Memorial Sloan Kettering Cancer Center

An Overview of Lymphoma: Diagnosis, Clinical Manifestations, and New Treatment Paradigms

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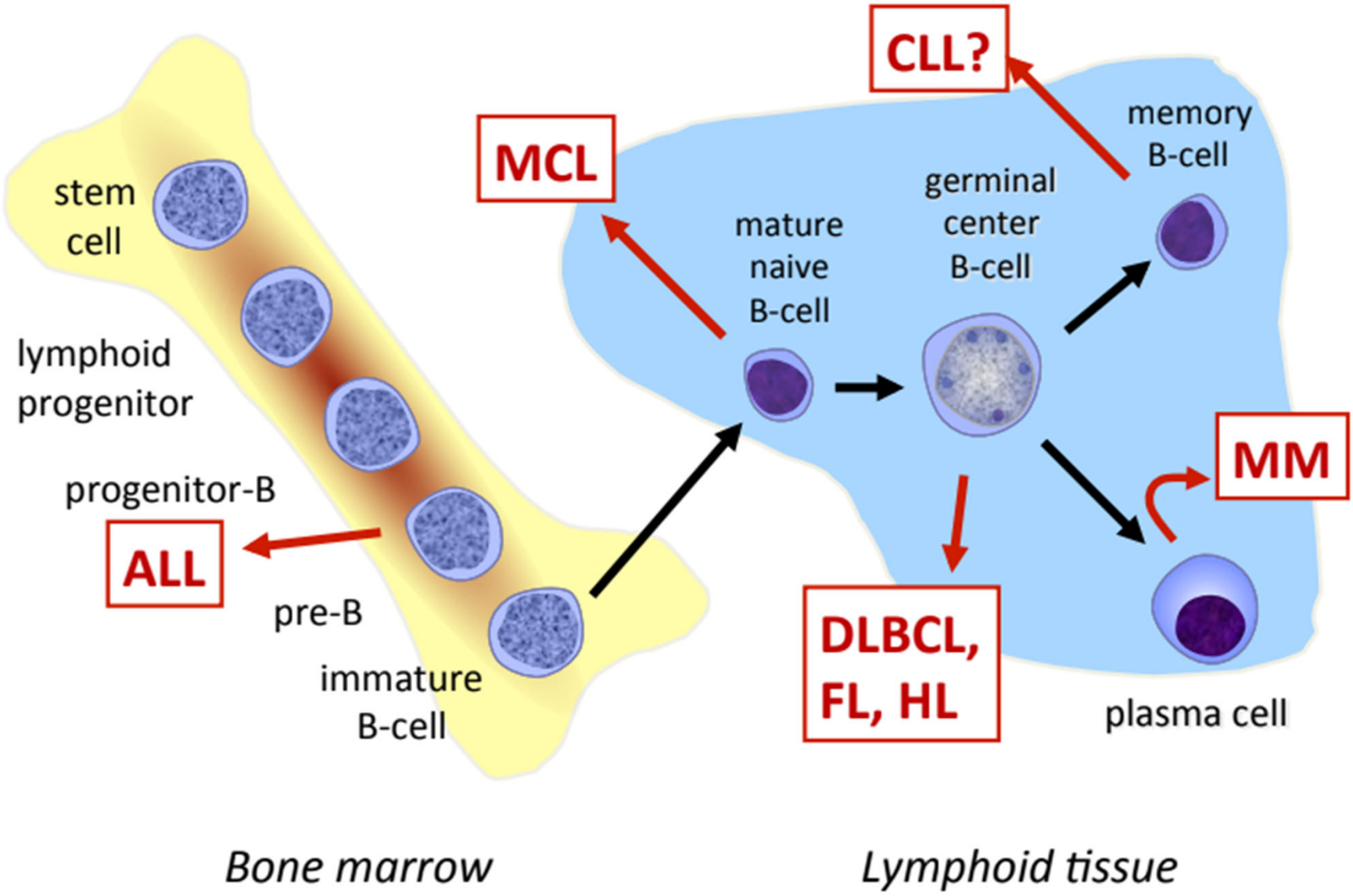
Talk Objectives

- Describe the epidemiology and classification of lymphoma including indolent vs aggressive, hodgkin vs non-hodgkin
- Describe the clinical features commonly associated with lymphoma, including B symptoms
- Provide an overview of how lymphoma is diagnosed
- Provide an overview of common lymphoma treatments and future trends

What is Lymphoma?

- Cancer derived from B cell progenitors, T cell progenitors, mature B cells, mature T cells, or (rarely) natural killer cells
  - Lymphocytes are cells that circulate in the lymphatic system (lymph nodes, spleen marrow, and thymus) to fight infection
- Non Hodgkin lymphoma (NHL)
  - T cell lymphomas are a subtype of NHL
- Hodgkin lymphoma (HL)

B-cell development and malignant counterparts



Types of Lymphoma

- Aggressive vs Indolent
- Hodgkin vs NHL
- B cell vs T cell

Practical way to think about Lymphoma

Category	Cure?	Survival if untreated	Treatment?
Indolent MZL FL	No	Years	Often can defer until criteria met
Aggressive/Very Aggressive Burkitts, DLBCL	Possibly	Weeks to months	Treat
Hodgkin	Most	Months	Treat

Mature B-cell lymphomas (about 85%-90% of NHL cases)

- **Aggressive**
  - Diffuse large B-cell lymphoma (DLBCL) (30%)
  - Mantle cell lymphoma (MCL) (3%)—has features of both indolent and aggressive NHL
  - Lymphoblastic lymphoma (2%)
  - Burkitt lymphoma (BL) (2%)
  - Primary mediastinal (thymic) large B-cell lymphoma (PMBCL)
  - Transformed follicular and transformed mucosa-associated lymphoid tissue (MALT) lymphomas
  - High-grade B-cell lymphoma with double or triple hits (HBL)
  - And others
- **Indolent**
  - Follicular lymphoma (FL) (22%)
  - Marginal zone lymphoma (MZL) (7%)
  - Chronic lymphocytic leukemia/small-cell lymphocytic lymphoma (CLL/SLL) (7%)
  - Gastric mucosa-associated lymphoid tissue (MALT) lymphoma (8%)
  - Lymphoplasmacytic lymphoma (1%)
  - Waldenström macroglobulinemia (WM)
  - Nodal marginal zone lymphoma (NMZL) (1%)
  - Splenic marginal zone lymphoma (SMZL)
  - And others

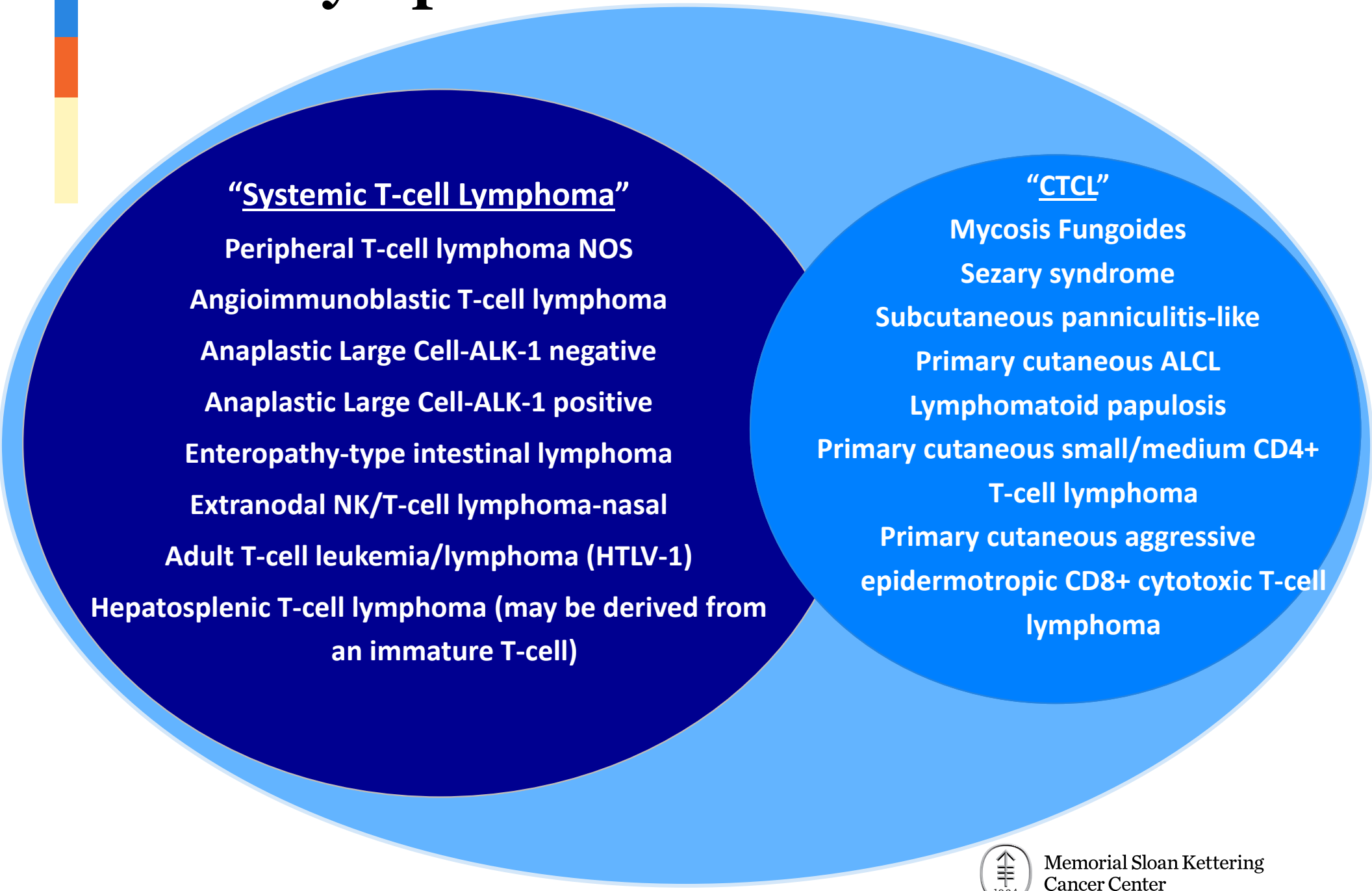
	Common Types of Cancer	Estimated New Cases 2023	Estimated Deaths 2023
1.	Breast Cancer (Female)	297,790	43,170
2.	Prostate Cancer	288,300	34,700
3.	Lung and Bronchus Cancer	238,340	127,070
4.	Colorectal Cancer	153,020	52,550
5.	Melanoma of the Skin	97,610	7,990
6.	Bladder Cancer	82,290	16,710
7.	Kidney and Renal Pelvis Cancer	81,800	14,890
8.	**Non-Hodgkin Lymphoma**	**80,550**	**20,180**
9.	Uterine Cancer	66,200	13,030
10.	Pancreatic Cancer	64,050	50,550

Non-Hodgkin lymphoma represents 4.1% of all new cancer cases in the U.S.

Hodgkin Lymphoma

- Distinct from Non-Hodgkin lymphoma
  - 4 subtypes, Classical Hodgkin
  - Nodular lymphocyte predominant Hodgkin lymphoma
- Approx 10 percent of all lymphomas
- Average age of onset: 34 years, bimodal distribution
- Highly Curable; OS >85%
- B Symptoms occur less than 20% stage I/II disease
- 8800 United States annual incidence

T-Cell Lymphomas



T-cell Lymphoma

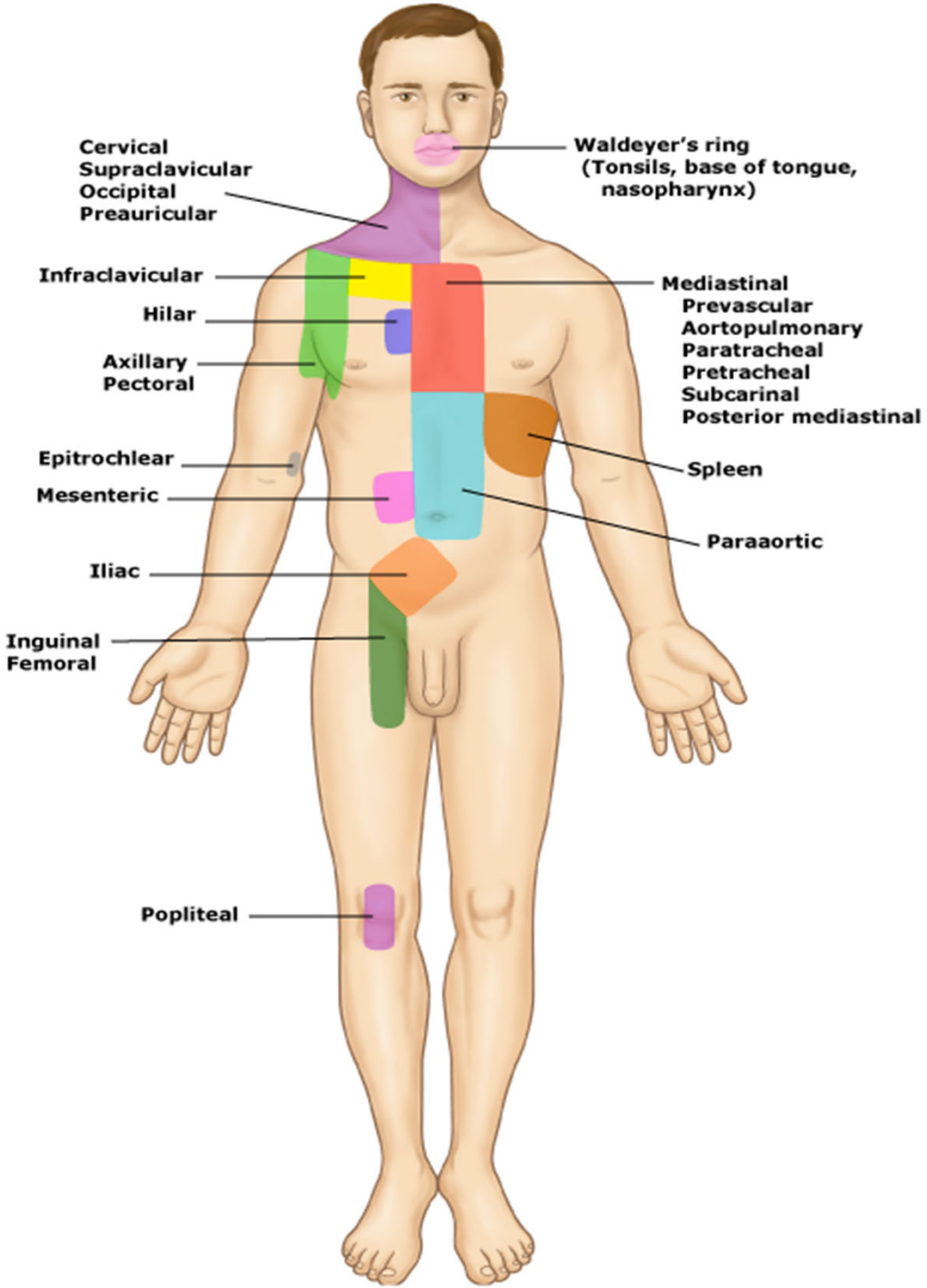
- ~10% of all NHL cases
- Systemic T cell neoplasms
  - Disease involved in lymph nodes, extranodal organs and/or skin
  - Typically aggressive in nature
- Cutaneous T cell lymphoma (CTCL)
  - Disease confined to the skin only
  - Typically indolent in nature

INDOLENT	AGGRESSIVE	HIGHLY AGGRESSIVE
Follicular lymphoma	DLBCL	Burkitt
CLL/SLL	PTCL	High grade B cell lymphoma with features b/t DLBCL and Burkitt
Marginal zone lymphoma	Anaplastic large cell	ATLL
Mycosis Fungoides	Hodgkin	Hepatosplenic TCL
Mantle cell lymphoma		

Lymphoma Clinical Presentation

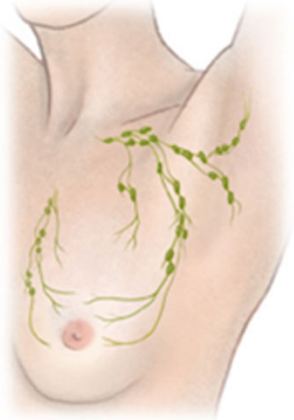
- Lymphadenopathy not explained by other causes – sometimes incidental finding
- Fever, night sweats, weight loss, pruritus, profound lethargy
- Alcohol induced pain (cHL)
- Indolent vs aggressive differences
- Paraneoplastic syndromes rare
- CNS Lymphoma
- Cytopenias varied detiology

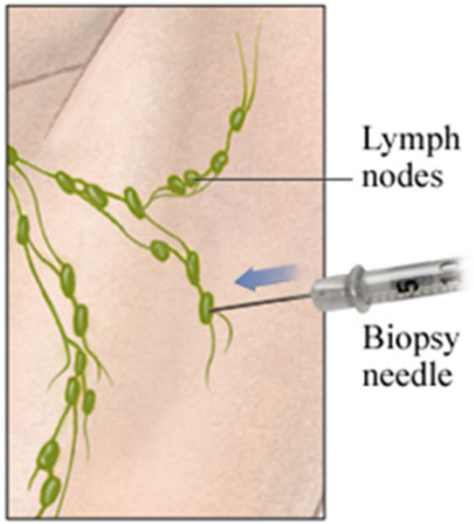
Lymph node regions in lymphoma

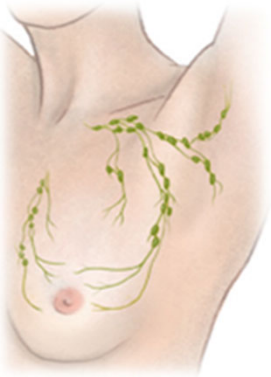


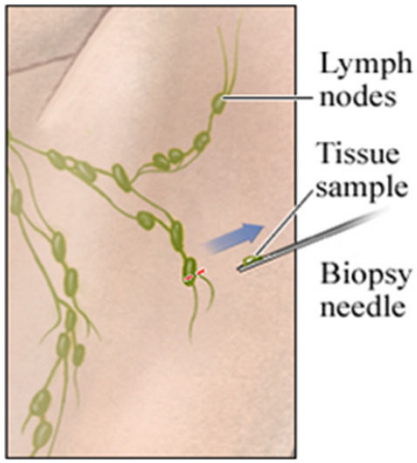
Diagnosis & Work up: Biopsy

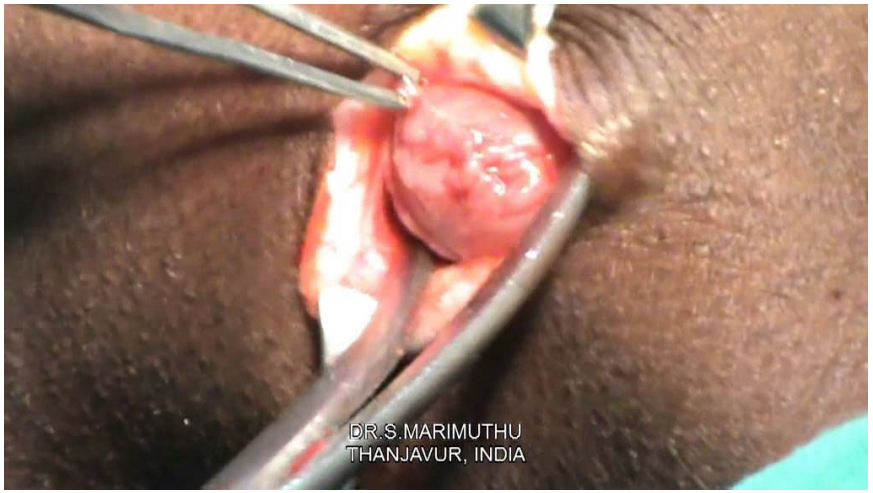
- Biopsy
  - Excisional biopsy
  - Core biopsy
    - FNA not preferred











Pathology Report

- Histology: what is seen under microscope
  - Morphology and growth pattern
  - Proliferation rate: Ki-67
- Immunophenotype: cell surface markers (stains)
  - Immunohistochemistry (IHC)
- Diagnostic molecular
  - Receptor gene rearrangement and clonality
  - T cell lymphomas
- FISH (fluorescence in situ hybridization)
  - Identify structural abnormalities, such as deletions, duplications, translocations
  - "double hit" or "triple hit"

Example Hematopathology Report

- 1: Right Inguinal Mass, Lymph Node
  DIAGNOSIS:
  1. Right Inguinal Mass, Lymph Node
     - High-grade B-cell lymphoma with reported MYC, BCL2 and BCL6 rearrangements.

  MORPHOLOGY
  Histologic section shows core biopsy of lymphoid tissue with a diffuse proliferation of predominant large-sized lymphoid cells with irregular nuclei, vesicular to dispersed chromatin and prominent nucleoli. Apoptotic bodies are frequently seen in the background. Patchy necrosis is present.

  IMMUNOHISTOCHEMISTRY
  Express: PAX5, CD20 (subset; ~20%), CD10 (diffuse), BCL6 (>30%), BCL2 (diffuse) and c-MYC (diffuse)
  CD3 highlights scattered T cells.
  Ki-67 proliferation index is ~80-90%.
  EBER-ISH is negative.

  FLOW CYTOMETRIC ANALYSIS
  Immunophenotypic analysis demonstrates 11.3% small T lymphocytes (CD4:CD8= 3.95:1), 1.0% small mature polytypic B lymphocytes (kappa:lambda=1.3:1), 0.9% NK cells, 58.6% granulocytes, and 5.8% monocytes. The remaining events are attributable to uncharacterized cells and debris.

  CYTOGENETIC STUDIES
  FISH:
  Abnormal:
  Positive for BCL6 (3q27) rearrangement - 96%,
  Positive for MYC (Bq24.1) rearrangement - 94.5%
  Positive for BCL2 (18q21) rearrangement - 95.5%.

Diagnosis & Work up: Scans

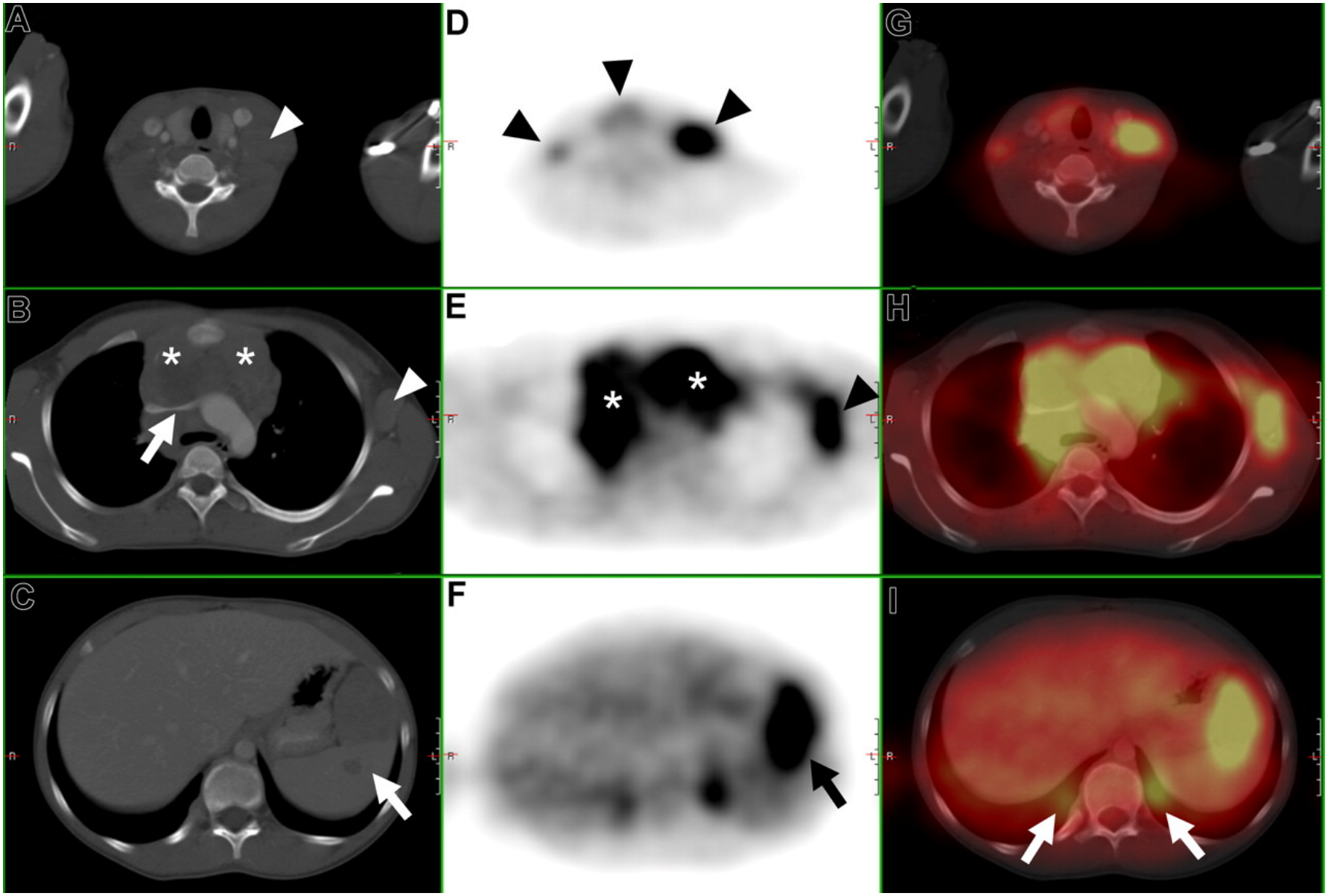
Positron Emission Tomography (PET)

- Radioactive glucose injected, uptake observed
- More radiation than CT, radioactive
- 2-4 hours

Computer Tomography (CT)

- Can visualize soft tissues and lymph nodes
- Accurate bone outline
- IV contrast dye
- No metabolic information

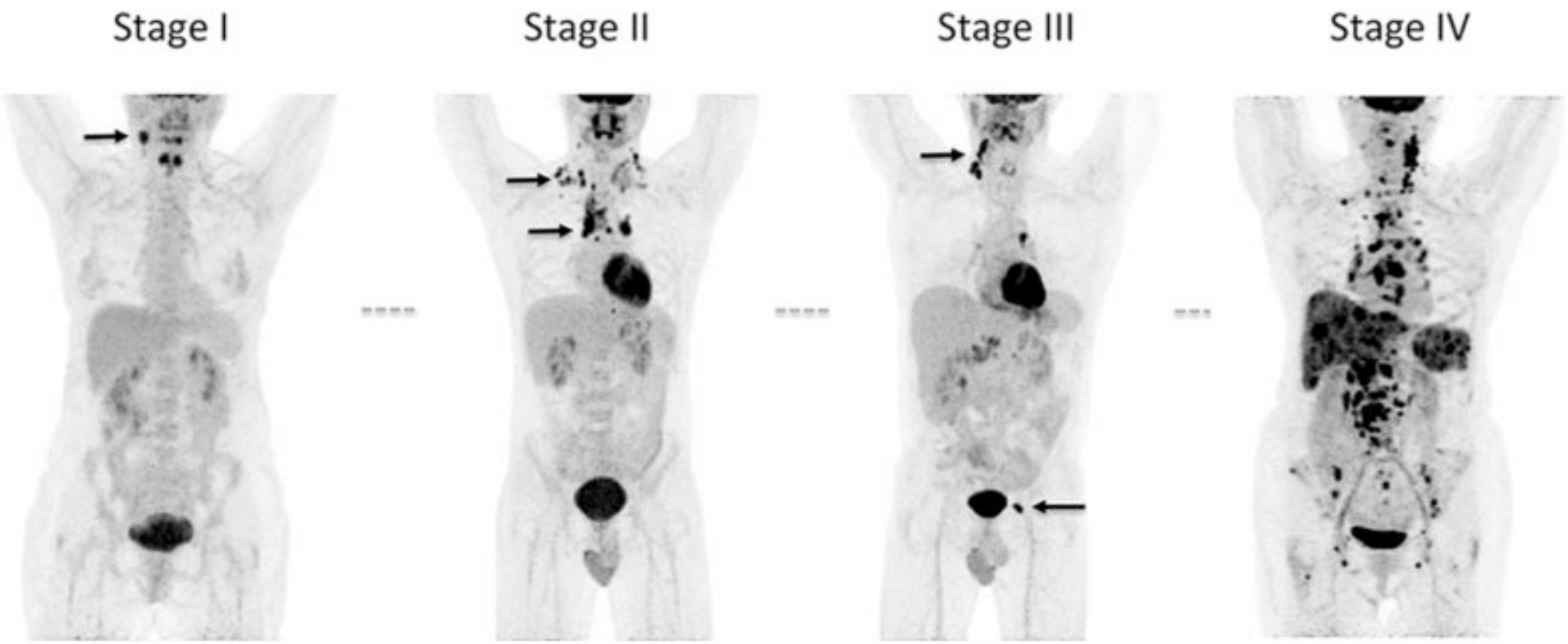
CT, FDG-PET, and FDG-PET/CT fusion



Thomas C. Kwee et al. Blood 2008;111:504-516

blood

Staging of lymphoma



Tarec Christoffer El-Galaly, MD, DMSc, Lars Christian Gormsen,MD, PhD, Martin Hutchings, MD, PhD
PET/CT for Staging; Past, Present, and Future. Seminars Nuc Med, vol 48(1):4-16, 2018
https://doi.org/10.1053/j.semnuclmed.2017.09.001

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Staging System

Stage	Involvement	Extranodal (E) status
Limited		
I	One node or a group of adjacent nodes	Single extranodal lesions without nodal involvement
II	Two or more nodal groups on the same side of the diaphragm	Stage I or II by nodal extent with limited contiguous extranodal involvement
II bulky*	II as above with "bulky" disease	
Advanced		
III	Nodes on both sides of the diaphragm; nodes above the diaphragm with spleen involvement	Not applicable
IV	Additional noncontiguous extralymphatic involvement	Not applicable

- "A": Absence of B symptoms
- "B": B symptoms: weight loss > 10% body weight during prior 6 months, recurrent fevers > 38C during prior month, recurrent drenching night sweats in prior month

*These designations are only used in HL

Performance Status

- Describes a patient's level of functioning in terms of their ability to care for self, daily activity, and physical ability (walking, working, etc.) in order to determine how "fit" they are for treatment.

- ECOG and KPS

ECOG PERFORMANCE STATUS	KARNOFSKY PERFORMANCE STATUS (KPS)
0—Fully active, able to carry on all pre-disease performance without restriction	100—Normal, no complaints; no evidence of disease 90—Able to carry on normal activity; minor signs or symptoms of disease
1—Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work	80—Normal activity with effort, some signs or symptoms of disease 70—Cares for self but unable to carry on normal activity or to do active work
2—Ambulatory and capable of all selfcare but unable to carry out any work activities; up and about more than 50% of waking hours	60—Requires occasional assistance but is able to care for most of personal needs 50—Requires considerable assistance and frequent medical care
3—Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours	40—Disabled; requires special care and assistance 30—Severely disabled; hospitalization is indicated although death not imminent
4—Completely disabled; cannot carry on any selfcare; totally confined to bed or chair	20—Very ill; hospitalization and active supportive care necessary 10—Moribund
5—Dead	0—Dead

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Diffuse Large B Cell Lymphoma

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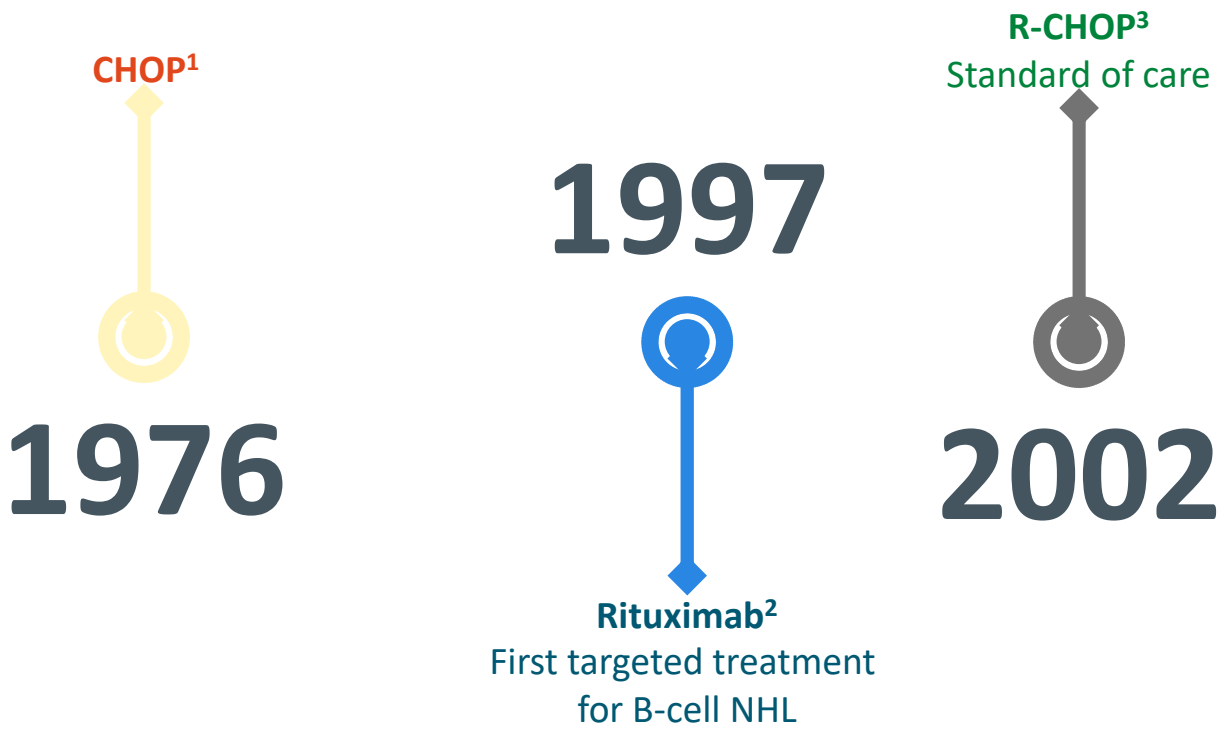
Diffuse Large B Cell Lymphoma

- Most common NHL ~30% of cases
- Median age 60s
- De novo vs transformation
  - Richter's (CLL), Follicular, MZL, Waldenstrom's
- Approx 60% of patients cured with 1st line
- Germinal center (GCB) v Non-Germinal Center (ABC) v PBML v. Unclassifiable
- CNS risk?

R-CHOP: First-line in DLBCL for 2+ Decades



1. McKelvey. Cancer. 1976;38:1484. 2. McLaughlin. JCO. 1998;16:2825. 3. Coiffier. NEJM. 2002;346:235.

DLBCL treatments

- Front line combination chemo-immunotherapy
  - R-CHOP (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and prednisone)
  - R-da-EPOCH (Rituximab, Etoposide, Prednisone, Vincristine, Cyclophosphamide, Doxorubicin)
  - R-Pola-CHP (Rituximab, Cyclophosphamide, Doxorubicin, Polatuzumab, and prednisone)

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Follicular Lymphoma

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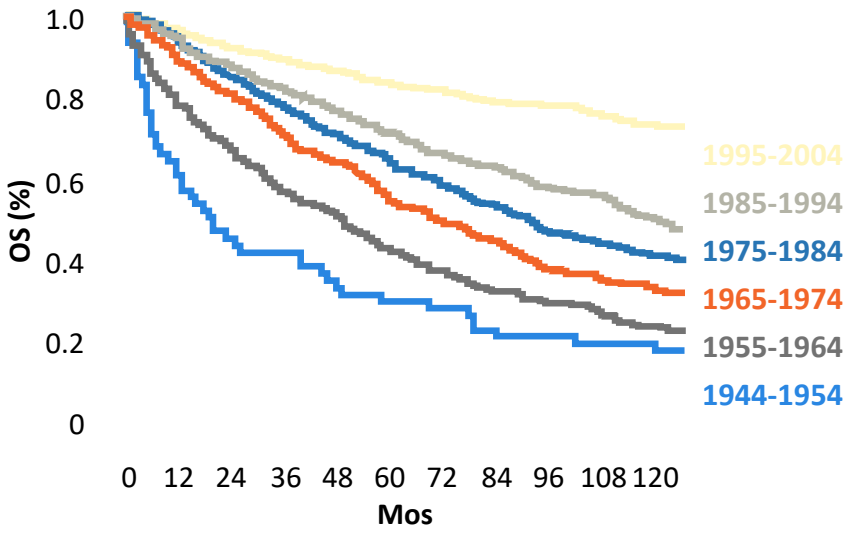
Follicular Lymphoma

- Second most common NHL
- Follicular(nodular) growth pattern
- Incidence increases with age; median 65
- Patients can live with the disease for many years
- Grade 1-2, 3a more indolent behaving. Grade 3b more aggressive and treated like DLBCL.
- GELF Criteria

Improved Prognosis for Patients With FL in New Treatment Era

- FL typically regarded as chronic disease with good responses to initial therapy, but with eventual relapses to subsequent therapy[1,2]
- Recent therapeutic advances, most notably rituximab, have improved disease control and long-term clinical outcomes[3-5]
  - 10-yr survival rate: 64% to 92%[3]
  - Median survival is ~ 20 yrs, similar to age matched controls[5-8]
- Current goal of treatment: maintain best QoL by delaying disease progression—will this translate into an OS benefit with longer follow-up?

OS Improvement in Indolent B-Cell Lymphoma from 1944 to 2004: the MDACC Experience[9]



1. WHO. Follicular lymphoma. 2014. 2. ACS. Treating B-cell non-Hodgkin lymphoma. 3. Freedman. Am J Hematol. 2020; 95:316. 4. Kahl. Blood. 2016;127:2055. 5. Provencio. PLoS ONE. 2017;12:e0177204. 6. Maurer. Am J Hematol. 2016;91:1096. 7. Swenson. JCO. 2005; 23:5019. 8. Tan. Blood. 2013;122:981. 9. Neelapu. 60 Years of Survival Outcomes at the MD Anderson Cancer Center. New York, NY: Springer; 2013. p. 241.

Slide credit: clinicaloptions.com

Treatment Considerations for Newly Diagnosed FL

- Disease stage
- Tumor grade
- Tumor burden
- Symptoms
- Patient age and fitness
- Patient goals and priorities

- CR and/or prolonged PFS
  - Prioritizes longer remissions over QoL
  - Usually requires more aggressive treatment that is more toxic in the short term
- Maximize QoL and/or reduce risk for AEs
  - Prioritizes QoL over longer remissions
  - Usually involves gentler treatment with fewer toxicities at the expense of efficacy

Blinman. Ann Oncol. 2012;23:1104. Dreyling. Ann Oncol. 2016;27(suppl 5):v83. Meropol. Cancer. 2008;113:3459.

Slide credit: clinicaloptions.com

GELF Criteria

- A person has high tumor burden if they have ≥ 1 of the following:
  - Any mass ≥ 7 cm in diameter
  - Involvement of ≥ 3 LNs, each ≥ 3 cm in diameter
  - Presence of B symptoms
  - Splenomegaly
  - Compression syndrome (ureteral, orbital, GI)
  - Ascites or pleural effusion
  - Cytopenias (WBC < 1 x 10^9/L or PLTs < 100 x 10^9/L)
  - Leukemia (> 5.0 x 10^9/L circulating malignant cells)
  - (Elevated LDH or β_2-microglobulin)

Solal-Céligny. JCO. 1998;16:2332. Brice. JCO. 1997;15:1110. Dreyling. Ann Oncol. 2016;27(suppl 5):v83.

Slide credit: clinicaloptions.com

First Line Treatments in FL

- Bendamustine + obinutuzumab or rituximab
- CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + obinutuzumab or rituximab
- CVP (cyclophosphamide, vincristine, prednisone) + obinutuzumab or rituximab
- Lenalidomide + rituximab
- Rituximab alone in select cases
- Radiation in select cases
  - Boom Boom or BOOM

Case Study #1. Mr. John

Diagnosed in 2019 with Follicular lymphoma, Grade 1-2, Stage IV

- 12/11/19 Cytopenias, Bone Marrow Bx done - involvement by FL (24% by flow).
- 12/15/19 PET/CT with non bulky LN above/below
- 12/2019 - 03/2020: Bendamustine/Rituximab x3 of 6 stopped amid COVID.
- 4/7/2020 PET/CT – CMR
- 2/29/21: generalized POD, not obviously meeting GELF criteria for treatment. Isolated leukemic phase without cytopenia not felt to be sufficient to treat

Progressive Anemia, Now Hgb 8.6

	/21 2	01/06/22 08:35	03/30/22 08:30	07/28/22 10:47	07/28/22 12:05	08/02/22 11:06	08/09/22 16:16	08/11/22 10:34	0
Hematology Lab									
Hematology									
WBC	4.0 *	↑ 11.3 *	↑ 14.5 *	↑ 15.1 *	↑ 14.2 *	↑ 15.2 *	↑ 16.5 *	↑ 15.9 *	
RBC	3.98 *	↓ 3.88 *	↓ 3.54 *	↓ 2.64 *	↓ 2.62 *	↓ 2.69 *	↓ 2.68 *	↓ 2.62 *	
HGB	13.1 *	12.5 *	↓ 11.4 *	↓ 8.7 *	↓ 8.6 *	↓ 8.8 *	↓ 8.5 *	↓ 8.6 *	
HCT	39.8 *	38.9 *	↓ 35.2 *	↓ 26.8 *	↓ 25.7 *	↓ 26.8 *	↓ 26.3 *	↓ 26.6 *	
Mean Corpuscular Volume (MCV)	100 *	↑ 100 *	↑ 99 *	↑ 102 *	98 *	↑ 100 *	98 *	↑ 102 *	
Mean Corpuscular Hemoglobin (MCH)	32.9 *	32.2 *	32.2 *	33.0 *	32.8 *	32.7 *	31.7 *	32.8 *	
Mean Corpuscular Hemoglobin Conc (MCHC)	32.9 *	32.1 *	32.4 *	32.5 *	33.5 *	32.8 *	32.3 *	32.3 *	
Red Blood Cell Distribution Width (RDW)	14.7 *	↑ 15.3 *	↑ 17.6 *	↑ 18.9 *	↑ 18.7 *	↑ 19.5 *	↑ 20.0 *	↑ 20.5 *	
Platelets.	123 *	↓ 104 *	↓ 110 *	↓ 117 *	↓ 116 *	↓ 118 *	↓ 144 *	↓ 135 *	
Neutrophil	54.5 *	↓ 24.0 *	↓ 13.0 *	↓ 17.0		* ↓ 28.0 *	↓ 17.0 *	↓ 19.0 *	
Mono	8.5 *	3.0 *	2.0 *	3.0		* 3.0 *	2.0 *	1.0 *	
Eos	0.2 *	1.0 *	0.0 *	0.0		* 0.0 *	0.0 *	0.0 *	
Baso	0.0 *	0.0 *	0.0 *	1.0		* 0.0 *	0.0 *	0.0 *	
Immature Granulocyte	6.2								

Restaging Biopsy July 2022

- DIAGNOSIS:
  1-2. Bone marrow, right posterior iliac crest, biopsy and aspirate, smears:
  - Involvement by follicular lymphoma (30%)
  - Hypercellular marrow with trilineage maturing hematopoiesis.

  IMMUNOHISTOCHEMISTRY
  CD20/PAX5 highlight the neoplastic lymphoid cells.
  CD3 highlights T cells

  FLOW CYTOMETRIC ANALYSIS, BONE MARROW (F22-8303) Interpretation:
  Abnormal B cell population represents 45% of WBC. Immunophenotype:
  Abnormal: CD5 (partial), CD10 (positive), CD19 (dim), CD22 (dim), surface Lambda (restriction)

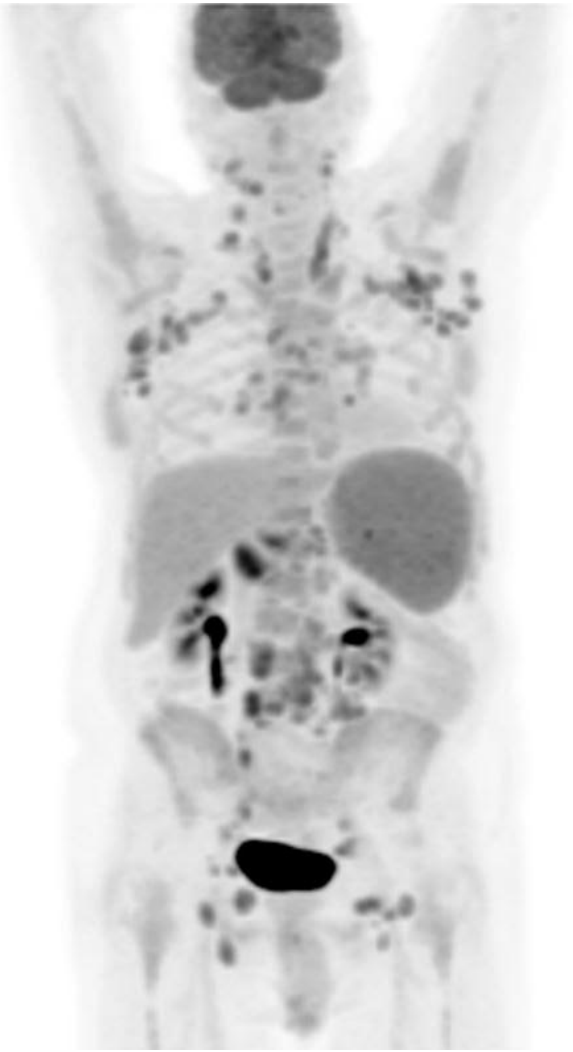
  Test Results:
  FISH ANALYSIS
  Interphase/Nuclear In Situ Hybridization [ISCN 2016]: nuc ish(IGHx3~4,BCL2x2~3)(IGH con BCL2x2~3)[92/300]

  FISH ANALYSIS:
  IGH-BCL2 fusion/ t(14;18) detected in 30.7% of cells, with a signal pattern of two to three fusions and one signal for IGH (14q32.3).

Restaging PET/CT Given POD July 2022

IMPRESSION:

1. Since last scan new FDG avid cervical, thoracic and abdominopelvic adenopathy, consistent with lymphoma. Most FDG avid lesion demonstrates maximum SUV 9.9.
2. New splenomegaly with diffuse FDG avidity, suspicious for involvement.
3. Increased diffuse bone marrow FDG avidity, suspicious for involvement.



Mr. John Assessment July 2022

- 83-year-old diagnosed with FL grade 1-2, stage 4 (marrow involvement), originally treated with bendamustine - rituximab for 3 cycles, interrupted in the setting of COVID-19 pandemic having achieved complete metabolic response, course complicated by reported severe infusion related reaction now with slow but progressive recurrence without obvious suspicion for transformation to DLBCL. The new element is worsening anemia, which is symptomatic. This will need to be addressed with anti lymphoma therapy.
- PMHx: CAD, BPH, HTN, HLD
- Started Rituximab and Lenalidomide

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Other lymphomas

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CLL/SLL

- Median age 70
- 25-30% percent of all leukemias in the US
- Can involve predominantly blood, lymph nodes or both
- Often present with painless adenopathy that wax/wanes or incidental lymphocytosis on routine CBC, cytopenias
  - At times associated with autoimmune phenomenon: hemolytic or anemia, immune thrombocytopenia or exaggerated reaction to insect bites
- Cytogenetics evaluated to help prognosticate:
  - ex: 17p deletion, CD38 positivity, unmutated IgHV, del11q, trisomy 12, del 13q

Front line CLL/SLL Treatment

- **BTKi**
- Convenience (no infusions, TLS monitoring) § Long-term efficacy data
- Phase III data compared with FCR and BR
- More data for efficacy of Ven at time of ibrutinib progression

- **Ven + Obin**
- Potential for 1 yr time-limited therapy
- No known cardiac or bleeding risks
- Less concern for long-term adherence
- Potential for cost saving if 1 yr of therapy is durable

Marginal Zone Lymphoma

- Consists of 3 diseases: Extranodal(MALT), Nodal and Splenic
- Some subtypes are a consequence of chronic infection/inflammation
  - H. pylori, Borrelia burgdorferi, Hepatitis C, Chlamydia psittaci, Campylobacter jejuni
  - Autoimmune d/o: Sjogren's, Hashimoto thyroiditis

Treatment of Hodgkin Lymphoma

- Early/Advanced stage? Favorable/Unfavorable?
- ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine)
- BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, prednisone, procarbazine)
- Brentuximab vedotin + AVD (doxorubicin, vinblastine, and dacarbazine)

Case #2. Ms. Jane

- 22 y/o F referred to head and neck surgery from PCP for evaluation of left supraclavicular adenopathy since Jan. 2023
- Asymptomatic, Normal CBC, LDH. Noted December 2019.
- PMHx: None

Ms. Jane MRI Neck

- 2/4/2023: MR w & w/o con soft tissue neck: reports there are multiple nodular masses involving the left lower neck, in particular the posterior triangle and supraclavicular region as well as the left axillary region, most likely representing lymphadenopathy, correlating to US. The largest node is located deep to the SCM muscle at the level of the thyroid measuring 1.4 x 2.4 cm. There is a left axillary node measuring 1.6 x 1.2cm.

Ms. Jane Work Up

- -2/20/23 Left supraclavicular lymph node core biopsy consistent with classic Hodgkin lymphoma.
- -3/3/23: PET/CR with >3 sites of above-the-diaphragm adenopathy

- What is the staging and treatment ?
- What is the prognosis?
- Considerations before treatment?

Infection ppx, fertility preservation,

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Noteworthy Treatment Advances

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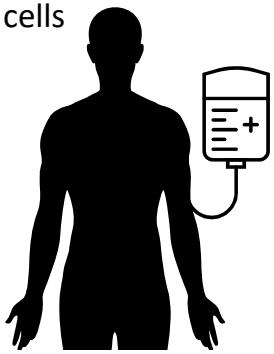
Autologous CAR T-Cell Therapy: Underlying Principles

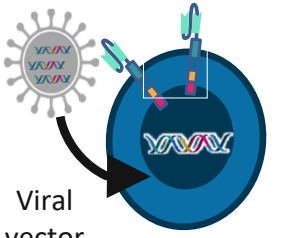
Leukapheresis

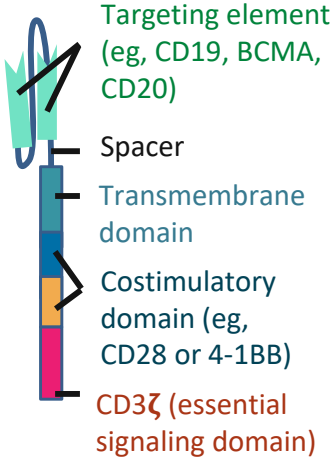
Collect patient's white blood cells



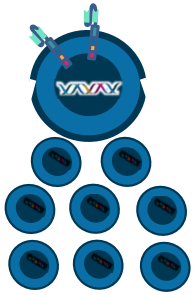
Isolate and activate T-cells

Engineer T-cells with CAR gene



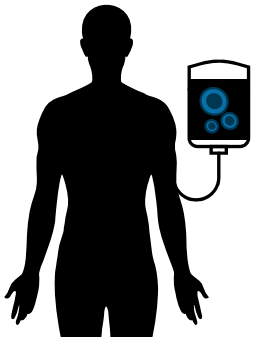


Expand CAR T-cells

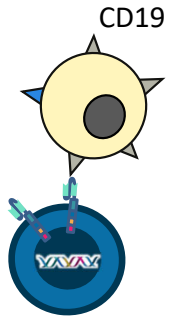


Infusion

Infuse same patient with CAR T-cells



Activity



Median manufacturing time: 17-28 days

Patients undergo lymphodepleting (and possibly salvage/bridging) therapy

Majors. EHA 2018. Abstr PS1156. Lim. Cell .2017;168:724. Sadelain. Nat Rev Cancer. 2003;3:35.
Brentjens. Nat Med. 2003;9:279. Park. ASH 2015. Abstr 682. Axicabtagene ciloleucel PI. Tisagenlecleucel PI.

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Memorial Sloan Kettering Cancer Center

FDA-Approved CAR T-Cell Therapies

Therapy	Indications	Cost*
CD19-Targeting Therapies		
Axicabtagene ciloleucel	▪ **Adults with R/R large B-cell lymphoma after ≥2 lines of systemic therapy,** including DLBCL NOS, DLBCL arising from follicular lymphoma, primary mediastinal large B-cell lymphoma, high-grade B-cell lymphoma ▪ **Adults with R/R follicular lymphoma after ≥2 lines of systemic therapy**	$373,000
Brexucabtagene autoleucel	▪ **Adults with R/R MCL**	$373,000
Lisocabtagene maraleucel	▪ **Adults with R/R large B-cell lymphoma after ≥2 lines of systemic therapy**, including DLBCL NOS (including DLBCL arising from indolent lymphoma), high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and follicular lymphoma grade 3B	$410,300
Tisagenlecleucel	▪ **Patients aged up to 25 yr with B-cell precursor ALL that is refractory or in second/later relapse** ▪ **Adults with R/R large B-cell lymphoma after ≥2 lines of systemic therapy**, including DLBCL NOS, DLBCL arising from follicular lymphoma, high-grade B-cell lymphoma	DLBCL: $373,000 ALL: $475,000

*Wholesale acquisition cost (USD).

Axicabtagene ciloleucel PI. Brexucabtagene autoleucel PI. Idecabtagene vicleucel PI. Lisocabtagene maraleucel PI. Tisagenlecleucel PI.
Geethakumari. Curr Hematol Malig Rep. 2021(Jun 5):1.

Slide credit: clinicaloptions.com

Acute CAR-T Toxicity

- Cytokine release syndrome
  - Sequelae of this sepsis like syndrome
  - Hemophagocytic lymphohistiocytosis (HLH)
- Neurotoxicity (immune effector cell-associated neurologic syndrome)
  - Most severe form cerebral edema, seizure, profound AMS
- Hypersensitivity reaction
- Tumor lysis syndrome

Acute CAR-T Toxicity continued…

- Persistent Cytopenia after T Cell Therapy
- B-cell aplasia and hypogammaglobulinemia (CD-19 specific)
- Coagulopathy
  - DIC in setting of severe CRS
- Infections
- Acute Kidney Injury/ Electrolyte Dyscrasias
- Cardiopulmonary toxicities
  - Arrhythmias, pulmonary edema
- Hemophagocytic lymphohistiocytosis (HLH)

Bispecific Antibody

- Epcoritamab / Glofitamab contains two antigen-recognition sites: one for human CD3, a T-cell surface antigen, and one for human CD20, a tumor-associated antigen (TAA) that is exclusively expressed on B cells during most stages of B-cell development and is often overexpressed in B-cell malignancies. Upon administration, binds to both T-cells and CD20-expressing B-lineage tumor cells. The resulting cross-linkage may trigger a potent cytotoxic T-lymphocyte response against the CD20-expressing tumor B cells.