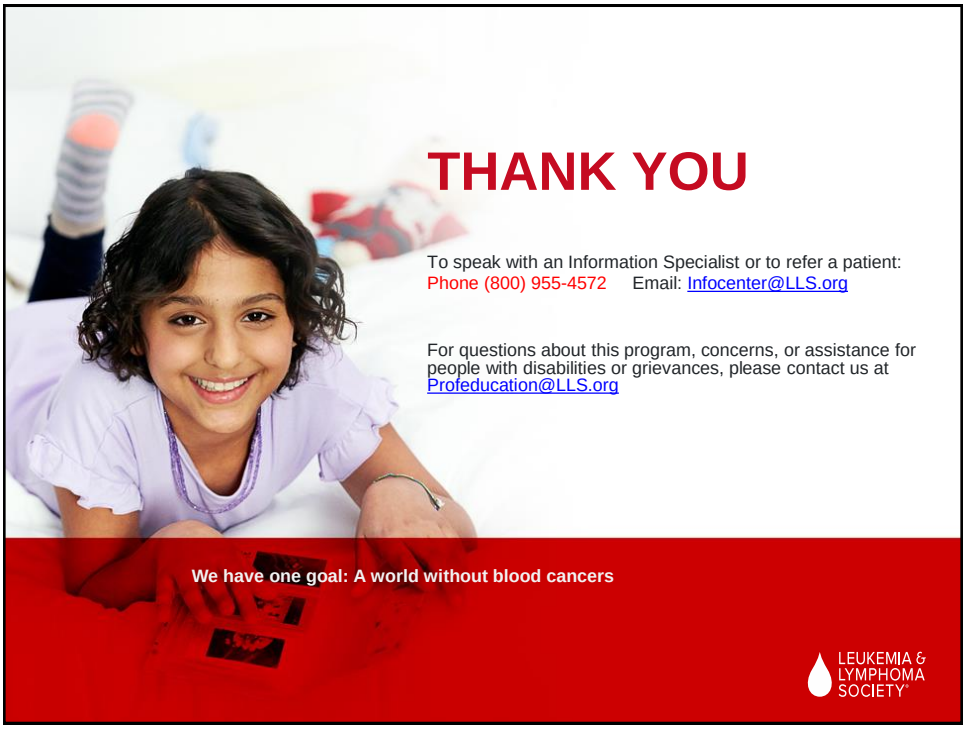




Booklets and Fact Sheets
English – www.LLS.org/Booklets
Spanish – www.LLS.org/Materiales

LEUKEMIA & LYMPHOMA SOCIETY

83



84