LEUKEMIA & LYMPHOMA SOCIETY®

# SPOTLIGHT ON AGGRESSIVE NON-HODGKIN LYMPHOMAS

**Jason Westin, MD**
**Director, Lymphoma Clinical Research**
**Section Chief, Aggressive Lymphoma**
**Department of Lymphoma & Myeloma**
**The University of Texas at MD Anderson Cancer Center**
**Houston, TX**

1

## WELCOMING REMARKS

SPOTLIGHT ON AGGRESSIVE NON-HODGKIN LYMPHOMAS

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

LEUKEMIA & LYMPHOMA SOCIETY®

2

# WELCOMING REMARKS

SPOTLIGHT ON AGGRESSIVE NON-HODGKIN LYMPHOMAS

**Stephanie Chuang**
**Diffuse Large B-cell Lymphoma Survivor**
**Journalist**
**Founder, The Patient Story**

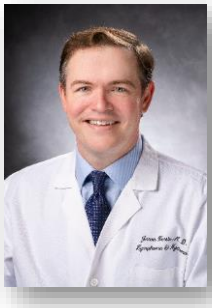

thepatientstory.com

LEUKEMIA & LYMPHOMA SOCIETY

3

# DISCLOSURES

SPOTLIGHT ON AGGRESSIVE NON-HODGKIN LYMPHOMAS



**Dr. James Westin**

**Consultant/Honoraria:**

**Abbvie, ADC Therapeutics, AstraZeneca, BMS, Genentech, Kite/Gilead, Morphosys/Incyte, Kymera, MonteRosa, Novartis, Nurix**

LEUKEMIA & LYMPHOMA SOCIETY

4


THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

# Spotlight on Aggressive Non-Hodgkin Lymphomas

The Leukemia & Lymphoma Society

**Jason Westin MD MS FACP**
**Director, Lymphoma Clinical Research**
**Section Chief, Aggressive Lymphoma**
**MD Anderson Cancer Center**

5



## Aggressive Lymphomas: Agenda

- What is Diffuse Large B cell Lymphoma?
- Signs and Symptoms
- Current Treatment Options
- New Important Treatment Advances
- Burkitt Lymphoma
- What do I need to remember?

6

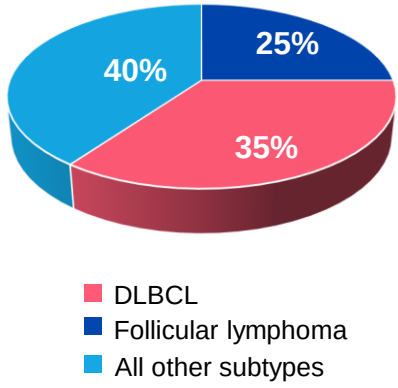
MD Anderson | Aggressive Lymphomas - Dr. Westin

# DLBCL IS THE MOST COMMON NHL SUBTYPE

**United States patients with DLBCL**

- Newly diagnosed ~30,000 per year
  - ~2/3 of newly diagnosed cured with 1L
- Relapsed/Refractory ~10,000 per year
  - 2/10 of r/r are cured

**NHL prevalence in the US**

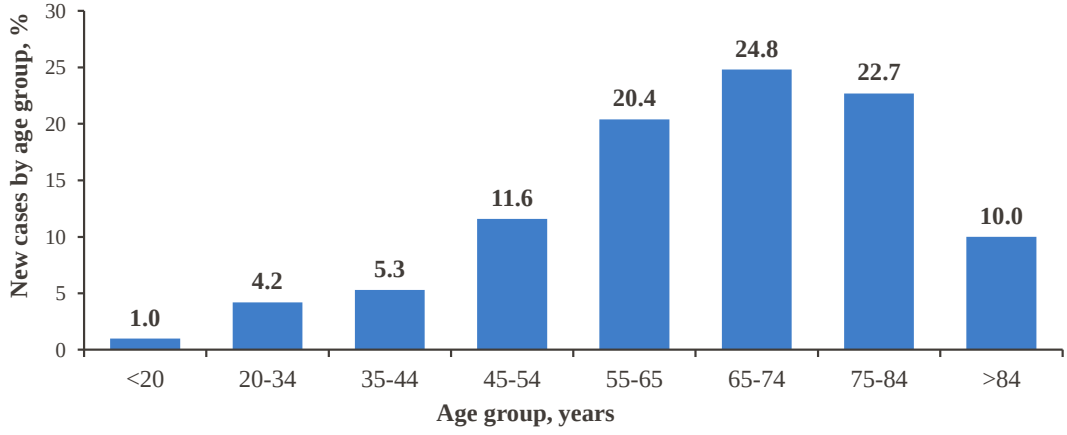



7

MD Anderson | Aggressive Lymphomas - Dr. Westin

# DLBCL INCIDENCE INCREASES WITH AGE

**Average patient at diagnosis is 60-65 years of age (median age = 69 years), where most are not fit for HDC/ASCT**




8

# Lymphoma Facts:

**Estimated New Cases**

| | Males | | | Females | | |
|---|---|---|---|---|---|---|
| Prostate | 161,360 | 19% | | Breast | 252,710 | 30% |
| Lung & bronchus | 116,990 | 14% | | Lung & bronchus | 105,510 | 12% |
| Colon & rectum | 71,420 | 9% | | Colon & rectum | 64,010 | 8% |
| Urinary bladder | 60,490 | 7% | | Uterine corpus | 61,380 | 7% |
| Melanoma of the skin | 52,170 | 6% | | Thyroid | 42,470 | 5% |
| Kidney & renal pelvis | 40,610 | 5% | | Melanoma of the skin | 34,940 | 4% |
| Non-Hodgkin lymphoma | 40,080 | 5% | | Non-Hodgkin lymphoma | 32,160 | 4% |
| Leukemia | 36,290 | 4% | | Leukemia | 25,840 | 3% |
| Oral cavity & pharynx | 35,720 | 4% | | Pancreas | 25,700 | 3% |
| Liver & intrahepatic bile duct | 29,200 | 3% | | Kidney & renal pelvis | 23,380 | 3% |
| **All Sites** | **836,150** | **100%** | | **All Sites** | **852,630** | **100%** |

Cancer Statistics, Siegel CA Cancer J Clin 2017, 67:7-30

9



# Lymphoma Facts:

**Estimated Deaths**

| | Males | | | Females | | |
|---|---|---|---|---|---|---|
| Lung & bronchus | 84,590 | 27% | | Lung & bronchus | 71,280 | 25% |
| Colon & rectum | 27,150 | 9% | | Breast | 40,610 | 14% |
| Prostate | 26,730 | 8% | | Colon & rectum | 23,110 | 8% |
| Pancreas | 22,300 | 7% | | Pancreas | 20,790 | 7% |
| Liver & intrahepatic bile duct | 19,610 | 6% | | Ovary | 14,080 | 5% |
| Leukemia | 14,300 | 4% | | Uterine corpus | 10,920 | 4% |
| Esophagus | 12,720 | 4% | | Leukemia | 10,200 | 4% |
| Urinary bladder | 12,240 | 4% | | Liver & intrahepatic bile duct | 9,310 | 3% |
| Non-Hodgkin lymphoma | 11,450 | 4% | | Non-Hodgkin lymphoma | 8,690 | 3% |
| Brain & other nervous system | 9,620 | 3% | | Brain & other nervous system | 7,080 | 3% |
| **All Sites** | **318,420** | **100%** | | **All Sites** | **282,500** | **100%** |

Cancer Statistics, Siegel CA Cancer J Clin 2017, 67:7-30

10

# Lymphoma Facts:

Estimated New Cancer Cases and Deaths by Sex, United States, 2017*

| | ESTIMATED NEW CASES | | | ESTIMATED DEATHS | | |
|---|---|---|---|---|---|---|
| | BOTH SEXES | MALE | FEMALE | BOTH SEXES | MALE | FEMALE |
| **Lymphoma** | **80,500** | **44,730** | **35,770** | **21,210** | **12,080** | **9,130** |
| Hodgkin lymphoma | 8,260 | 4,650 | 3,610 | 1,070 | 630 | 440 |
| Non-Hodgkin lymphoma | 72,240 | 40,080 | 32,160 | 20,140 | 11,450 | 8,690 |
| **Myeloma** | **30,280** | **17,490** | **12,790** | **12,590** | 6,660 | **5,930** |

Cancer Statistics, Siegel CA Cancer J Clin 2017, 67:7-30

11



# Lymphoma Facts:

TABLE 8. Probability (%) of Developing Invasive Cancer Within Selected Age Intervals by Sex, United States, 2011 to 2013*

| | | BIRTH TO 49 | 50 TO 59 | 60 TO 69 | ≥70 | BIRTH TO DEATH |
|---|---|---|---|---|---|---|
| **All sites†** | Male | 3.4 (1 in 30) | 6.3 (1 in 16) | 14.0 (1 in 7) | 33.3 (1 in 3) | 40.8 (1 in 2) |
| | Female | 5.4 (1 in 18) | 6.0 (1 in 17) | 10.0 (1 in 10) | 25.9 (1 in 4) | 37.5 (1 in 3) |
| **Breast** | Female | 1.9 (1 in 52) | 2.3 (1 in 44) | 3.5 (1 in 29) | 6.8 (1 in 15) | 12.4 (1 in 8) |
| **Colorectum** | Male | 0.3 (1 in 294) | 0.7 (1 in 149) | 1.2 (1 in 84) | 3.5 (1 in 28) | 4.6 (1 in 22) |
| | Female | 0.3 (1 in 318) | 0.5 (1 in 198) | 0.8 (1 in 120) | 3.2 (1 in 31) | 4.2 (1 in 24) |
| **Kidney & renal pelvis** | Male | 0.2 (1 in 457) | 0.3 (1 in 289) | 0.6 (1 in 157) | 1.3 (1 in 75) | 2.1 (1 in 48) |
| | Female | 0.1 (1 in 729) | 0.2 (1 in 582) | 0.3 (1 in 315) | 0.7 (1 in 135) | 1.2 (1 in 83) |
| **Leukemia** | Male | 0.2 (1 in 410) | 0.2 (1 in 574) | 0.6 (1 in 259) | 1.4 (1 in 72) | 1.8 (1 in 57) |
| | Female | 0.2 (1 in 509) | 0.1 (1 in 901) | 0.4 (1 in 447) | 0.9 (1 in 113) | 1.2 (1 in 81) |
| **Lung & bronchus** | Male | 0.2 (1 in 643) | 0.7 (1 in 149) | 1.9 (1 in 53) | 6.2 (1 in 16) | 7.0 (1 in 14) |
| | Female | 0.2 (1 in 598) | 0.6 (1 in 178) | 1.5 (1 in 68) | 4.8 (1 in 21) | 6.0 (1 in 17) |
| **Melanoma of the skin‡** | Male | 0.5 (1 in 220) | 0.5 (1 in 198) | 0.9 (1 in 111) | 2.5 (1 in 40) | 3.5 (1 in 28) |
| | Female | 0.6 (1 in 155) | 0.4 (1 in 273) | 0.5 (1 in 212) | 1.6 (1 in 57) | 2.3 (1 in 44) |
| **Non-Hodgkin lymphoma** | Male | 0.3 (1 in 385) | 0.3 (1 in 353) | 0.4 (1 in 175) | 1.8 (1 in 55) | 2.4 (1 in 42) |
| | Female | 0.2 (1 in 547) | 0.2 (1 in 483) | 0.2 (1 in 245) | 1.3 (1 in 74) | 1.9 (1 in 54) |
| **Prostate** | Male | 0.3 (1 in 354) | 1.9 (1 in 52) | 5.4 (1 in 19) | 9.1 (1 in 11) | 12.9 (1 in 8) |
| **Thyroid** | Male | 0.2 (1 in 533) | 0.1 (1 in 799) | 0.2 (1 in 620) | 0.2 (1 in 429) | 0.6 (1 in 163) |
| | Female | 0.8 (1 in 127) | 0.4 (1 in 275) | 0.3 (1 in 292) | 0.4 (1 in 258) | 1.8 (1 in 57) |
| **Uterine cervix** | Female | 0.3 (1 in 371) | 0.1 (1 in 868) | 0.1 (1 in 899) | 0.2 (1 in 594) | 0.6 (1 in 161) |
| **Uterine corpus** | Female | 0.3 (1 in 352) | 0.6 (1 in 169) | 1.0 (1 in 105) | 1.3 (1 in 76) | 2.8 (1 in 36) |

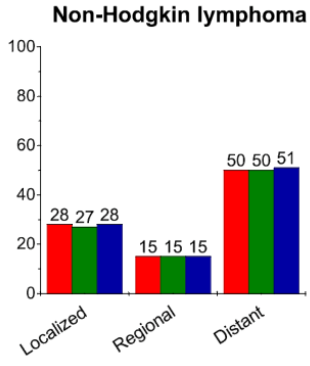
Cancer Statistics, Siegel CA Cancer J Clin 2017, 67:7-30

12

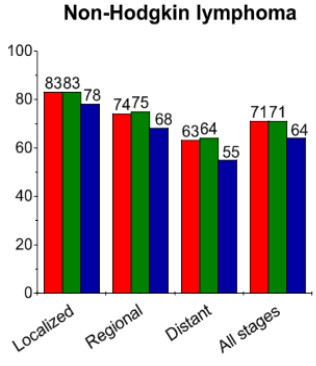
MD Anderson | Aggressive Lymphomas - Dr. Westin

# Lymphoma Facts:


Stage at diagnosis



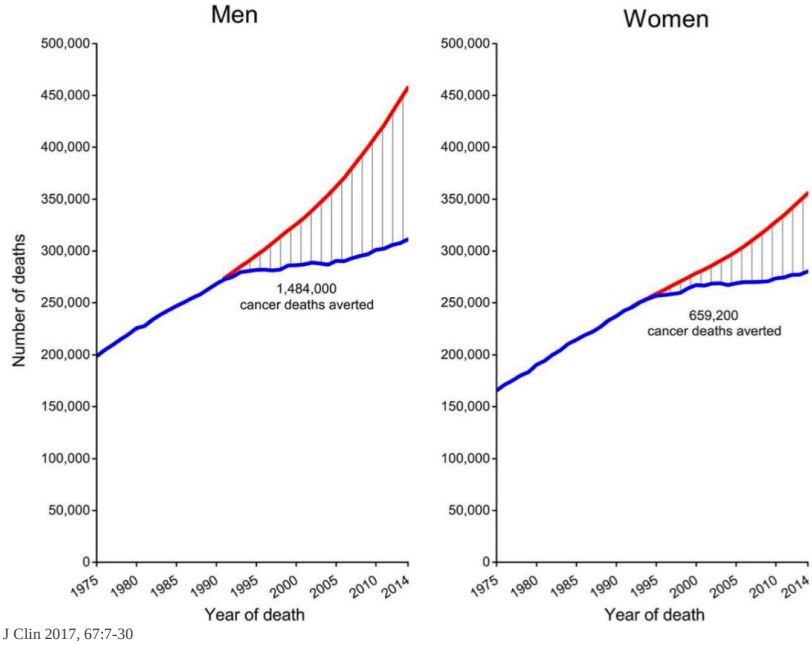

5 year overall survival




Cancer Statistics, Siegel CA Cancer J Clin 2017, 67:7-30

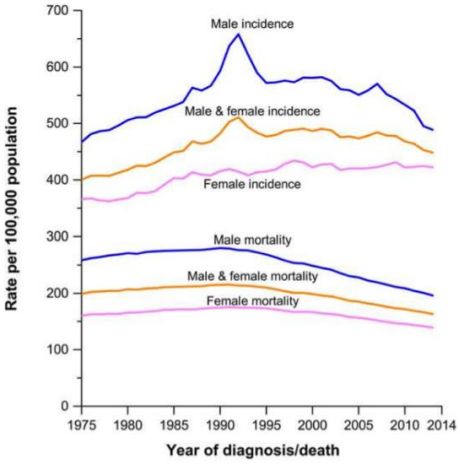
13

MD Anderson | Aggressive Lymphomas - Dr. Westin




Cancer Statistics, Siegel CA Cancer J Clin 2017, 67:7-30

14




Cancer Statistics, Siegel CA Cancer J Clin 2017, 67:7-30

15



## How is Diffuse Large B-cell Lymphoma diagnosed?

A new lump in the neck, under the arm, in the groin

A new pain that lacks explanation

Significant and worsening fatigue

None of the above (serendipity)

16

## How is Diffuse Large B-cell Lymphoma diagnosed?

- A biopsy is required for diagnosis
- Radiology reports may say “suspicious for lymphoma”
  - Not good enough
- Usually a core needle or surgical biopsy is required
- Fine needle aspiration gives a smear of cells – not good enough for subtyping lymphoma

17

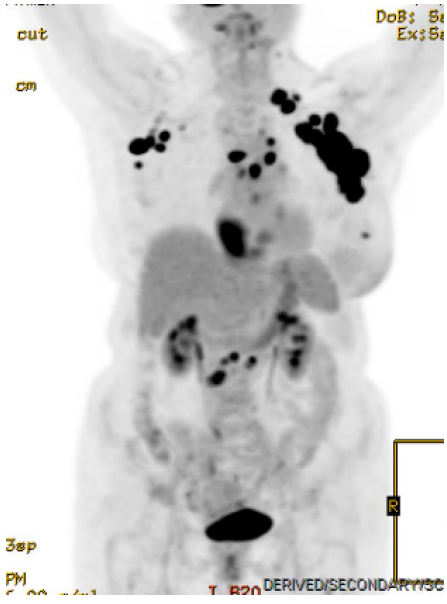


## Clinical Case

63F without significant past medical history has a new mass under her left arm. She feels ok but has lost 5 pounds over the past month without trying.

On exam, she has bilateral small LN, a PET Scan and biopsy are ordered.

LDH is up, labs otherwise normal




18

## We have the biopsy – now what?

THE UPDATED WHO CLASSIFICATION OF HEMATOLOGICAL MALIGNANCIES

**The 2016 revision of the World Health Organization classification of lymphoid neoplasms**

Steven H. Swerdlow,[1] Elias Campo,[2] Stefano A. Pileri,[3] Nancy Lee Harris,[4] Harald Stein,[5] Reiner Siebert,[6] Ranjana Advani,[7] Michele Ghielmini,[8] Gilles A. Salles,[9] Andrew D. Zelenetz,[10] and Elaine S. Jaffe[11]

BLOOD, 19 MAY 2016 • VOLUME 127, NUMBER 20

19



## How do we classify Lymphomas?

1. The type of lymphocyte the lymphoma started from
2. How the lymphoma looks under the microscope
3. The presence of genetic and protein changes of the lymphoma

20

## DLBCL Diagnosis

Lymph Node core or excisional biopsy (NOT FNA)

Immunohistochemistry for B-cell markers

- Cell of Origin (WHO recommends)
- MYC and BCL protein expression
- CD19 is usually assessed

FISH

- MYC followed by BCL2 and BCL6

Bone Marrow biopsy

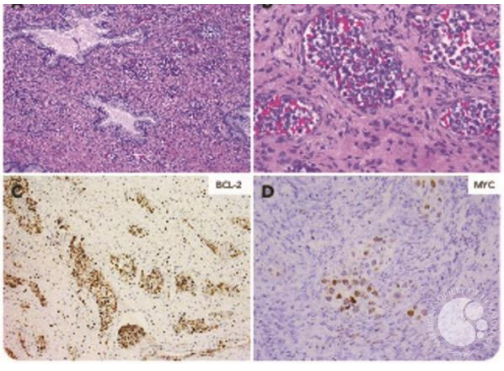
- Sometimes not done if PET – but controversy

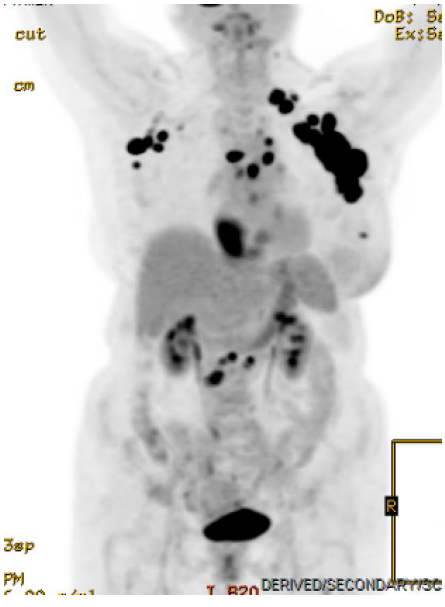
21



## Clinical Case

A core needle biopsy shows






22

MD Anderson

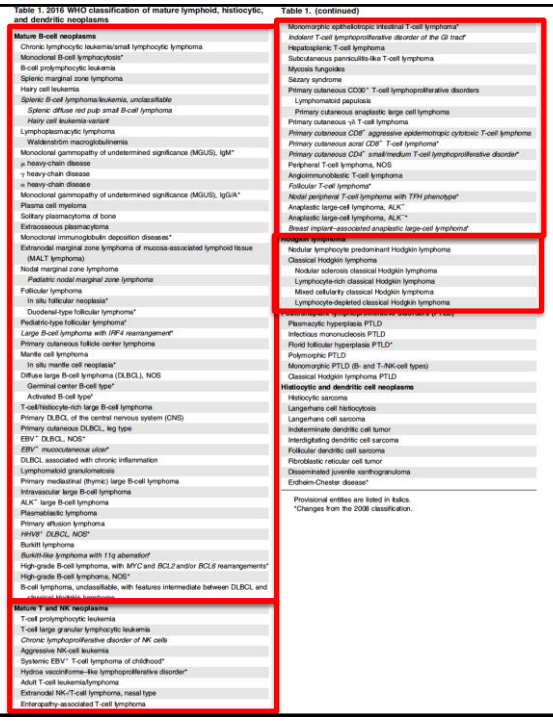


**Table 1. 2016 WHO classification of mature lymphoid, histiocytic, and dendritic neoplasms**

**Mature B-cell neoplasms**
- Chronic lymphocytic leukemia/small lymphocytic lymphoma
- Monoclonal B-cell lymphocytosis*
- B-cell prolymphocytic leukemia
- Splenic marginal zone lymphoma
- Hairy cell leukemia
- *Splenic B-cell lymphoma/leukemia, unclassifiable*
  - *Splenic diffuse red pulp small B-cell lymphoma*
  - *Hairy cell leukemia-variant*
- Lymphoplasmacytic lymphoma
  - Waldenström macroglobulinemia
- Monoclonal gammopathy of undetermined significance (MGUS), IgM*
- μ heavy-chain disease
- γ heavy-chain disease
- α heavy-chain disease
- Monoclonal gammopathy of undetermined significance (MGUS), IgG/A*
- Plasma cell myeloma
- Solitary plasmacytoma of bone
- Extraosseous plasmacytoma
- Monoclonal immunoglobulin deposition diseases*
- Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)
- Nodal marginal zone lymphoma
  - *Pediatric nodal marginal zone lymphoma*
- Follicular lymphoma
  - In situ follicular neoplasia*
  - Duodenal-type follicular lymphoma*
- Pediatric-type follicular lymphoma*
- *Large B-cell lymphoma with IRF4 rearrangement**
- Primary cutaneous follicle center lymphoma
- Mantle cell lymphoma
  - In situ mantle cell neoplasia*
- Diffuse large B-cell lymphoma (DLBCL), NOS
  - Germinal center B-cell type*
  - Activated B-cell type*
- T-cell/histiocyte-rich large B-cell lymphoma
- Primary DLBCL of the central nervous system (CNS)
- Primary cutaneous DLBCL, leg type
- EBV+ DLBCL, NOS*
- *EBV+ mucocutaneous ulcer**
- DLBCL associated with chronic inflammation
- Lymphomatoid granulomatosis
- Primary mediastinal (thymic) large B-cell lymphoma
- Intravascular large B-cell lymphoma
- ALK+ large B-cell lymphoma
- Plasmablastic lymphoma
- Primary effusion lymphoma
- *HHV8+ DLBCL, NOS**
- Burkitt lymphoma
- *Burkitt-like lymphoma with 11q aberration**
- High-grade B-cell lymphoma, with *MYC* and *BCL2* and/or *BCL6* rearrangements*
- High-grade B-cell lymphoma, NOS*
- B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and classical Hodgkin lymphoma

**Mature T and NK neoplasms**
- T-cell prolymphocytic leukemia
- T-cell large granular lymphocytic leukemia
- *Chronic lymphoproliferative disorder of NK cells*
- Aggressive NK-cell leukemia
- Systemic EBV+ T-cell lymphoma of childhood*
- Hydroa vacciniforme–like lymphoproliferative disorder*
- Adult T-cell leukemia/lymphoma
- Extranodal NK/T-cell lymphoma, nasal type
- Enteropathy-associated T-cell lymphoma
- Monomorphic epitheliotropic intestinal T-cell lymphoma*
- *Indolent T-cell lymphoproliferative disorder of the GI tract**
- Hepatosplenic T-cell lymphoma
- Subcutaneous panniculitis-like T-cell lymphoma
- Mycosis fungoides
- Sézary syndrome
- Primary cutaneous CD30+ T-cell lymphoproliferative disorders
  - Lymphomatoid papulosis
  - Primary cutaneous anaplastic large cell lymphoma
- Primary cutaneous γδ T-cell lymphoma
- *Primary cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma*
- *Primary cutaneous acral CD8+ T-cell lymphoma**
- *Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder**
- Peripheral T-cell lymphoma, NOS
- Angioimmunoblastic T-cell lymphoma
- *Follicular T-cell lymphoma**
- *Nodal peripheral T-cell lymphoma with TFH phenotype**
- Anaplastic large-cell lymphoma, ALK−*
- Anaplastic large-cell lymphoma, ALK+*
- *Breast implant–associated anaplastic large-cell lymphoma**

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

**Immunodeficiency and myeloid neoplasm associated (partial list)**
- Plasmacytic hyperplasia PTLD
- Infectious mononucleosis PTLD
- Florid follicular hyperplasia PTLD*
- Polymorphic PTLD
- Monomorphic PTLD (B- and T-/NK-cell types)
- Classical Hodgkin lymphoma PTLD

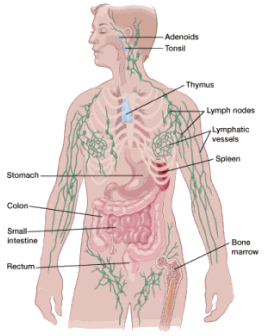
**Histiocytic and dendritic cell neoplasms**
- Histiocytic sarcoma
- Langerhans cell histiocytosis
- Langerhans cell sarcoma
- Indeterminate dendritic cell tumor
- Interdigitating dendritic cell sarcoma
- Follicular dendritic cell sarcoma
- Fibroblastic reticular cell tumor
- Disseminated juvenile xanthogranuloma
- Erdheim-Chester disease*

Provisional entities are listed in italics.
*Changes from the 2008 classification.

23

MD Anderson | Aggressive Lymphomas - Dr. Westin

# How do we classify Lymphomas?




What are Lymphocytes?

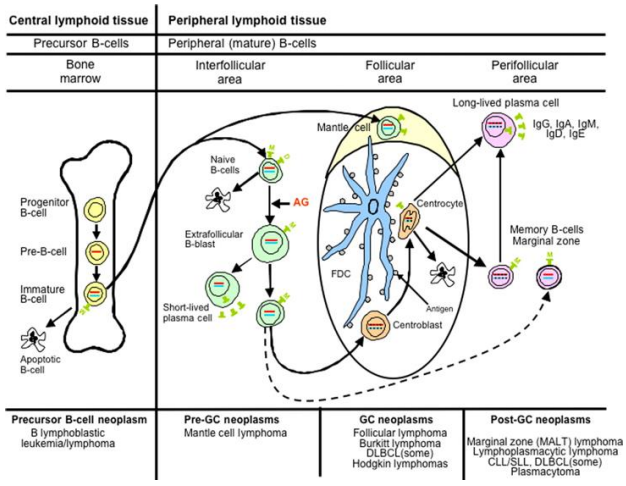
- Latin: lympha = water
- Lymphatic system
  - circulatory system for lymphocytes and fluid
- Lymphocytes are also called white blood cells

What are the types of lymphocytes?

- B cells (antibodies)
- T cells (kill infection or abnormal cells, help/hurt other immune cells)
- NK cells (“natural killer” cells

24

## How do we classify Lymphomas?

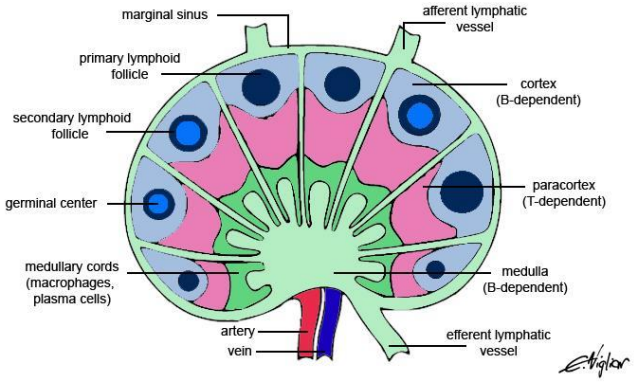



25



## How do we classify Lymphomas?

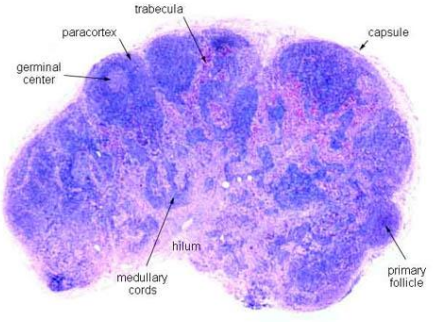
How does the lymphoma looks under the microscope




26

## How do we classify Lymphomas?

How does the lymphoma looks under the microscope

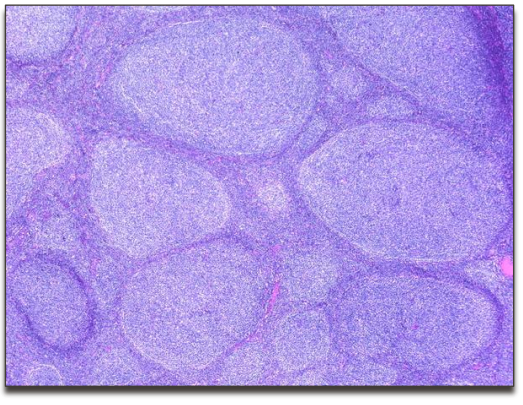



27



## How do we classify Lymphomas?

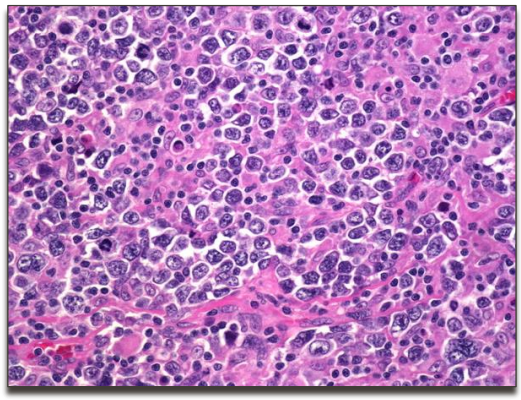
How does the lymphoma looks under the microscope



28

## How do we classify Lymphomas?

How does the lymphoma looks under the microscope

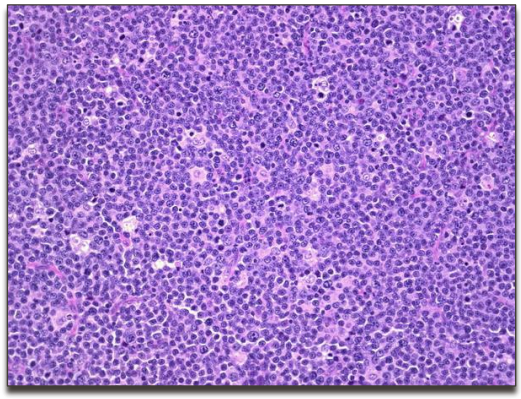


29



## How do we classify Lymphomas?

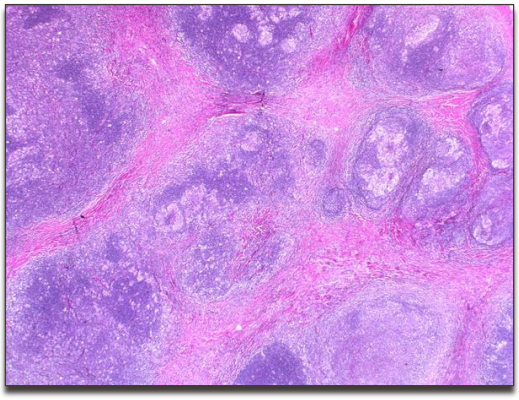
How does the lymphoma looks under the microscope



30

## How do we classify Lymphomas?

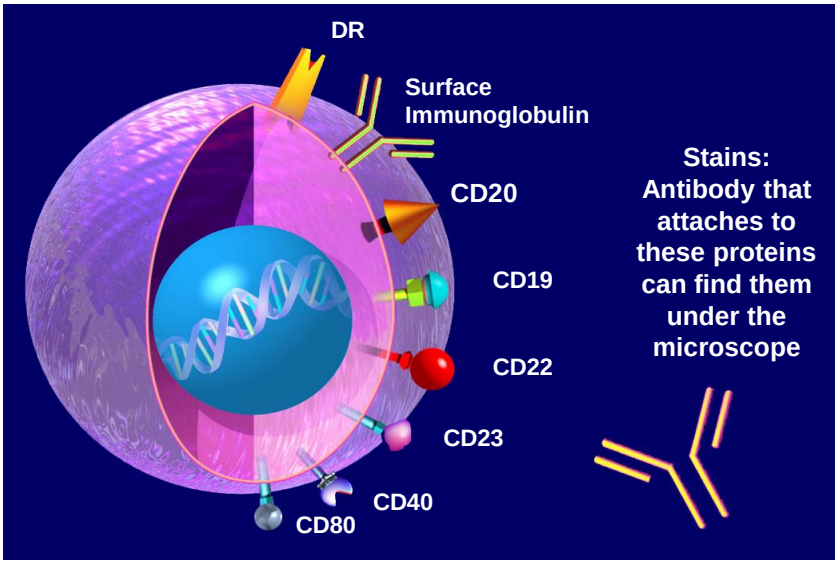
How does the lymphoma looks under the microscope



31



## Examples of Various Proteins Associated with Various B-Cell Lymphomas




CD = Cluster of Differentiation

32

## "Markers" That Make a Difference in Diagnosis of Some Lymphomas

- "Markers" are sugar/protein complexes that are produced by cells
- They can be produced by both cancer cells and normal cells
- These can be studied under the microscope to identify certain types of lymphomas

| Marker | FL | SLL/CLL | MCL | MZL | T Cell |
|---|---|---|---|---|---|
| CD20 | Pos | Pos | Pos | Pos | Neg |
| CD10 | Pos | Neg | Neg | Neg | Neg |
| CD5 | Neg | Pos | Pos | Neg | Pos |
| CD23 | Neg | Pos | Pos | Neg | Neg |
| Cyclin D1 | Neg | Neg | Pos | Neg | Neg |
| Cytogenetics | t(14;18) | Various | t(11;14) | Various | Various |

- CD: Cluster of Differentiation
- Not all are absolute: There are often variations in positivity/negativity
- Note: The genetics are only in the cancer cells

33



## Signs and Symptoms of Diffuse Large B-cell Lymphoma

Could have any (or none) of below:

Tired

"Don't feel well"

Night sweats

Unintentional Weight Loss

Pain

A new swelling or lump

34

## What happens after diagnosis?

Testing to see where the lymphoma exists in the body

- PET/CT scan
- Bone Marrow Biopsy
- Blood tests

Testing to see if any limitations on treatment due to other medical problems

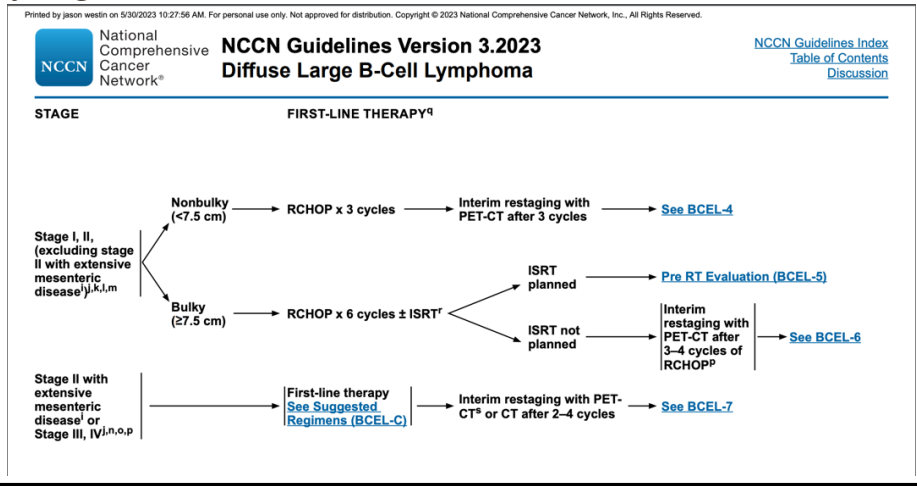
- Echocardiogram
- EKG
- Blood tests

35



## What are the current treatment options for Diffuse Large B-cell Lymphoma?

For newly diagnosed disease:




36

## Current Therapy

RCHOP

*Cancer* 38:1484–1493, 1976.

37



HYDROXYLDAUNOMYCIN (ADRIAMYCIN) COMBINATION CHEMOTHERAPY IN MALIGNANT LYMPHOMA

EUGENE M. MCKELVEY, MD, JEFFREY A. GOTTLIEB, MD, HENRY E. WILSON, MD, ARTHUR HAUT, MD, ROBERT W. TALLEY, MD, RONALD STEPHENS, MD, MONTAGUE LANE, MD, JESS F. GAMBLE, MD, STEPHEN E. JONES, MD, PETRE N. GROZEA, MD, JORDON GUTTERMAN, MD, CHARLES COLTMAN, JR., MD, AND THOMAS E. MOON, PHD

*Cancer* 38:1484–1493, 1976.

38

# HYDROXYLDAUNOMYCIN (ADRIAMYCIN) COMBINATION CHEMOTHERAPY IN MALIGNANT LYMPHOMA

Eugene M. McKelvey, MD, Jeffrey A. Gottlieb, MD, Henry E. Wilson, MD, Arthur Haut, MD, Robert W. Talley, MD, Ronald Stephens, MD, Montague Lane, MD, Jess F. Gamble, MD, Stephen E. Jones, MD, Petre N. Grozea, MD, Jordon Gutterman, MD, Charles Coltman, Jr., MD, and Thomas E. Moon, PhD

Table 1. CHOP–HOP Chemotherapy for Non-Hodgkin's Lymphoma

| | | | |
|---|---|---|---|
| C | Cyclophosphamide | 750 mg/m² | d1 |
| H | Adriamycin | 50 mg/m² | d1 |
| O | Vincristine | 1.4 mg/m² (max 2 mg) | d1 |
| P | Prednisone | 100 mg daily × 5 | d1–5 |
| H | Adriamycin | 80 mg/m² | d1 |
| O | Vincristine | 1.4 mg/m² (max 2 mg) | d1 |
| P | Prednisone | 100 mg daily × 5 | d1–5 |

Courses repeated every 2–3 weeks

*Cancer* 38:1484–1493, 1976.

39





# COMPARISON OF A STANDARD REGIMEN (CHOP) WITH THREE INTENSIVE CHEMOTHERAPY REGIMENS FOR ADVANCED NON-HODGKIN'S LYMPHOMA

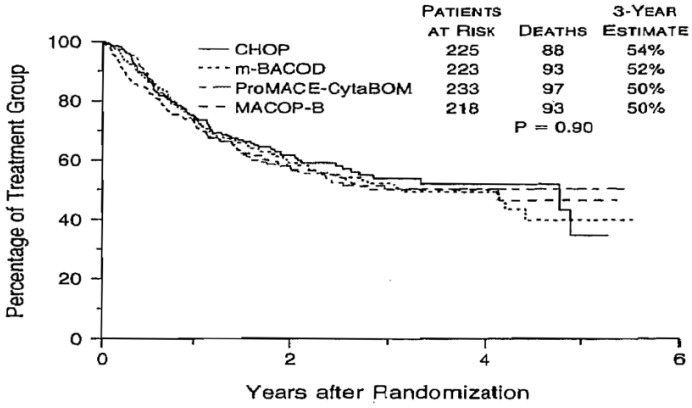
Richard I. Fisher, M.D., Ellen R. Gaynor, M.D., Steve Dahlberg, M.S., Martin M. Oken, M.D., Thomas M. Grogan, M.D., Evonne M. Mize, John H. Glick, M.D., Charles A. Coltman, Jr., M.D., and Thomas P. Miller, M.D.

40

Aggressive Lymphomas - Dr. Westin

## COMPARISON OF A STANDARD REGIMEN (CHOP) WITH THREE INTENSIVE CHEMOTHERAPY REGIMENS FOR ADVANCED NON-HODGKIN'S LYMPHOMA

RICHARD I. FISHER, M.D., ELLEN R. GAYNOR, M.D., STEVE DAHLBERG, M.S., MARTIN M. OKEN, M.D., THOMAS M. GROGAN, M.D., EVONNE M. MIZE, JOHN H. GLICK, M.D., CHARLES A. COLTMAN, JR., M.D., AND THOMAS P. MILLER, M.D.




| | Patients at Risk | Deaths | 3-Year Estimate |
|---|---|---|---|
| CHOP | 225 | 88 | 54% |
| m-BACOD | 223 | 93 | 52% |
| ProMACE-CytaBOM | 233 | 97 | 50% |
| MACOP-B | 218 | 93 | 50% |

Figure 2. Overall Survival in the Treatment Groups. The three-year estimate is of overall survival.

**m-BACOD**

**MTX, Bleo, Dox, CTX, VCR, Dex**

**MACOP-B**

**MTX, Dox, CTX, VCR, Pred, Bleo**

**ProMACE-CytaBOM**

**CTX, Dox, Etop, Pred**

**AraC, Bleo, VCR, Bleo**

NEJM, 1993:328:1002-6

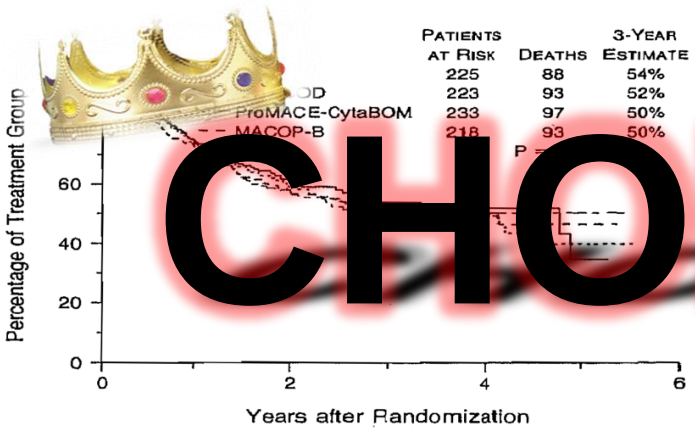
41

1002 THE NEW ENGLAND JOURNAL OF MEDICINE April 8, 1993

Aggressive Lymphomas - Dr. Westin

COMPARISON OF A STANDARD REGIMEN (CHOP) WITH THREE INTENSIVE CHEMOTHERAPY REGIMENS FOR ADVANCED NON-HODGKIN'S LYMPHOMA

RICHARD I. FISHER, M.D., ELLEN R. GAYNOR, M.D., STEVE DAHLBERG, M.S., MARTIN M. OKEN, M.D., THOMAS M. GROGAN, M.D., EVONNE M. MIZE, JOHN H. GLICK, M.D., CHARLES A. COLTMAN, JR., M.D., AND THOMAS P. MILLER, M.D.




| | Patients at Risk | Deaths | 3-Year Estimate |
|---|---|---|---|
| CHOP | 225 | 88 | 54% |
| m-BACOD | 223 | 93 | 52% |
| ProMACE-CytaBOM | 233 | 97 | 50% |
| MACOP-B | 218 | 93 | 50% |

Figure 2. Overall Survival in the Treatment Groups. The three-year estimate is of overall survival.

**m-BACOD**

**MTX, Bleo, Dox, CTX, VCR, Dex**

**MACOP-B**

**MTX, Dox, CTX, VCR, Pred, Bleo**

**ProMACE-CytaBOM**

**CTX, Dox, Etop, Pred**

**AraC, Bleo, VCR, Bleo**

NEJM, 1993:328:1002-6

42

## How is RCHOP given?

IV usually via port or PICC

• Drugs are vessicants

IV portion is over 1 day every 3 weeks

Oral is daily for 5 days, every 3 weeks from start date

43



## What are the main side effects of RCHOP?

Fatigue

Nausea

Infection risk

44

## What are rare but serious side effects of RCHOP?

Low chance of heart failure

Low chance of bone marrow problems like myleodysplasia or leukemia

Low chance of bleeding from the bladder

45



## How likely is RCHOP to work?

Remember the IPI: APLES

- **A**ge >60
- **P**erformance status – impaired
- **L**DH – elevated
- **E**xtranodal sites >=2
- **S**tage III/IV

46

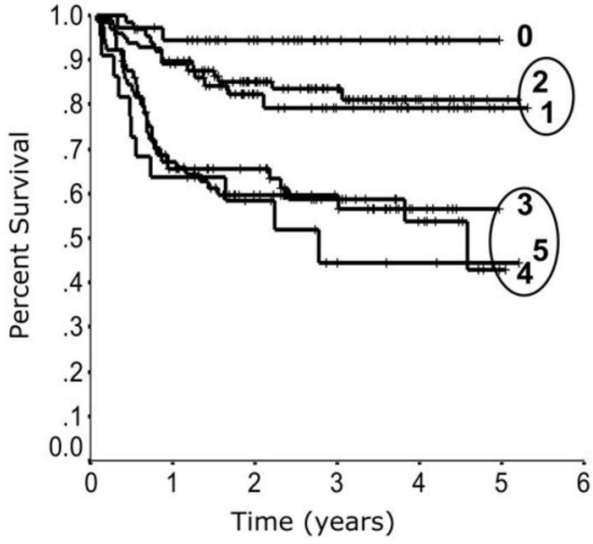
MD Anderson | Aggressive Lymphomas - Dr. Westin

## IPI vs progression free survival

0 = 90+%

1 & 2 = 80%

3/4/5 = 55%




Sehn et al, Blood 2007

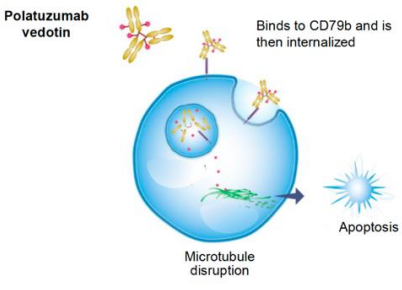
47

MD Anderson | Aggressive Lymphomas - Dr. Westin

## Polarix trial

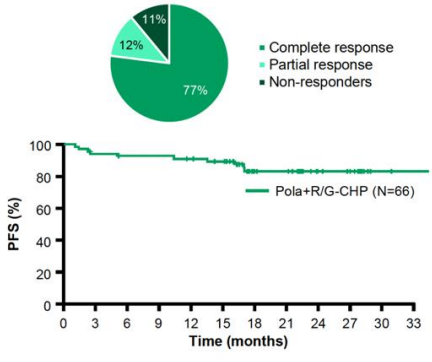
### Polatuzumab vedotin is an ADC targeting CD79b

**CD79b is ubiquitously expressed on DLBCL cells[1–3]**




ADC, antibody–drug conjugate; G, obinutuzumab.

**Pola+R/G-CHP demonstrated activity in first-line DLBCL[4]**

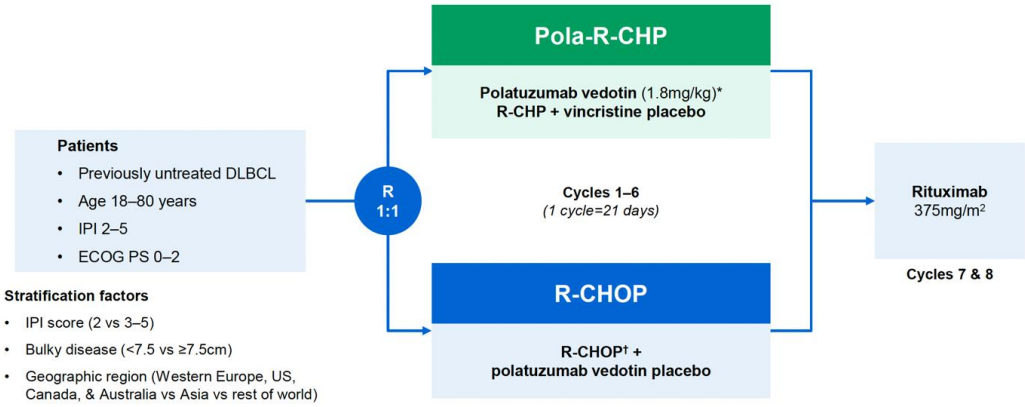



1. Dornan D, et al. Blood 2009;114:2721–9; 2. Polson AG, et al. Expert Opin Invest Drugs 2011;20:75–85; 3. Doronina SO, et al. Nat Biotechnol 2003;21:778–84; 4. Tilly H, et al. Lancet Oncol 2019;20:998–1010.

Tilly et al, ASH 2021

48

# POLARIX: A randomized double-blinded study



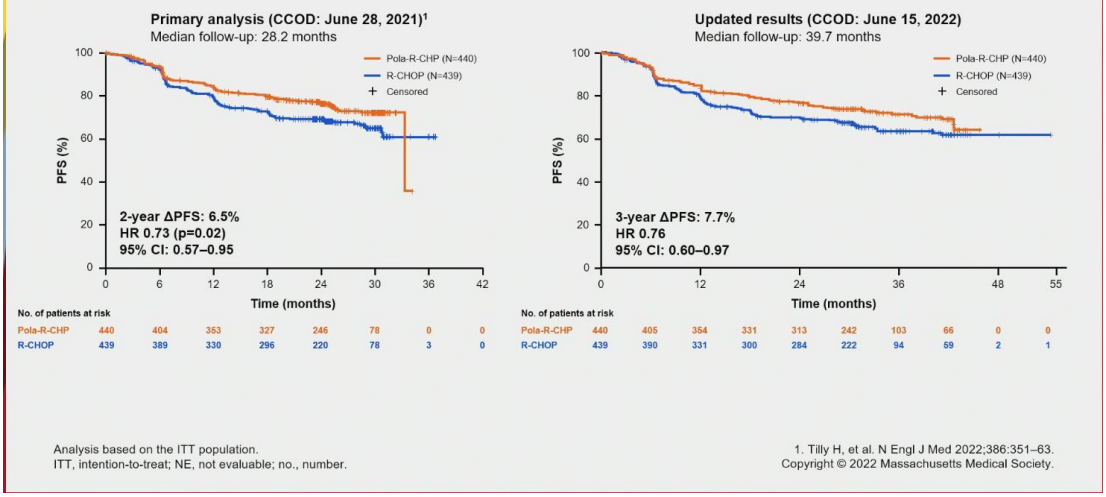

*IV on Day 1; †R-CHOP: IV rituximab 375mg/m², cyclophosphamide 750mg/m², doxorubicin 50mg/m², and vincristine 1.4mg/m² (max. 2mg) on Day 1, plus oral prednisone 100mg once daily on Days 1–5.
IPI, International prognostic index; ECOG PS, Eastern Cooperative Oncology Group performance status; R, randomized.

Tilly et al, ASH 2021

49



# PFS benefit with Pola-R-CHP vs R-CHOP was maintained with longer follow-up




Analysis based on the ITT population.
ITT, intention-to-treat; NE, not evaluable; no., number.

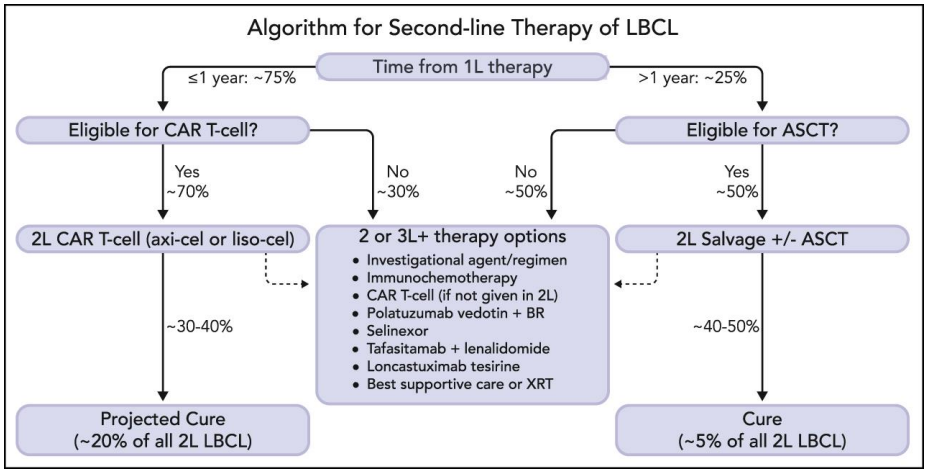
1. Tilly H, et al. N Engl J Med 2022;386:351–63.


Tilly et al, ASH 2021, Herrera et al, ASH 2022

50

## What are the current treatment options for Diffuse Large B-cell Lymphoma?

For relapsed disease




Westin & Sehn, Blood 2022

51



## What is an Autologous Stem Cell Transplant?

Intensive chemotherapy

If a good response

- Stem cells are collected
- Higher dose chemotherapy
- Stem cells are re-infused

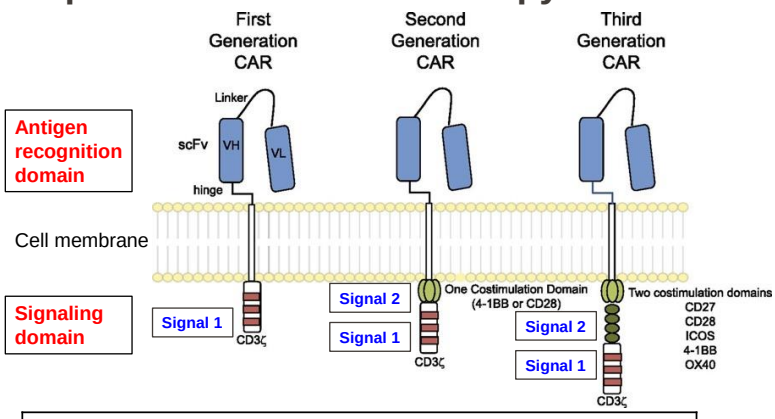
If a bad response

- CAR T-cell

52

MD Anderson | Aggressive Lymphomas - Dr. Westin

## Development of CAR T cell therapy




| | | | |
|---|---|---|---|
| Killing ability | + | + | ++ |
| Ability to multiply | | + | ++ |
| Cytokine secretion | | + | ++ |
| Persistence | | + | ++ |

Adapted from Maus et al. Blood 2014;123:2625-2635

53

MD Anderson | Aggressive Lymphomas - Dr. Westin

## CAR targets in development

| Target(s) | Tumor |
|---|---|
| **CD19**, CD20, CD22, CD23 | B cell leukemia/lymphoma |
| CD30 | T cell leukemia/lymphoma, Hodgkin lymphoma |
| CD38, BCMA, SLAM-F7 | Multiple myeloma |
| CD123 | Acute myeloid leukemia |
| Mesothelin | Pancreatic carcinoma |
| α-folate receptor | Ovarian Carcinoma |
| CAIX | Renal Cell Carcinoma |
| CEA | Colon Carcinoma |
| Her2 | Breast Carcinoma |
| GD2 | Neuroblastoma |
| GD3 | Melanoma |
| Lewis-Y | Colon Carcinoma |
| PSMA | Prostate Carcinoma |

54

MD Anderson | Aggressive Lymphomas - Dr. Westin

# CAR T cell production

Apheresis Product

T cell separation

Ready for bedside use

Viral transduction

Cell transfer to bag for growth

Wash, Concentrate & Freeze

Expand cells

The CAR is introduced into T cells using viruses and other means

55

MD Anderson | Aggressive Lymphomas - Dr. Westin

# Treatment Schema

2-4 wks manufacturing

**Apheresis / Blood draw**

**Days -5 to -3**

Conditioning chemotherapy
Cyclophosphamide
Fludarabine

**Day 0**

CAR T cells
(100-500 million cells)

- Patient-specific product; infused in <30 mins
- CAR T cells frozen at ≤ -150° C in GMP facility until the subject is ready for infusion
- Subject will be hospitalized for infusion of CAR T cells and remain hospitalized for at least 7 days following treatment

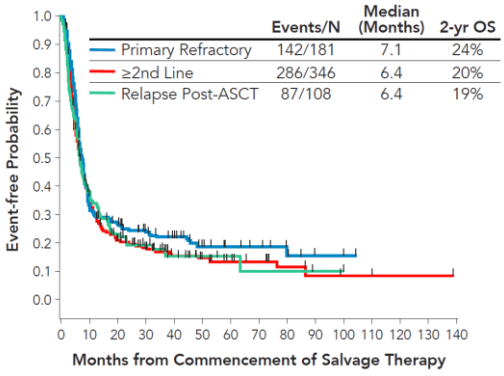
56

# Outcomes poor in refractory aggressive B-cell NHL

**(SCHOLAR - Retrospective Non-Hodgkin Lymphoma Research)**

- Meta-analysis to evaluate the outcomes in chemorefractory DLBCL
- CORAL, CCTG-LY12, MDACC, Mayo-Iowa
- Chemorefractory patient population
  - ✓ SD/PD after primary or later-lines of therapy
  - ✓ Relapse ≤12 months after ASCT
- N = 635
- ORR = 26%; CR rate = 8%
- Median OS = 6.6 months

**Overall survival**




*Crump, Westin, Neelapu et al, ASCO 2016*

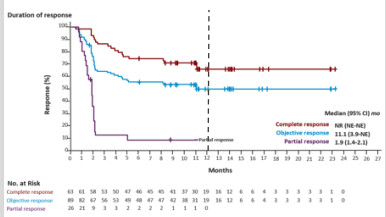




# Efficacy – Duration of Response

**ZUMA-1[1,2]**

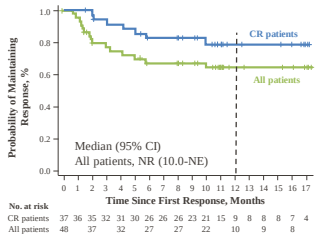
**Median follow-up, 15.4 months**




- 42% of patients had an ongoing response at long-term follow-up; 40% had CR
- 23 patients with either a PR (11/35) or SD (12/25) at the first tumor assessment (1 month post-Yescarta) achieved CR up to 15 months postinfusion without additional therapy
  - Median time to conversion from PR to CR: 64 days (range, 49-424 days)

**JULIET[3]**

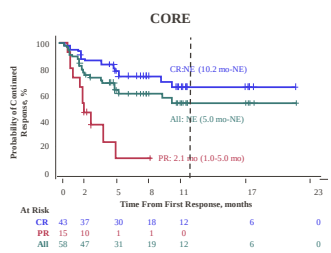
**Median follow-up, 13.9 months**




- 54% (13/24) patients converted from PR to CR, including 2 patients 9-12 months after initial response

**TRANSCEND[4]**

**Median follow-up, 8 months**



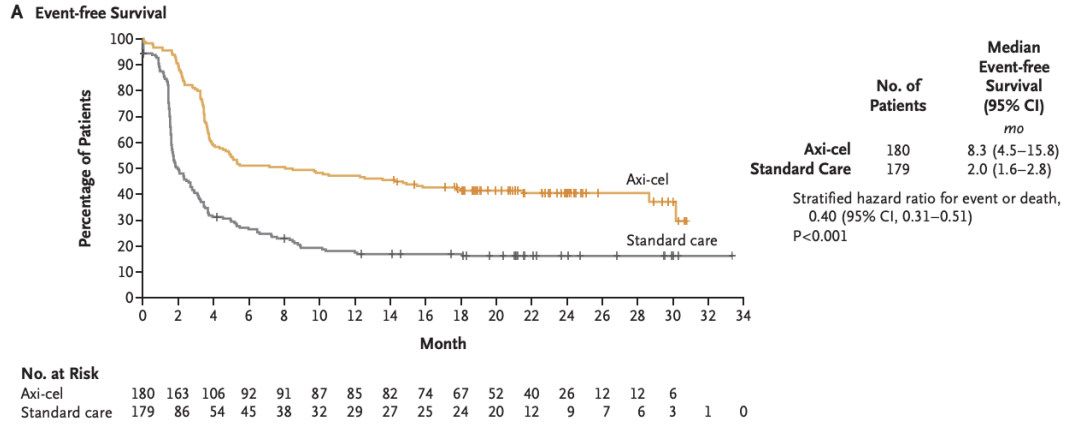

- In CORE group, 88% of patients with CR at 3 months stayed in CR at 6 months; 93% of patients in CR at 6 months had ongoing response

Full Group = Patients with relapsed or refractory DLBCL, HGBCL, PMBCL, or FL3B. CORE Group = Patients with r/r DLBCL or HGBCL.

[1]Neelapu SS, et al. *N Engl J Med*. 2017;377(26):2531-2544. [2]Neelapu SS et al. ASH 2017. [abstract 578].
[3]Borchmann P et al, EHA 2018. [abstract S799]. [4]Abramson JS et al, ASCO 2018. [abstract 7505].

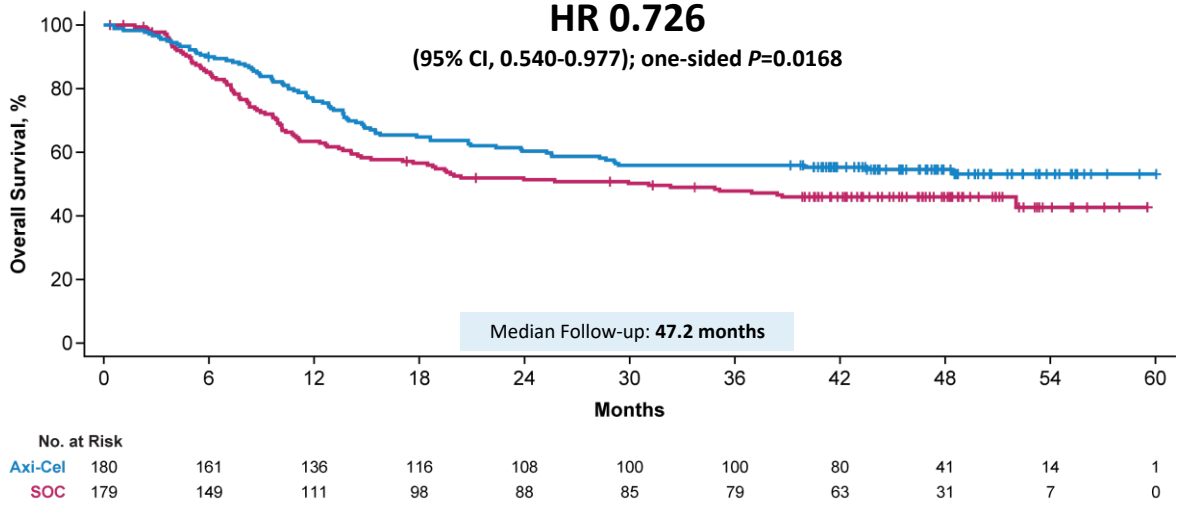
MD Anderson | Aggressive Lymphomas - Dr. Westin

## Axi-cel in 2L therapy vs chemo/SCT




59

## Axi-Cel Improved Overall Survival Versus Standard of Care



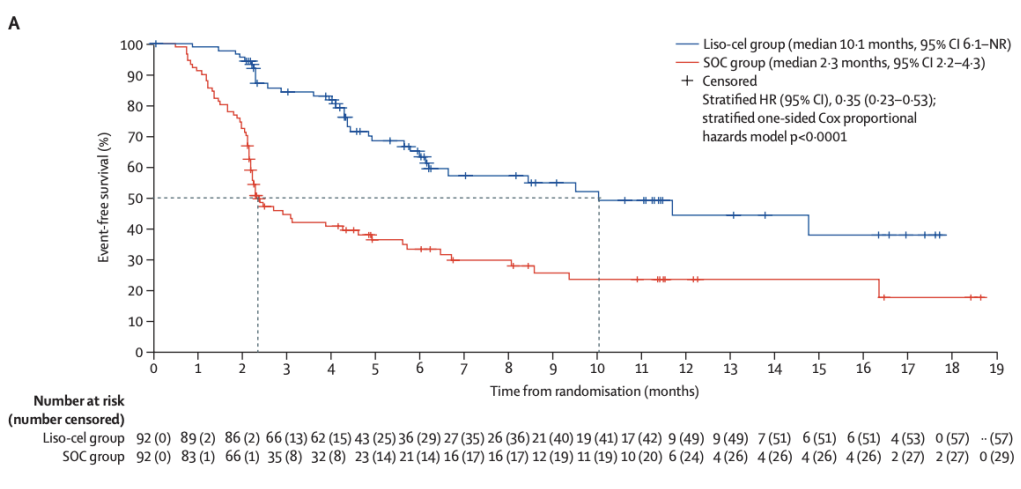

Axi-cel, axicabtagene ciloleucel; HR, hazard ratio; SOC, standard of care.

Westin et al ASCO 2023 Late-Breaking Abstract 107 12

60

MD Anderson | Aggressive Lymphomas - Dr. Westin

## Liso-cel in 2L therapy vs chemoSCT




61

MD Anderson | Aggressive Lymphomas - Dr. Westin

## What are the side effects of CAR T-cells?

Cytokine Release Syndrome (CRS)

- Fever
- Hypotension
- Organ dysfunction
- Usually reversible but can be severe and require ICU care

Neurologic toxicity

- Confusion
- Seizures
- Aphasia
- Tremor

62

## What are the side effects of CAR T-cells?

Cytokine Release Syndrome (CRS)

- Treated with supportive care when mild (tylenol, cooling blankets, etc)
- Treated with drugs targeting IL6 when moderate/severe (tocilizumab, siltuxumab)
- Treated with corticosteroids when severe

Cell therapy Related Encephalopathy Syndrome

- Treated with supportive care when mild (re-orientation, avoid sedation)
- Treated with drugs targeting IL6 when moderate/severe with CRS (tocilizumab, siltuxumab)
- Treated with corticosteroids when severe

63



## What do I need to know about being a CAR T cell patient?

Risk of infection

- Immunosuppressed
- Bacterial infections
- PCP/PJP pneumonia
- HSV
- CMV

Late cytopenias

Can relapse, but usually not after 6 months

64

## What do I need to remember about Diffuse Large B-cell Lymphoma?

DLBCL is common, curable, and complicated

A biopsy is required for diagnosis

Treatment is chemotherapy with immune therapy

- 1L RCHOP or R-CHP-Pola
- 2L CAR T-cell for <12m, chemo/SCT for >12m

Many drugs approved for 3rd line treatment

Clinical trials are essential for future progress

65



## Patient Story

66

# Ongoing 15+mo CR in refractory DLBCL

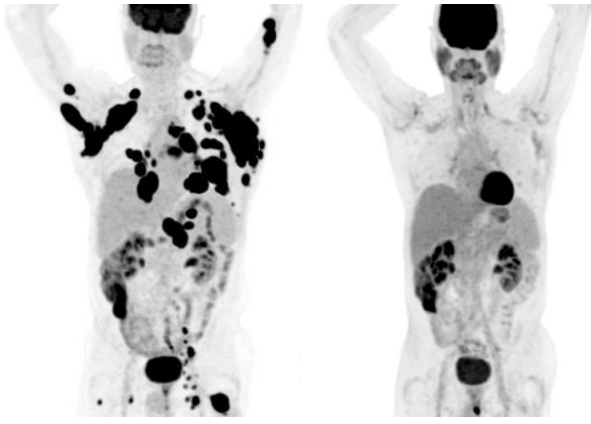
62-yo M with DLBCL

Prior therapies

- R-CHOP
- R-GDP
- R-ICE
- R-lenalidomide

No response to last 3 lines of therapy

Baseline Day 90



- **Responses can be rapid, complete, and durable**
- **Antitumor responses may be observed in all parts of the body**

67

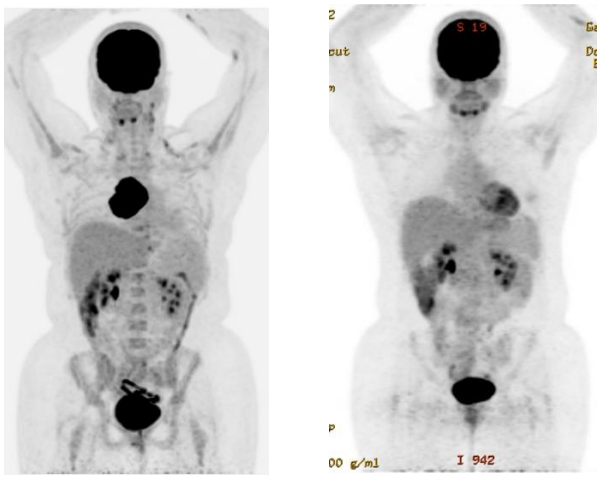


# Ongoing 12+ mo CR in refractory PMBCL

28 y/o female
Prior therapies:

- R-CHOP
- R-ICE
- R-DHAP

Baseline 6 months



68

## New Drugs

Polatuzumab

Antibody drug conjugate vs CD79B

Tafasitamab

Antibody vs CD19

Loncastuximab

Antibody drug conjugate vs CD19

Epcoritomab (others coming soon)

Bi-specific antibody vs CD20/CD3

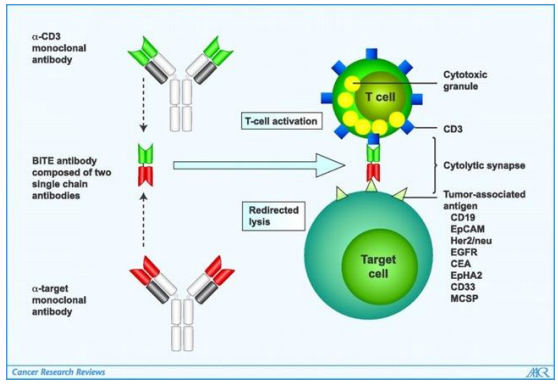
69



## Bispecific Abs

- BsAbs are protein constructs with specificity to 2 different antigens[1]
- Commonly bind a tumor-specific antigen and an immune effector cell antigen[1]
- BsAbs appose cytotoxic immune effector cells with a tumor cell via binding of a specific tumor antigen, creating an "immune synapse"[2]
- Antitumor activity is a result of activation of the immune effector cell and direct cytotoxic activity[2]
- Activation of T cells occurs only when BsAb also binds tumor antigen[2]

**Bispecific Antibody Principle[2]**

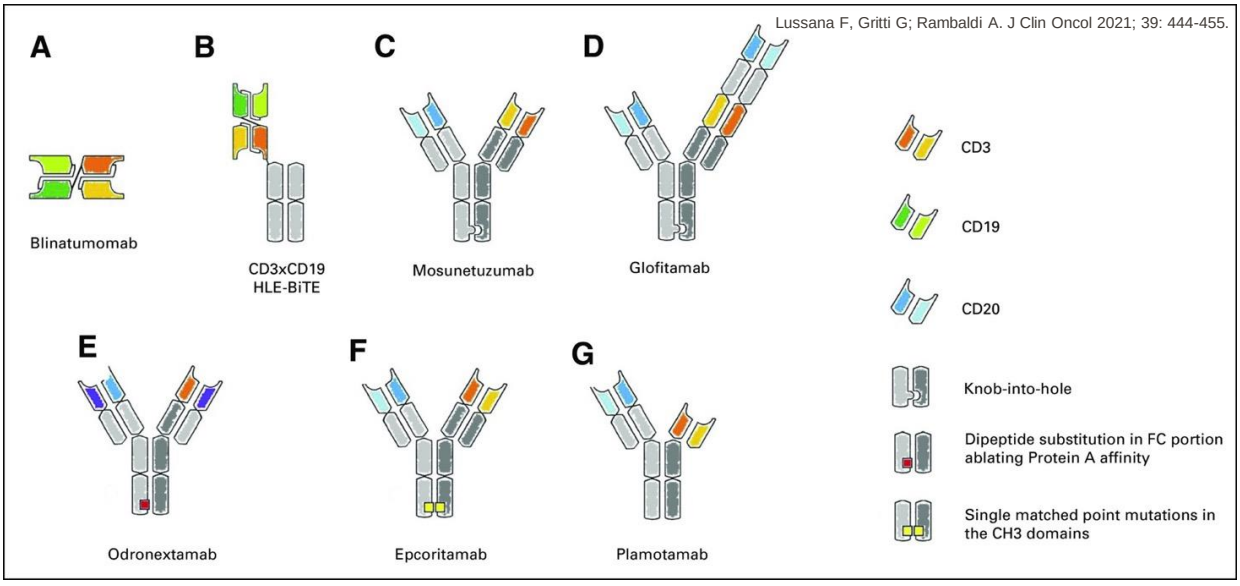



1. Lum LG, Thakur A. *BioDrugs.* 2011;25(6):365-379. 2. Baeuerle P, Reinhardt C. *Cancer Res.* 2009;69(12):4941-4944.

70

MD Anderson

# Bispecific CD3/CD20 antibodies in B-NHL




71

MD Anderson | Aggressive Lymphomas - Dr. Westin

## Burkitt Lymphoma

Curable with aggressive chemotherapy

- REPOCH, CODOX-M/IVAC, HyperCVAD

Relapsed disease is dangerous

- Clinical trials are best option

Should be seen at major cancer center

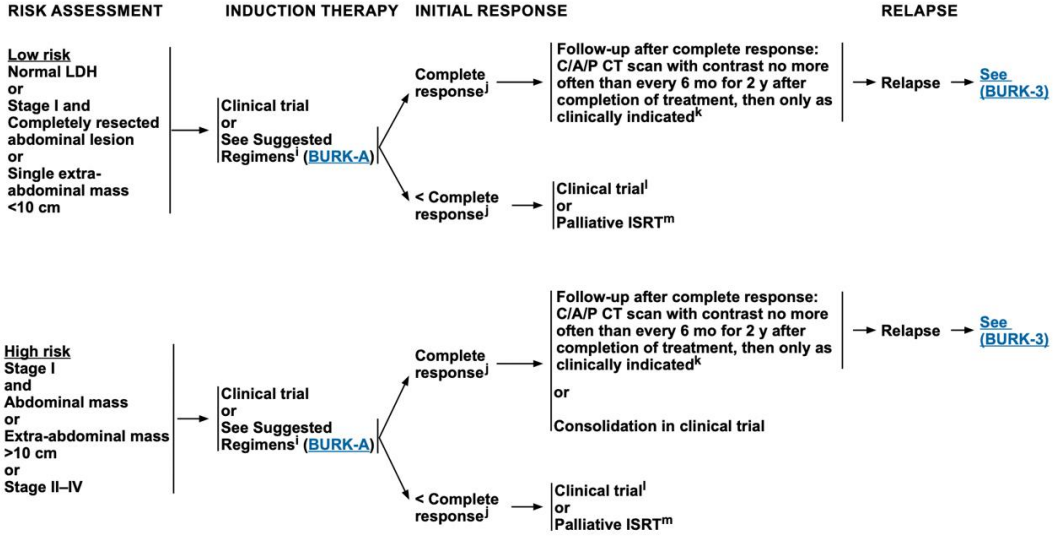
72

MD Anderson | Aggressive Lymphomas - Dr. Westin

National Comprehensive Cancer Network®

## NCCN Guidelines Version 3.2023
## Burkitt Lymphoma

NCCN Guidelines Index
Table of Contents
Discussion




73

MD Anderson | Aggressive Lymphomas - Dr. Westin

National Comprehensive Cancer Network®

## NCCN Guidelines Version 3.2023
## Burkitt Lymphoma

NCCN Guidelines Index
Table of Contents
Discussion

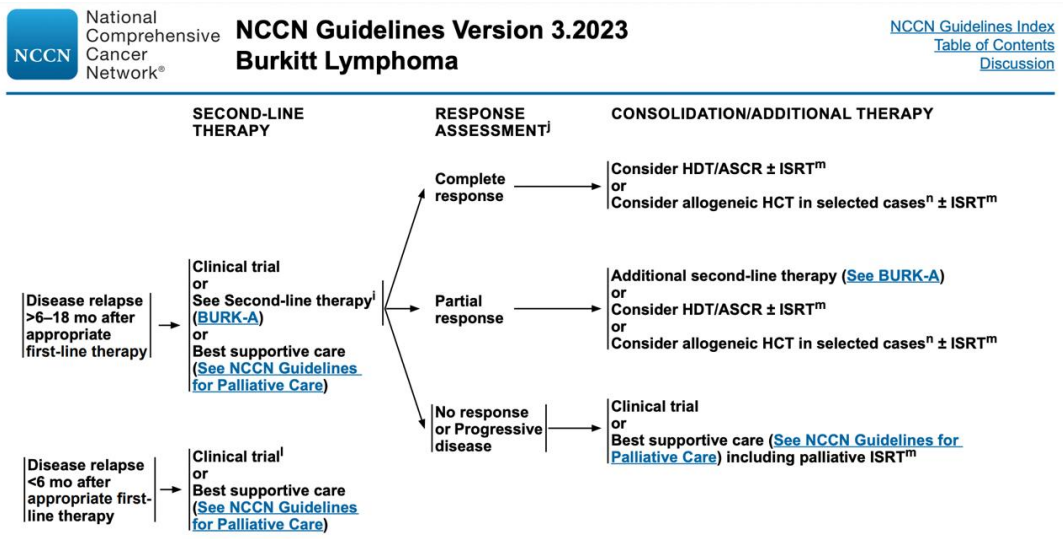
**SUGGESTED TREATMENT REGIMENS[a,b]**

**An FDA-approved biosimilar is an appropriate substitute for rituximab.**

**CHOP is not an adequate therapy.**

| AGE | RISK | INDUCTION THERAPY |
|---|---|---|
| <60 y | Low Risk | Preferred regimens (alphabetical order)<br>• CODOX-M (original or modified) (cyclophosphamide, doxorubicin, vincristine with intrathecal methotrexate and cytarabine followed by high-dose systemic methotrexate) + rituximab (3 cycles)<br>• Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) + rituximab (minimum 3 cycles with one additional cycle beyond CR) (regimen includes intrathecal methotrexate)<br>• HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone) alternating with high-dose methotrexate and cytarabine + rituximab (regimen includes intrathecal therapy) |
| | High Risk | Preferred regimens (alphabetical order)<br>• High-risk patients presenting with symptomatic CNS disease should be started with the portion of the systemic therapy that contains CNS-penetrating drugs.<br>• CODOX-M (original or modified) (cyclophosphamide, doxorubicin, vincristine with intrathecal methotrexate and cytarabine followed by high-dose systemic methotrexate) alternating with IVAC (ifosfamide, cytarabine, etoposide, intrathecal methotrexate) + rituximab<br>• HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone) alternating with high-dose methotrexate and cytarabine + rituximab (regimen includes intrathecal therapy)<br>Other recommended regimen<br>• Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) + rituximab (for high-risk patients with baseline CNS disease not able to tolerate aggressive treatments) (regimen includes intrathecal methotrexate) (Data included patients with leptomeningeal CNS disease; patients with parenchymal CNS disease were excluded in the clinical trials of this regimen.) |
| ≥60 y | Low and High Risk | Preferred regimen<br>• Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) + rituximab (minimum 3 cycles with one additional cycle beyond CR) (regimen includes intrathecal methotrexate) (Data included patients with leptomeningeal CNS disease; patients with parenchymal CNS disease were excluded in the clinical trials of this regimen.)<br>‣ In high-risk patients presenting with symptomatic CNS disease, the management of the CNS disease should be addressed with the initial regimen. |

74




75



# Mantle Cell Lymphoma

76

# Three-Year Follow-Up of Outcomes With KTE-X19 in Patients With Relapsed/Refractory Mantle Cell Lymphoma in ZUMA-2

Michael L. Wang, MD[1]; Javier Munoz, MD, MS, FACP[2]; Andre Goy, MD[3]; Frederick L. Locke, MD[4]; Caron A. Jacobson, MD, MMSc[5]; Brian T. Hill, MD, PhD[6]; John M. Timmerman, MD[7]; Houston Holmes, MD, MBA, FACP[8]; Ian W. Flinn, MD, PhD[9]; David B. Miklos, MD, PhD[10]; John M. Pagel, MD, PhD, DSc[11]; Marie José Kersten, MD, PhD[12]; Roch Houot, MD, PhD[13]; Amer Beitinjaneh, MD[14]; Weimin Peng, PhD[15]; Xiang Fang, PhD[15]; Rhine R. Shen, PhD[15]; Rubina Siddiqi, PhD[15]; Ioana Kloos, MD[15]; Patrick M. Reagan, MD[16]

*[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Banner MD Anderson Cancer Center, Gilbert, AZ, USA; [3]John Theurer Cancer Center, Hackensack University, Hackensack, NJ, USA; [4]Moffitt Cancer Center, Tampa, FL, USA; [5]Dana-Farber Cancer Institute, Boston, MA, USA; [6]Cleveland Clinic Foundation, Cleveland, OH, USA; [7]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [8]Texas Oncology, Dallas, TX, USA; [9]Sarah Cannon Research Institute and Tennessee Oncology, Nashville, TN, USA; [10]Stanford University School of Medicine, Stanford, CA, USA; [11]Swedish Cancer Institute, Seattle, WA, USA; [12]Amsterdam UMC, University of Amsterdam, Amsterdam, Cancer Center Amsterdam, The Netherlands, on behalf of HOVON/LLPC; [13]CHU Rennes, Université Rennes, INSERM & EFS, Rennes, France; [14]University of Miami, Miami, FL, USA; [15]Kite, a Gilead Company, Santa Monica, CA; and [16]University of Rochester Medical Center, Rochester, NY, USA*

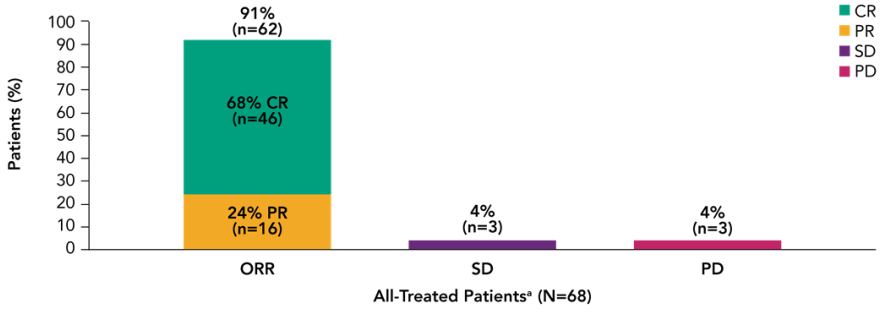
Wang ML et al. ASCO 2022. Abstract 7518.







## Objective Response Rate (ORR) in All Treated Patients (N=68)




After a median follow-up of 35.6 months (range, 25.9-56.3), the ORR (CR + partial response [PR]) was 91% (95% CI, 81.8-96.7), with a 68% CR rate (95% CI, 55.2-78.5) and a median DOR of 28.2 months (95% CI, 13.5-47.1)
In the ITT population, ORR was 84% (95% CI, 73.4-91.3), with a 62% CR rate (95% CI, 50.1-73.2)

With 3-years of follow-up, these data demonstrate that a single infusion of KTE-X19 resulted in high rates of durable responses in R/R MCL.

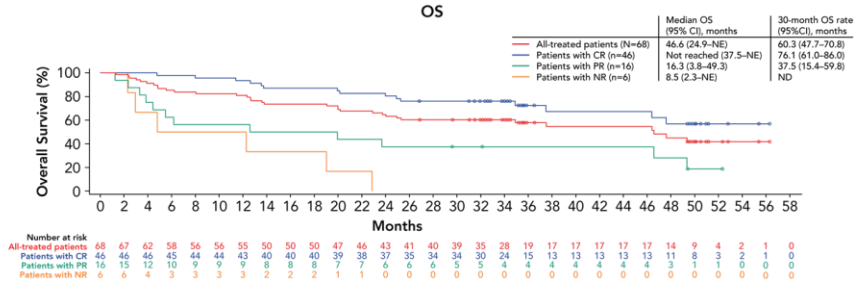
Assessed by an IRRC according to the Lugano Classification.[1] [a] Since the previous report,[2] IRRC review determined that 1 patient who was previously reported as best response of PR had no disease at baseline; this patient is reported as PD in the current report. 1. Cheson BD, et al. J Clin Oncol. 2014;32:3059-3068. 2. Wang M, et al. *Blood*. 2020;136(suppl 1):20-22.

Wang ML et al. ASCO 2022. Abstract 7518.

7th POSTGRADUATE Lymphoma Conference

Rome, March 16-17 2023

## Overall Survival (OS) in All Treated Patients (N=68)




- The median progression-free survival (PFS) was 25.8 months, as shown in the full poster
- In the ITT population (data not shown), the median PFS was 24.0 months and the median OS was 47.4 months

Median OS among treated patients was 46.6 months and was not reached among those who achieved CR.

Median follow-up 35.6 months.
CR, complete remission; mo, month; NE, not estimable; NR, no response; OS, overall survival; PFS, progression-free survival.

Wang ML et al. ASCO 2022. Abstract 7518.

79

79

## ASK A QUESTION

SPOTLIGHT ON AGGRESSIVE NON-HODGKIN LYMPHOMAS

### 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.

LEUKEMIA & LYMPHOMA SOCIETY

80

# LLS EDUCATION & SUPPORT RESOURCES

**HOW TO CONTACT US:**

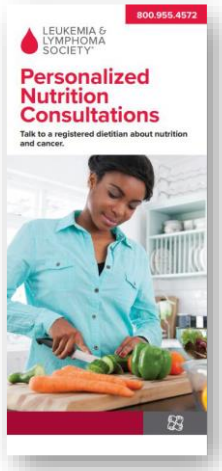
To contact an **Information Specialist** about disease, treatment and support information, resources and clinical trials:

**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.LLS.org/Consult.**

LEUKEMIA & LYMPHOMA SOCIETY

81

# LLS EDUCATION & SUPPORT RESOURCES


**Online Chats**

Online Chats are free, live sessions, moderated by oncology social workers. To register for one of the chats below, 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**

LEUKEMIA & LYMPHOMA SOCIETY

82

# 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

83

# 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

84