Non-Hodgkin Lymphoma: A Primer

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  - Speaker's Bureau for: none
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  - Institutional research funding: Portola, Genentech, Acerta, Pharmacyclics, Celgene, Curis, BMS, TG Therapeutics, Merck, Forty-Seven, Novartis
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What is lymphoma?

Lymphoma is a family of blood cancers derived from mature lymphocytes

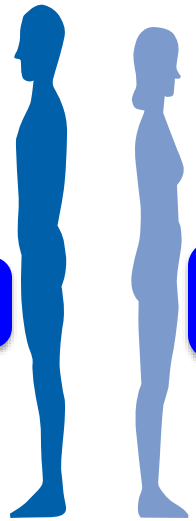
B-cells **T-cells** **NK-cells**

- Lymphocytes normally fight viruses, bacteria, fungi, and foreign organisms
- Lymphocytes travel in lymphatic system
- These cells can grow in nodal and extranodal locations

NHL: US Burden of Disease 2020

Estimated New Cases

Male			Female		
Prostate	191,930	21%	Breast	276,480	30%
Lung & bronchus	116,300	13%	Lung & bronchus	112,520	12%
Colon & rectum	78,300	9%	Colon & rectum	69,650	8%
Urinary bladder	62,100	7%	Uterine corpus	65,620	7%
Melanoma of the skin	60,190	7%	Thyroid	40,170	4%
Kidney & renal pelvis	45,520	5%	Melanoma of the skin	40,100	4%
Non-Hodgkin lymphoma	42,380	5%	Non-Hodgkin lymphoma	34,860	4%
Oral cavity & pharynx	38,380	4%	Kidney & renal pelvis	29,230	3%
Leukemia	35,470	4%	Pancreas	27,200	3%
Pancreas	30,400	3%	Leukemia	25,060	3%
All sites	893,660		All sites	912,930	



80,000 new cases/year
20,000 deaths/year

662,789 people living with lymphoma

American Cancer Society. *Cancer Facts & Figures 2020*. Atlanta, GA: American Cancer Society; 2020.

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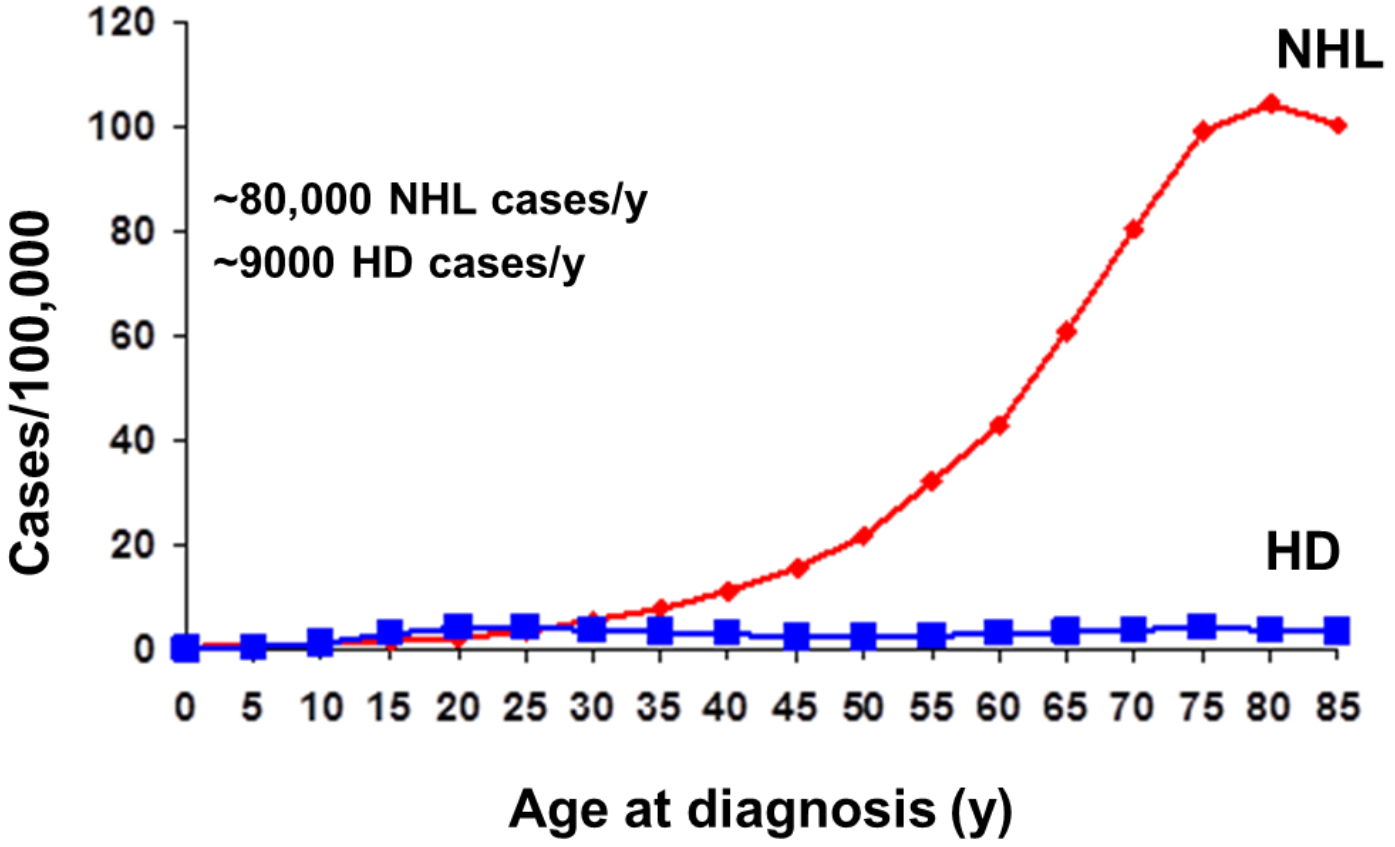
Etiology

- Increasing age
- Abnormalities of the immune system
  - Inherited
  - Related to treatment of another condition
  - Acquired (HIV)
- Viruses
  - Hepatitis B and C
  - Human herpes virus 6
- Exposure to certain chemicals
- Bacteria
  - Helicobacter pylori

Genetics?
Environment?
Diet/lifestyle?

Age Distribution of NHL vs. HL

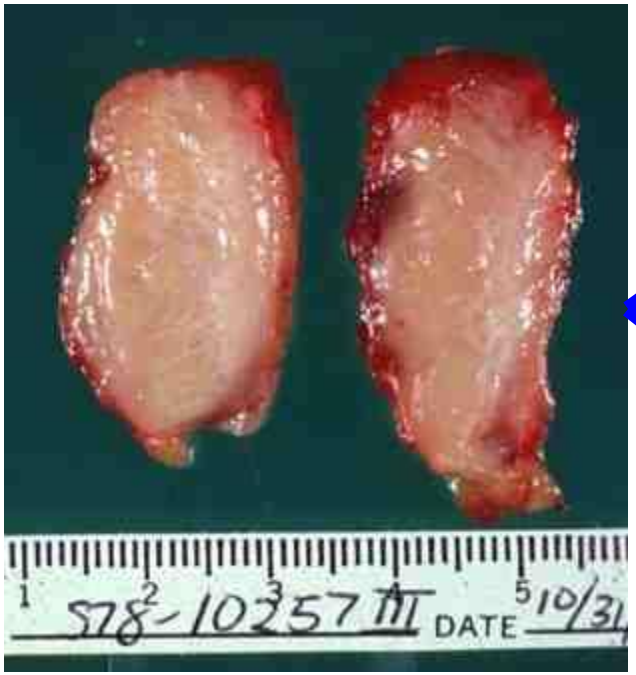


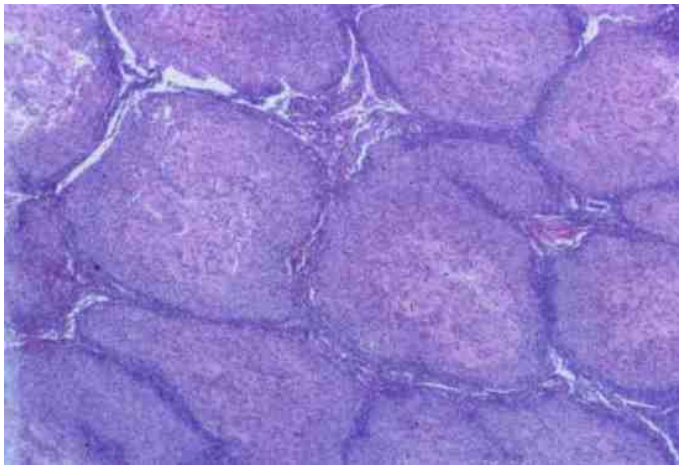
DIAGNOSIS

"Tissue is the issue," and "more is better"

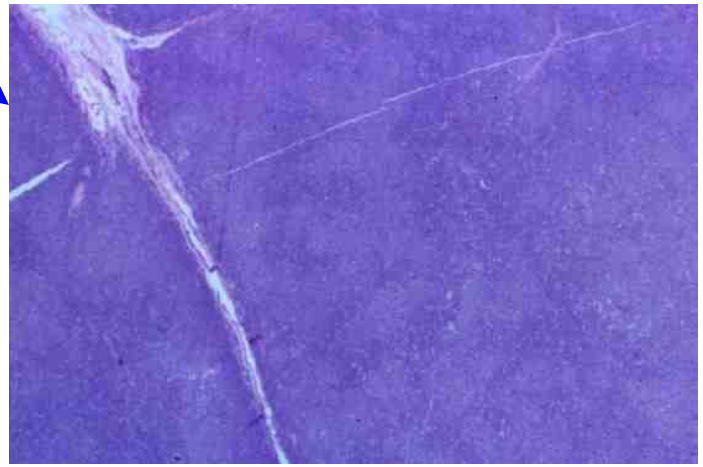
	PRO	CON
Fine needle aspirate	•can distinguish lymphoma from other cancers •Quick, easy, office-based	•Unable to give architectural detail •Insufficient for most prognostic tests
Core needle biopsy	•Can be done in hard to reach places (stomach, spinal cord)	•Unable to give architectural detail •Insufficient for most prognostic tests
Incisional or excisional biopsy	•Gold standard •Allows architectural evaluation •Allows tests for prognosis •Can be used for research	•May be more invasive •May require surgery and anesthesia

Excisional lymph node biopsy





"nodular"



"diffuse"

NHL Classification Systems

- 1970's:
  - Rappaport classification
  - Kiel classification
  - Lukes & Collins classification
  - British National Lymphoma classification
  - Dorfman classification
- 1981:
  - Working formulation
- 1990's:
  - Updated Kiel classification
  - REAL classification
- **2001, 2008, 2017: WHO classification**

1. Overall pattern
2. Cell size
3. Nuclear shape

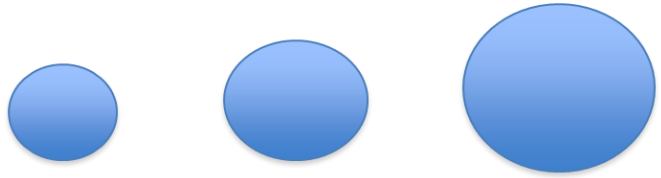
Working formulation

1. Overall pattern
2. Cell size
3. Nuclear shape

Overall architectural pattern

- Follicular (or nodular)
- Diffuse

Cell size



Small Intermediate Large

Shape of the nucleus

Cleaved Non-cleaved

Conceptual approach to lymphomas

Clinical behavior

B-cell development

WHO classification

Conceptual approach to lymphomas: clinical behavior

Low grade/indolent lymphoma

1. Slow growing
2. Incurable
3. More common in elderly

MCL?

Intermediate grade/aggressive lymphoma

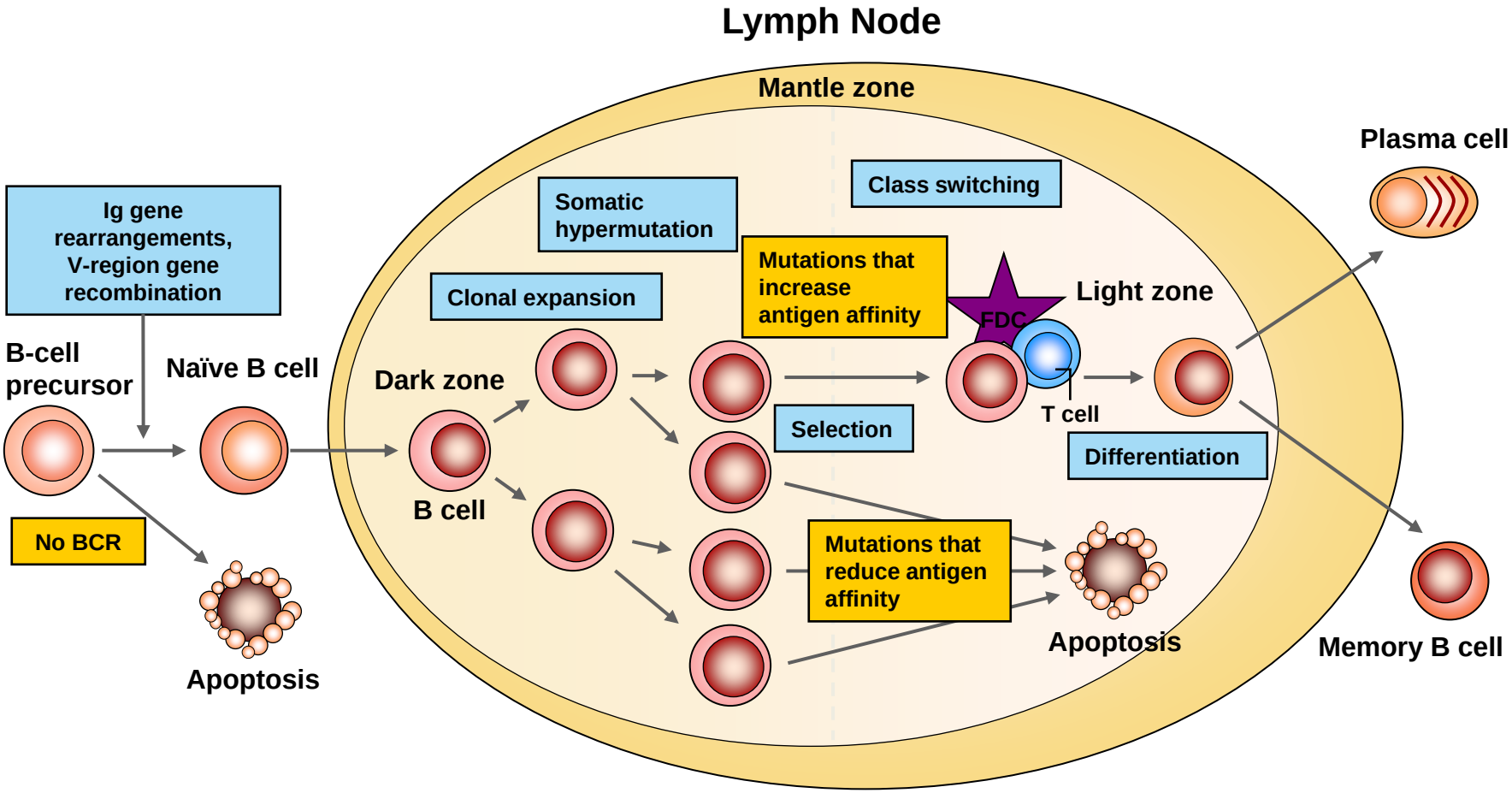
1. Fast growing
2. Potentially curable
3. Occurs in all age groups

T-NHL?

High grade/highly aggressive lymphoma

1. Very fast growing
2. Highly curable
3. Bimodal peak (i.e. Burkitt lymphoma)

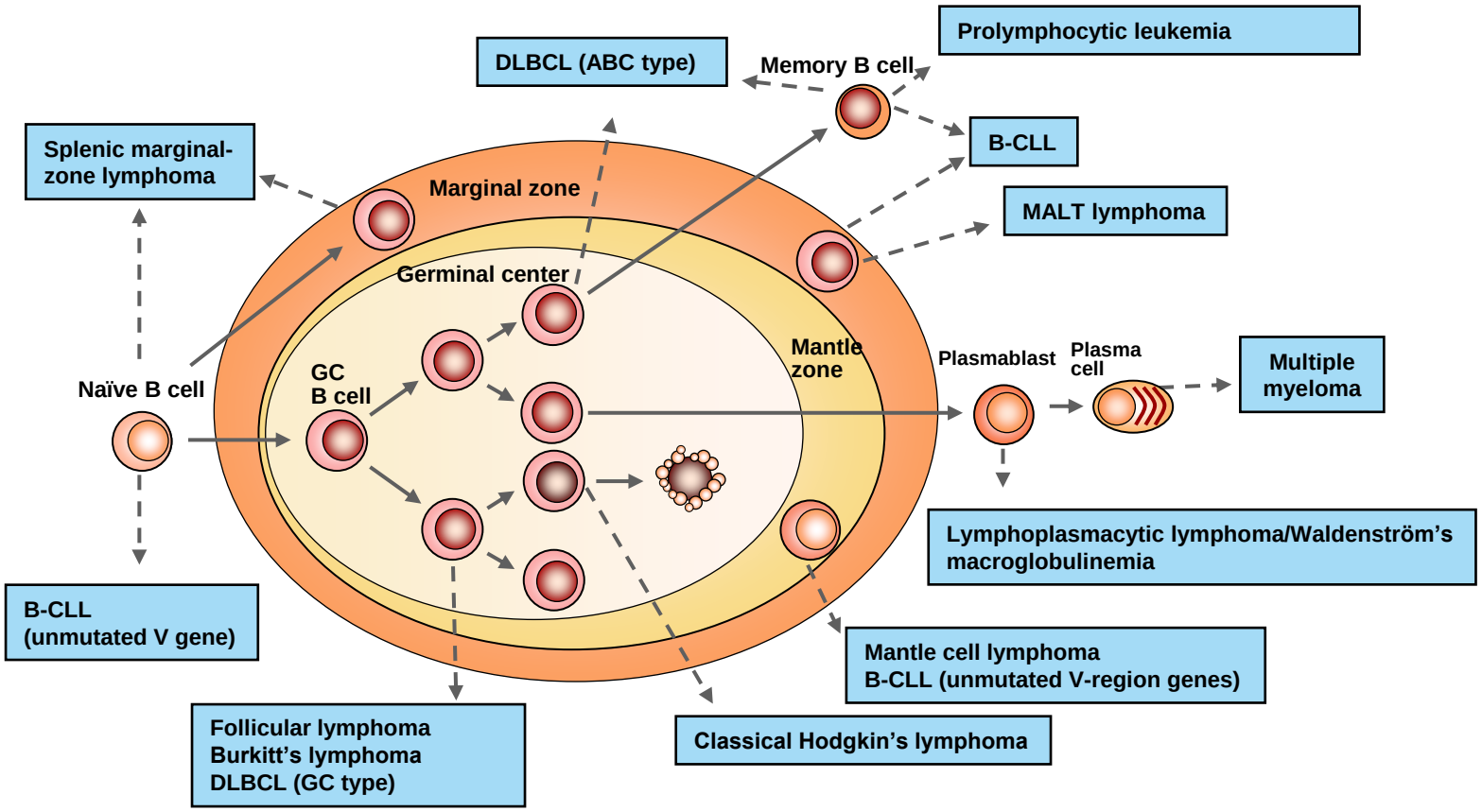
Conceptual approach to B-NHL: normal B-cell development



Küppers R. *Nat Rev Cancer.* 2005;5:251-262.

Cellular Origin of B-Cell Lymphomas

Most B-Cell Lymphomas Are Derived From the Germinal Center



Küppers R. *Nat Rev Cancer.* 2005;5:251-262.

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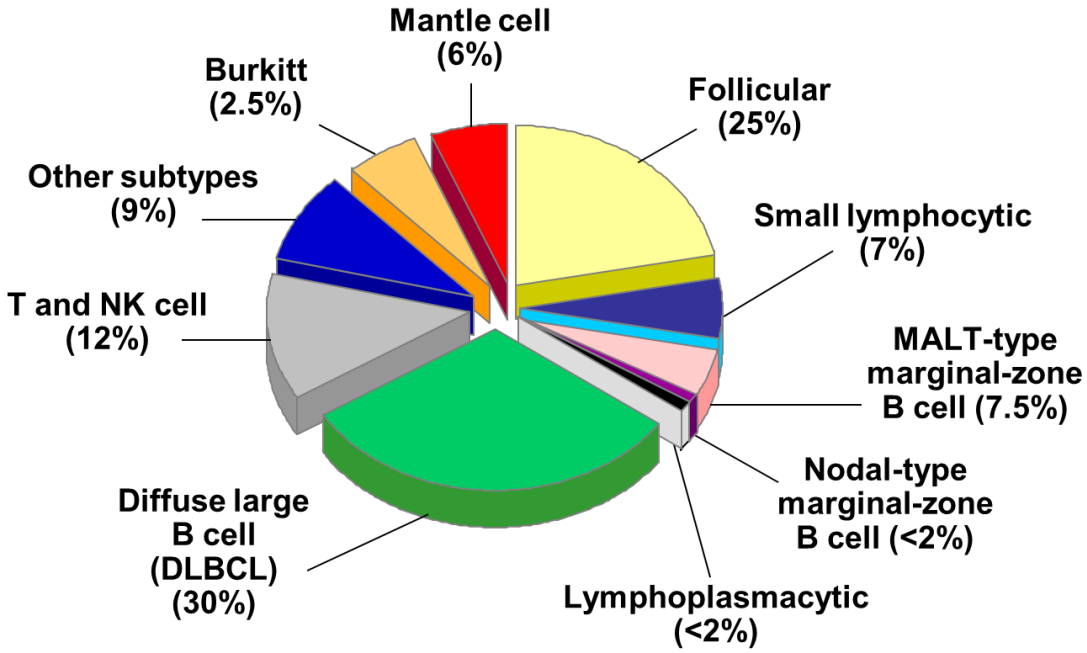
Conceptual approach to lymphoma: WHO classification

- Lineage is the starting point of disease definition
  - B, T, or NK cells
- Each disease is a distinct entity based on a constellation of clinical and laboratory features
  - Morphology
  - Immunophenotype
  - Genetic features
  - Clinical presentation and course
- Site of involvement is often a signpost for important biological distinctions

Use of clinical features is a novel aspect; diagnosis is not made in vacuum

There are nearly 100 types of lymphoma



Goals of therapy vary by histology and expected clinical behavior:

- ❑ **Curative intent**
- ❑ **Palliative intent**

WHO Classification of Lymphoid Malignancies 2008, 2016 update

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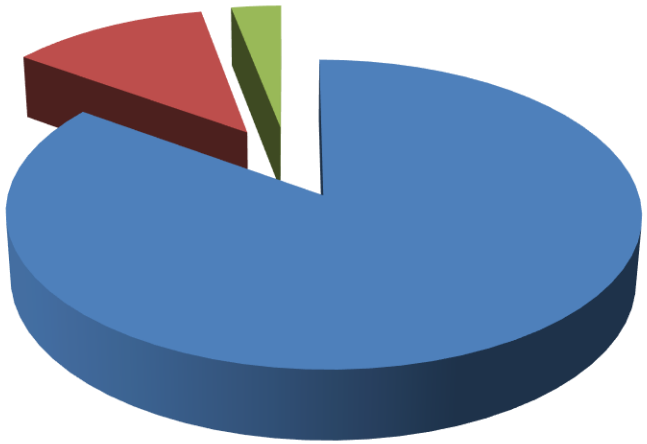
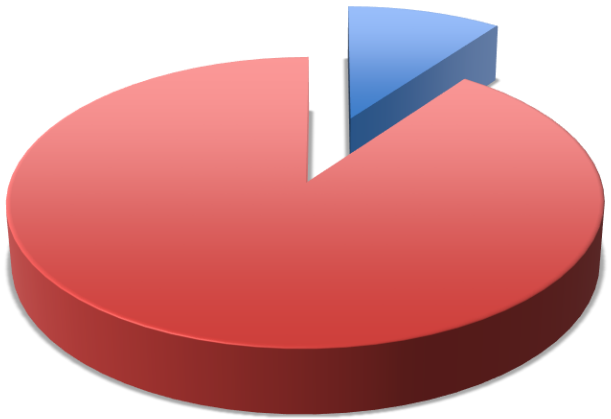
There are many ways to slice the “lymphoma pie”

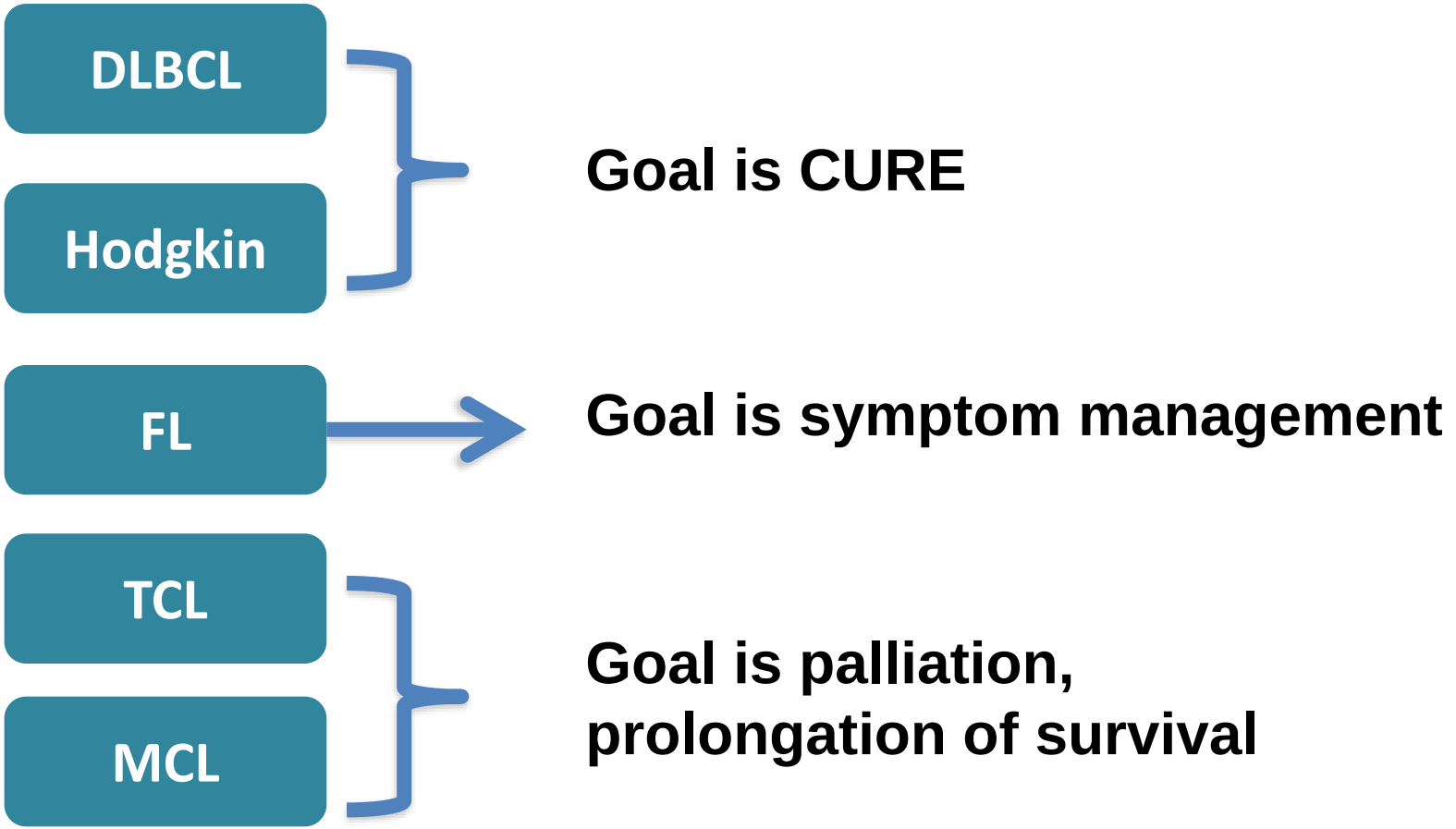




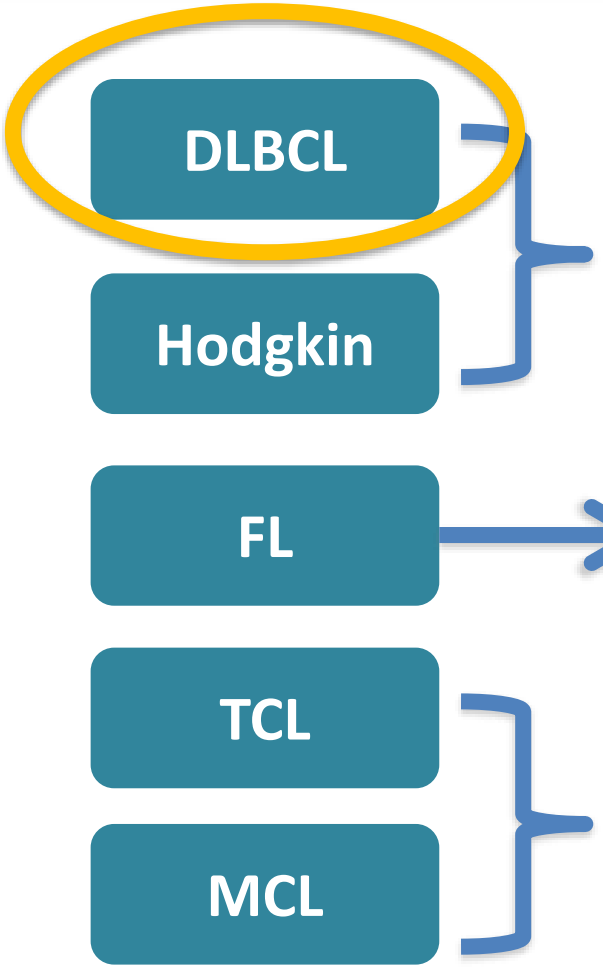
Treatment: General Principles

- Accurate histologic diagnosis essential
- Treatment decisions based primarily on HISTOLOGY rather than STAGE
  - Age
  - Pace of illness
  - Systemic symptoms

Goal of treatment depends on the disease



Type of treatment depends on the disease



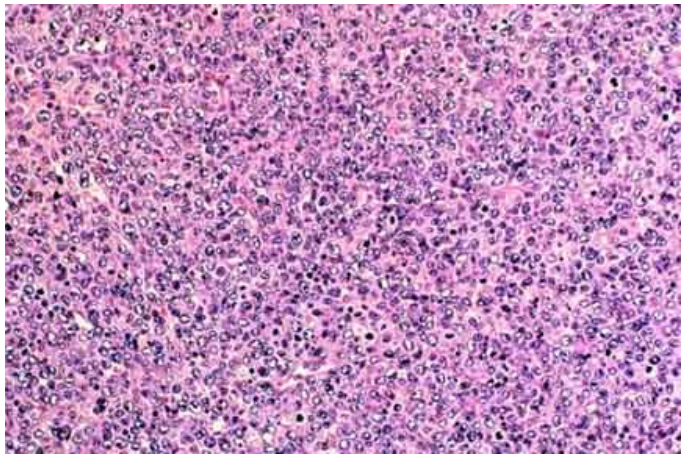
Combination chemotherapy, stem cell transplant

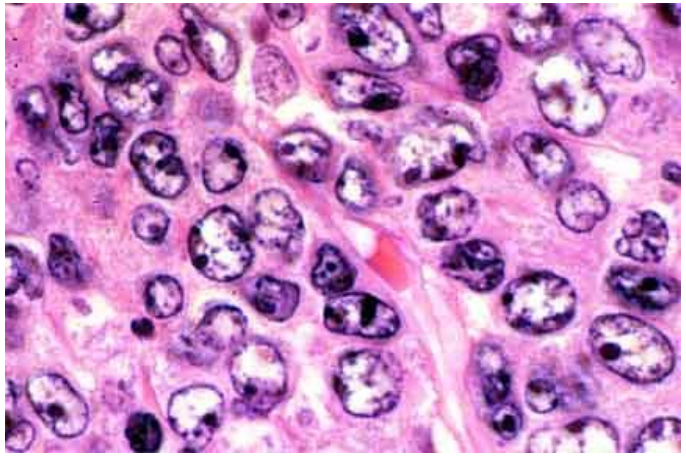
Observation, monoclonal antibodies, targeted agents, chemoimmunotherapy

Aggressive chemotherapy, stem cell transplant

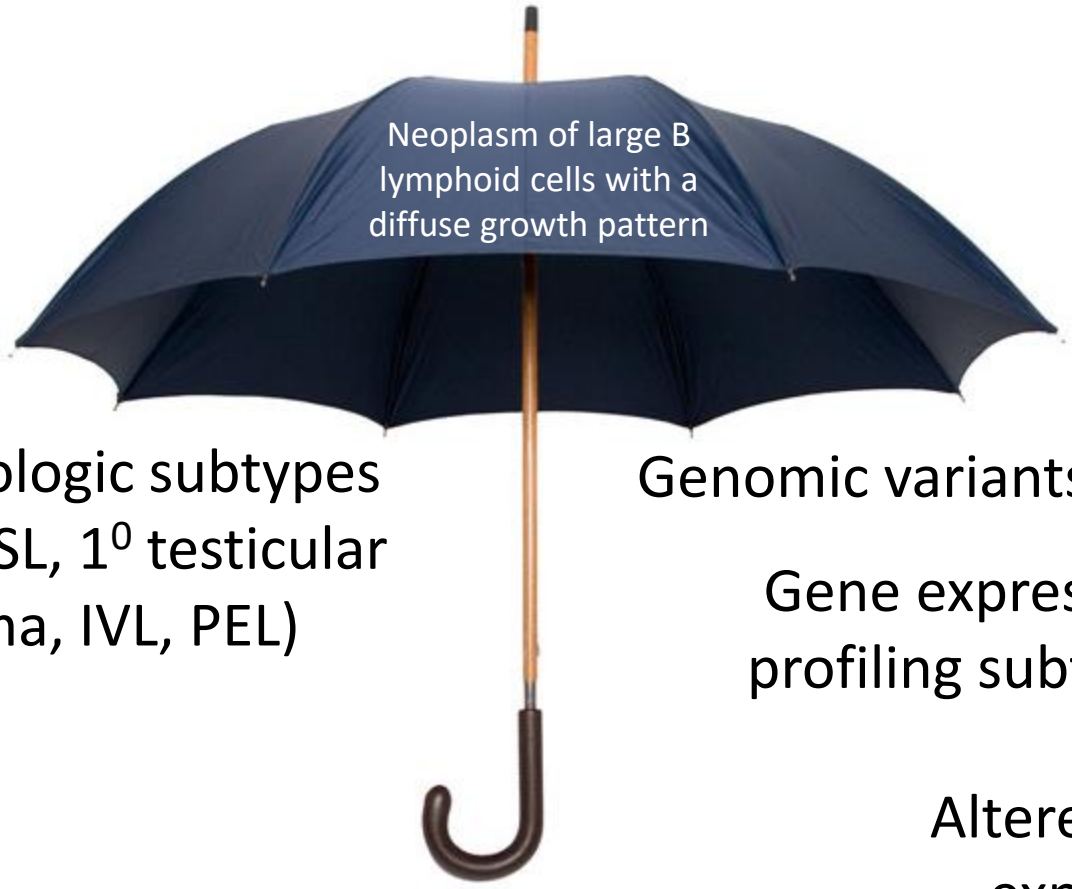
DLBCL

- Most common NHL, peak incidence 6th decade
- Large cells with loss of follicular architecture of node
- May present as extranodal disease (stomach, CNS, testis, skin)
- Median survival, weeks to months if not treated
- Immunophenotype: CD19+, CD20+, CD22+, CD79a+
- Cytogenetics: t(14;18) in 20-30%; 3q27 in 30%
- Curable in 30-90%





DLBCL: a study in clinical and biologic heterogeneity



Clinicopathologic subtypes (PMBL, PCNSL, 1^0 testicular lymphoma, IVL, PEL)

Genomic variants

Gene expression profiling subtypes

Altered protein expression

Morphologic variants

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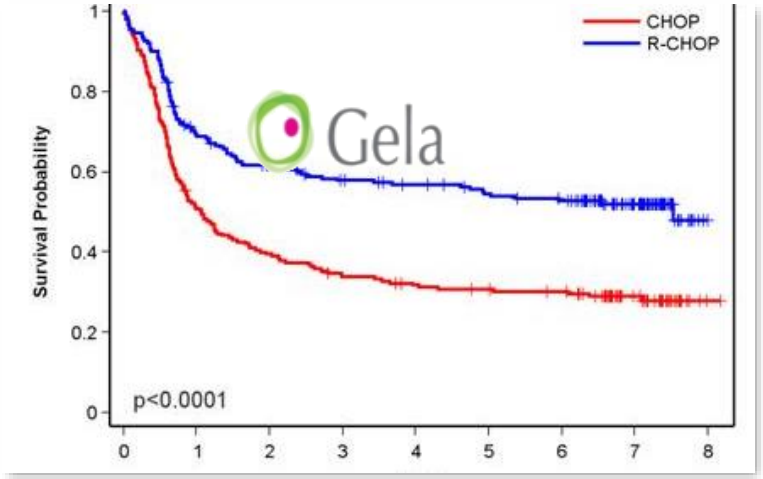
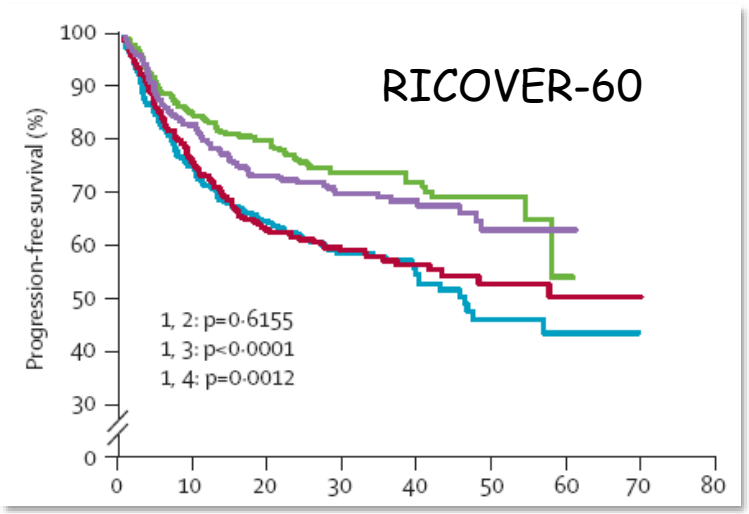
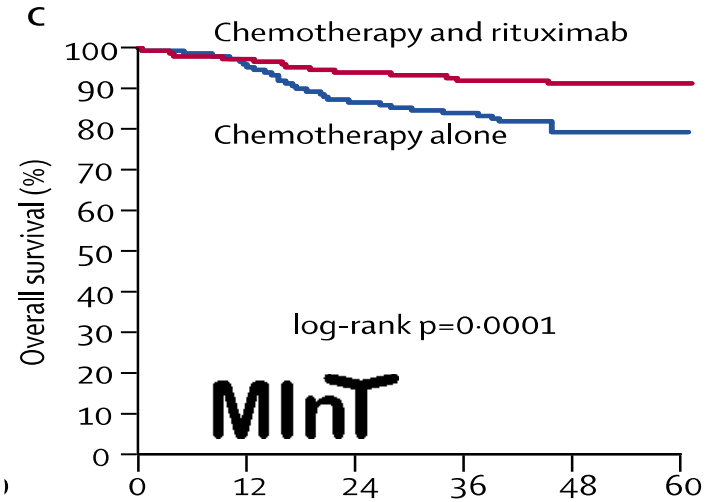
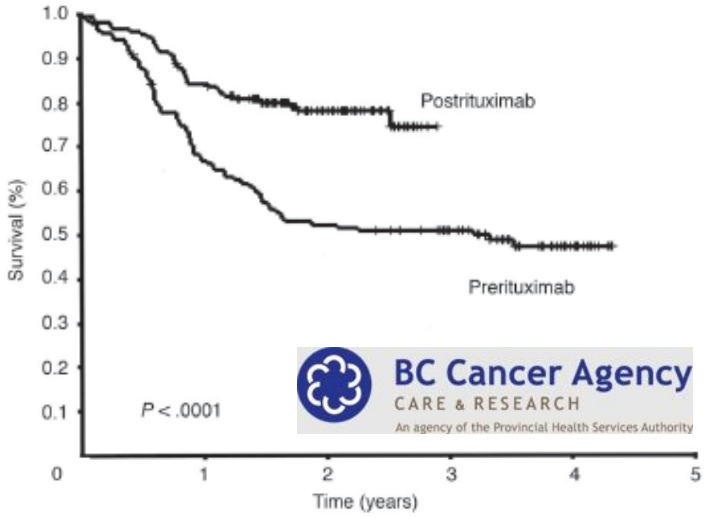
2002+: Rituximab plus CHOP-like regimens improves overall survival







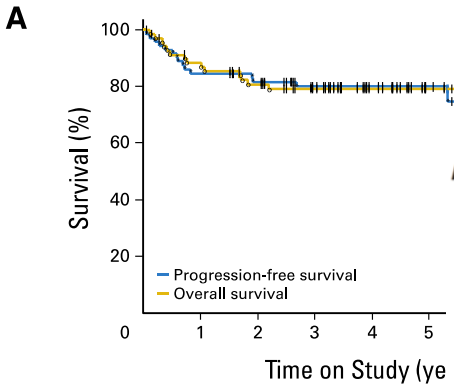


Pfreundschuh et al., Lancet Oncol. 2008; 9: 105. Pfreundschuh et al., Lancet Oncol. 2006; 7: 379. Habermann et al., JCO. 2006; 24: 3121. Feugier et al., JCO. 2005; 23: 4117.

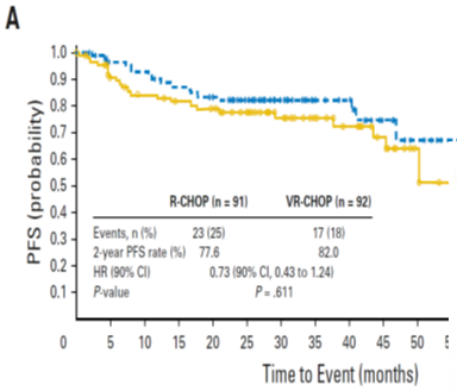
CAN WE MOVE BEYOND R-CHOP?

Challenging R-CHOP

DA-EPOCH-R

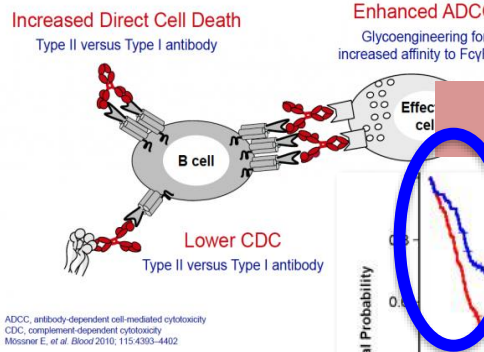


Add biologic agents



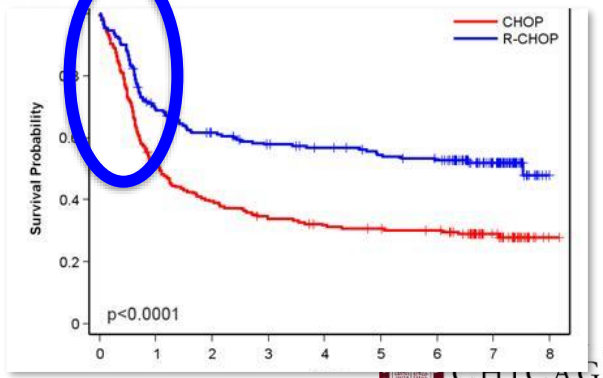
Obinutuzumab

GA101: Mechanisms of action



ADCC, antibody-dependent cell-mediated cytotoxicity
CDC, complement-dependent cytotoxicity
Mössner E, *et al. Blood* 2010; 115:4393–4402

Consolidation



2020: R-CHOP-21 remains the standard of care

Possible reasons for equivalent outcomes

- Trials enrolled all-comers with DLBCL
  - Not stratified for GC and non-GC
  - Inadvertent inclusion of double hit lymphomas
  - Mixture of DEL and non DEL
- Not powered to detect differences based on outcomes of subgroups
- Unexpectedly good outcomes for the control arm

ABBREVIATIONS: DLBCL, diffuse large B-cell lymphoma; GC, germinal center; DEL, dual expression lymphoma

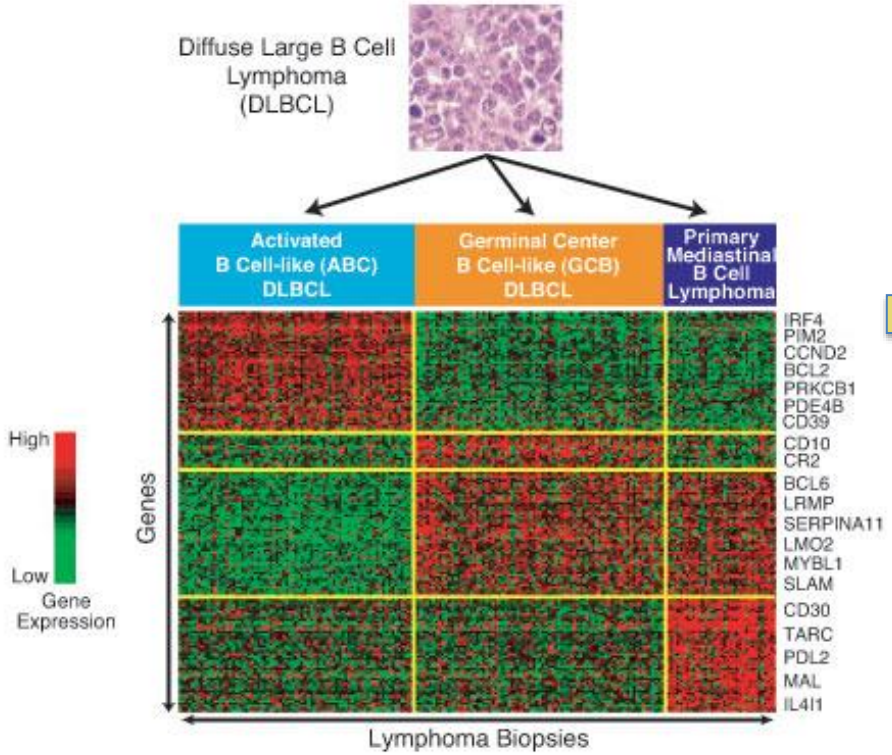
Retrospective data identifies high-risk groups unlikely to be cured with R-CHOP

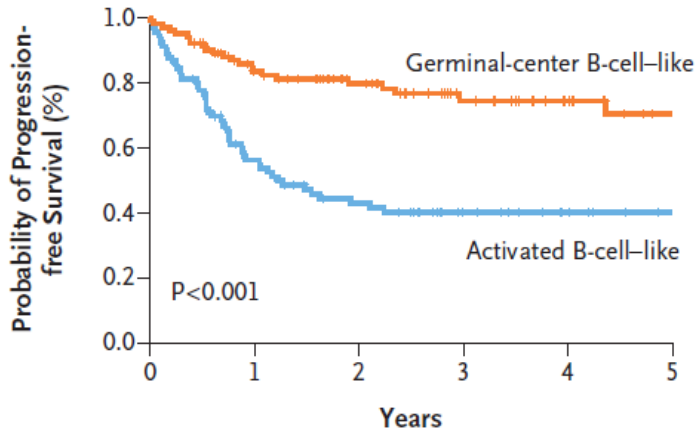
SUBSET	FREQ	R-CHOP		
		CR	PFS	OS
ABC DLBCL	30-50%	NR	2-yr 28%	2-yr 46%
Double hit lymphoma	3-12%	40%	1-yr %	<1yr
Dual expression of MYC/BCL2	21%	NR	5-yr 27%	5-yr 30%
Elderly DLBCL>60y	50%	70-80%	5-yr 50%	5-yr 58%
High IPI	45%	NR	4-yr 53%	4-yr 55%

*DPL: dual protein expression of MYC *and* BCL2

Ref: Aukema Blood 2011) Hu Blood 2013; Oki 2014, Maurer 2014, Feugier 2005, Sehn 2005; Nowakowski 2014; Johnson JCO. 2012.

Cell-of-origin (COO) model: there are two biologic subgroups in DLBCL





Two molecular subtypes with disparate outcomes

Lenz et al. *N Engl J Med.* 2008;359:2313-2323.

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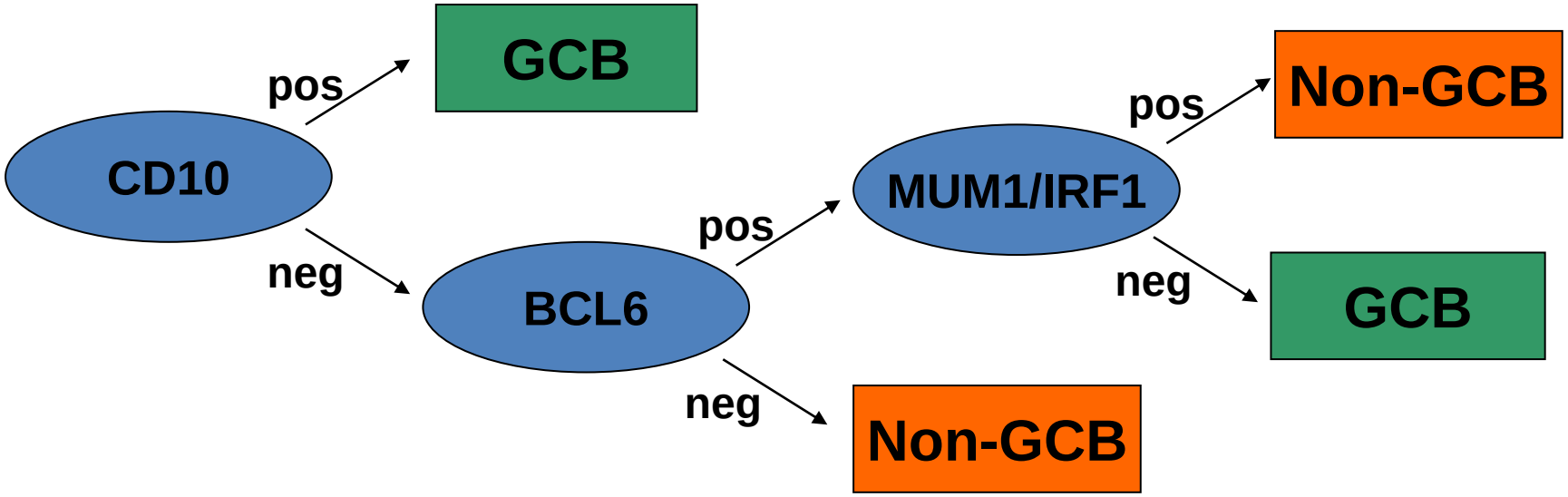
Cell of origin Subtypes of DLBCL: Immunophenotypic Classification



Approximately 20% error rate

Figure 4. Immunohistochemical algorithm to identify germinal center B-cell like DLBCL (GCB) from non-germinal center B-cell like DLBCL.

Smith SM and Vose JM. Management of Diffuse Large B-cell Lymphoma. In: O'Brien S, Kantarjian H, Vose JM, eds. Management of Hematologic Malignancies Cambridge University Press 2009

Beyond Cell of Origin: *MYC* and *BCL2* abnormalities

MYC + **BCL2** = **"DOUBLE HIT LYMPHOMA"**

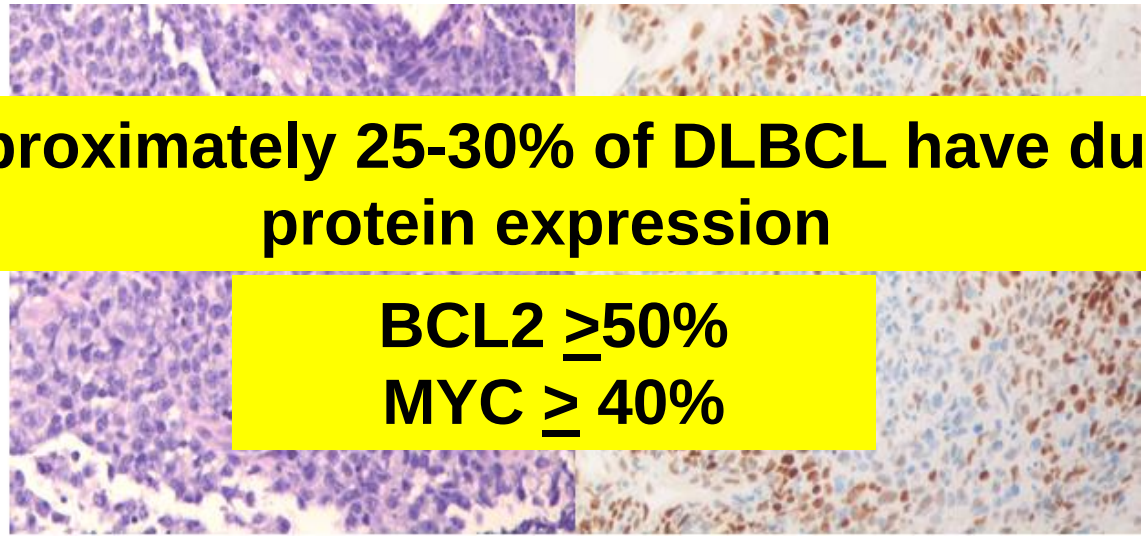
proliferation

Anti-apoptosis

- Either the GENES or the PROTEINS can be abnormal
- If it's the GENES/CHROMOSOMES: "Double Hit Lymphoma"
- If it's the PROTEINS WITHOUT THE GENES: DLBCL with dual expression ""dual expressor lymphoma"

DHL ≠ Dual expression

Diffuse large B-cell lymphoma, NOS	• Distinction of GCB vs ABC/non-GC type required with use of immunohistochemical algorithm acceptable, may affect therapy. • Coexpression of MYC and BCL2 considered new prognostic marker (double-expressor lymphoma). • Mutational landscape better understood but clinical impact remains to be determined.



Approximately 25-30% of DLBCL have dual protein expression

BCL2 ≥50%
MYC ≥ 40%

Swerdlow, et al., BLOOD, 19 MAY 2016 x VOLUME 127, NUMBER 20

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Double hit lymphoma *vs*. DLBCL, not otherwise specified with dual expression of MYC and BCL2

Double-hit lymphoma

- High grade B-cell lymphoma with translocations of *MYC*, *BCL2*, +/- *BCL6*
- Accounts for 5-7% of all DLBCL
- New category:
  - 2016 WHO category: "High grade B-cell lymphoma, with rearrangements of *MYC* and *BCL2* and/or *BCL6*"
- Outcome poor with standard therapies

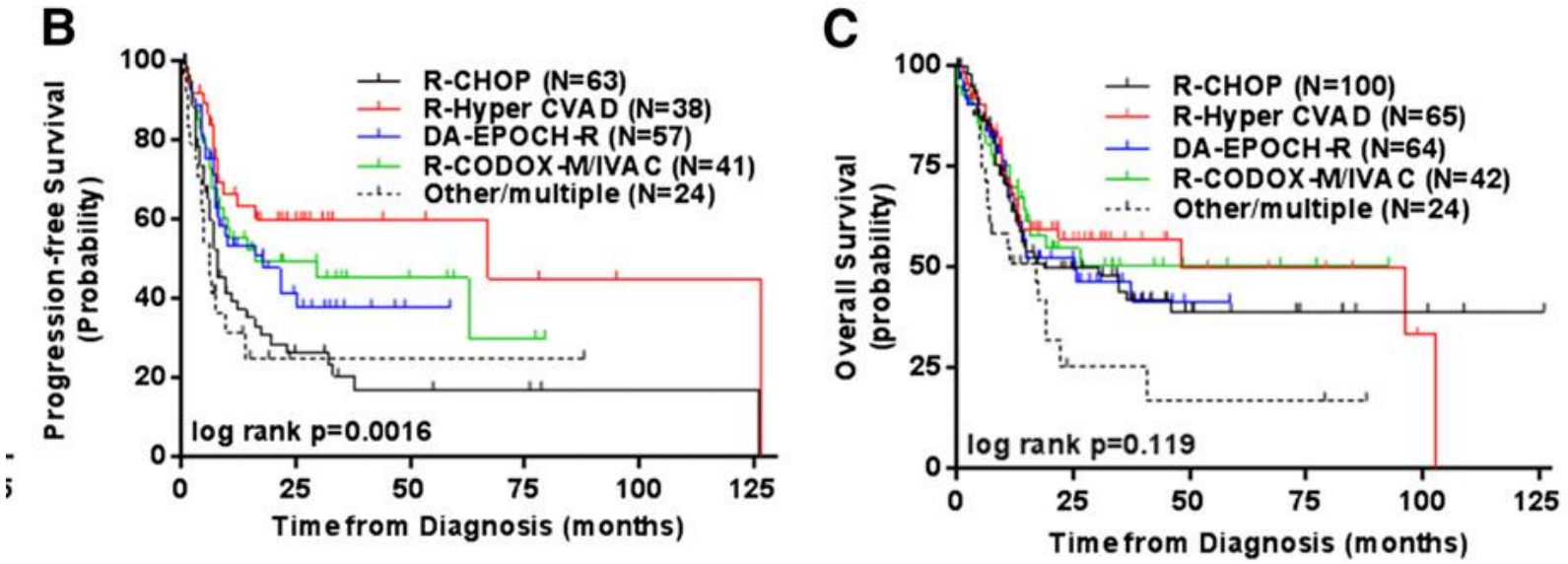
Majority are germinal center DLBCL

Double-expressing lymphomas

- DLBCL with immunohistochemical expression of MYC (≥40%) and BCL2 (≥50% recommended in 2016 WHO revision) ***in the absence of translocations***
- Accounts for 20-30% of all DLBCL
- Not a distinct entity but an adverse prognostic factor
- Outcome inferior to other DLBCLs treated with R-CHOP, but not as poor as DHL

Majority are non-germinal center DLBCL

R-CHOP is insufficient in DHL

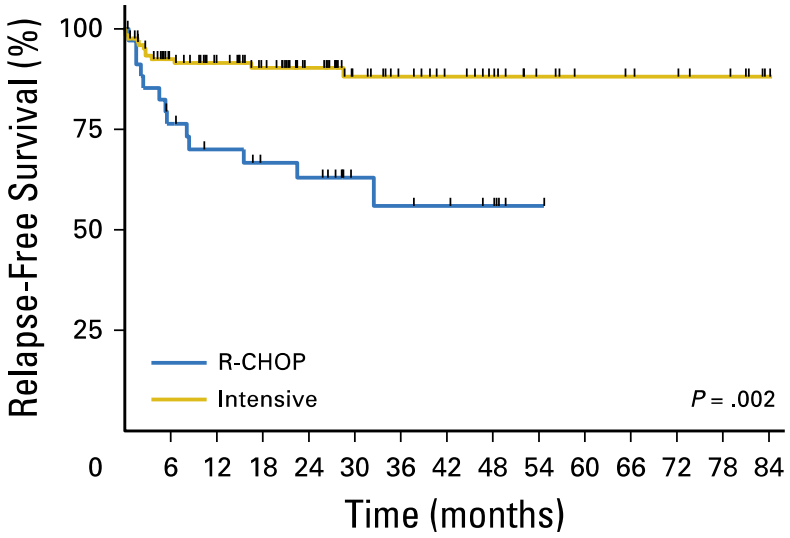


R-CHOP was inferior to intensive treatment: HR 0.53 (95% CI 0.29-0.98, P 5 .042).

Petrich Blood 2014 Oct 9;124(15):2354-61

R-CHOP is insufficient in DHL

C



No. at risk

R-CHOP	35	25	21	18	17	9	8	7	5	1	0	0	0	0	0
Intensive	124	96	79	67	52	38	32	26	22	16	13	12	11	9	3

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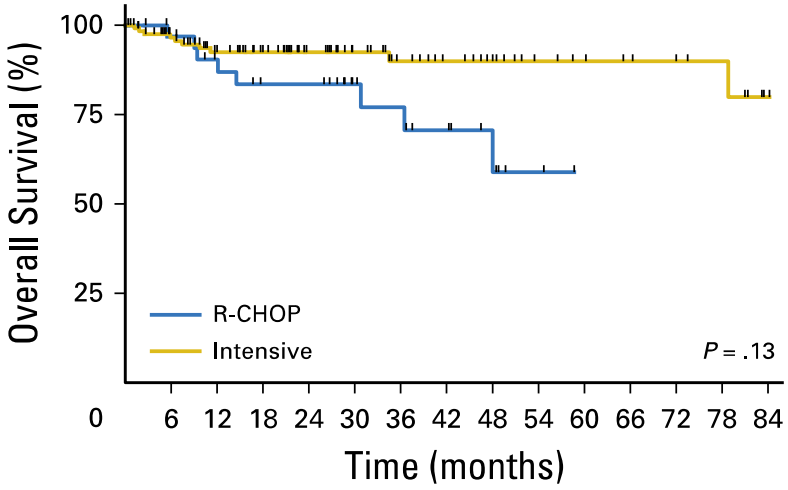

No. at risk

R-CHOP	35	31	26	22	22	14	12	9	6	2	0	0	0	0	0
Intensive	124	101	81	69	54	41	32	26	22	16	14	12	11	9	3

Landsburg J Clin Oncol. 2017 Jul 10;35(20):2260-2267

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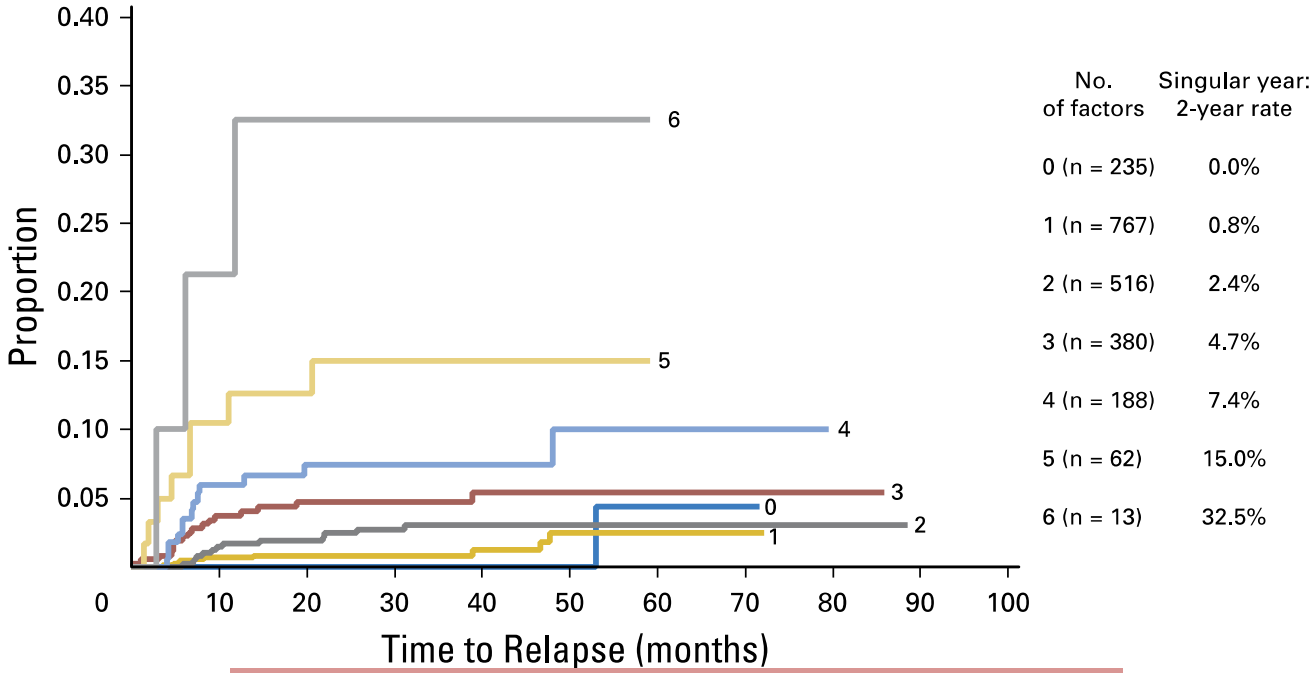
CNS PROPHYLAXIS

Who needs CNS prophylaxis?



- ❑ Kidney and/or adrenal involvement
- ❑ Age > 60 years
- ❑ LDH > normal
- ❑ PS > 1
- ❑ Stage III/IV disease
- ❑ EN involvement

Schmitz JCO 2016

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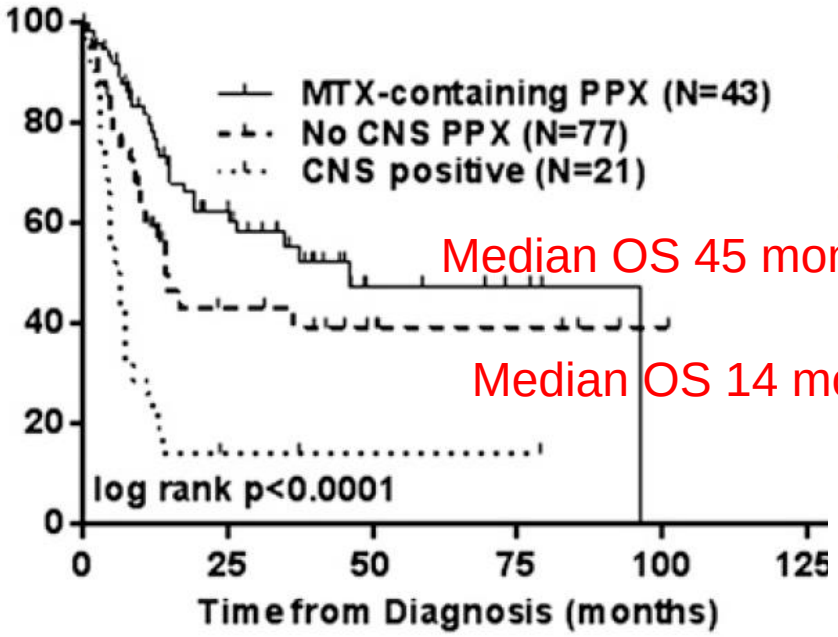
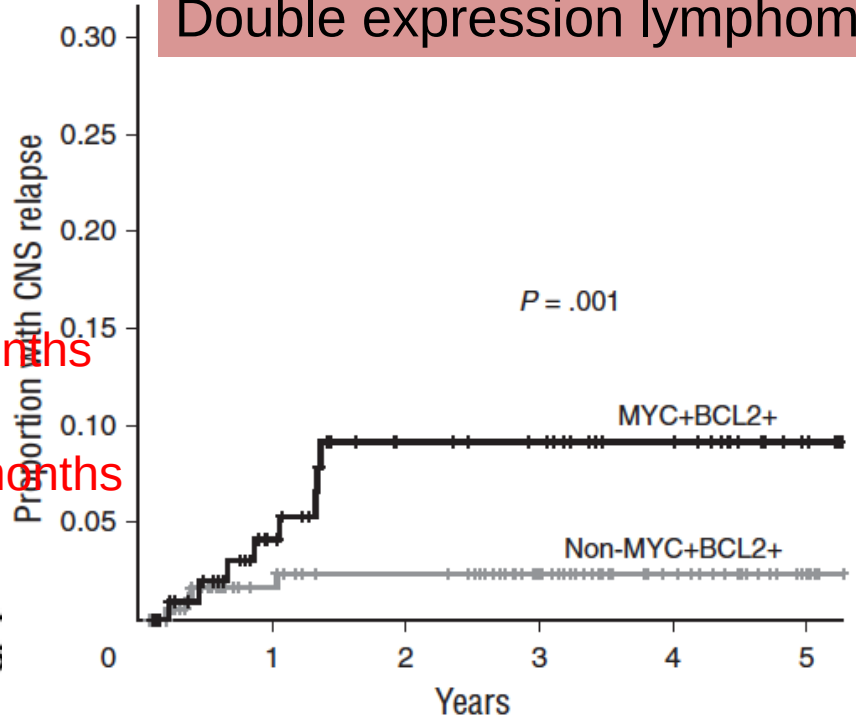
Who needs CNS prophylaxis?

Double hit lymphoma



Petrich et al. Blood. 2014;124(15):2354-2361

Double expression lymphoma



Savage et al. Blood 2016.127.2182-2188

Suggested treatment approach for aggressive B-cell lymphomas: 2017

- Diffuse large B-cell lymphoma
  - Cell of origin
    - GCB vs. non-GCB
  - Double expressor
    - MYC and BCL2 protein overexpression
- High grade B-cell lymphoma with MYC, BCL2 and/or BCL6 rearrangements
  - Double/Triple hit lymphoma

→ **R-CHOP**

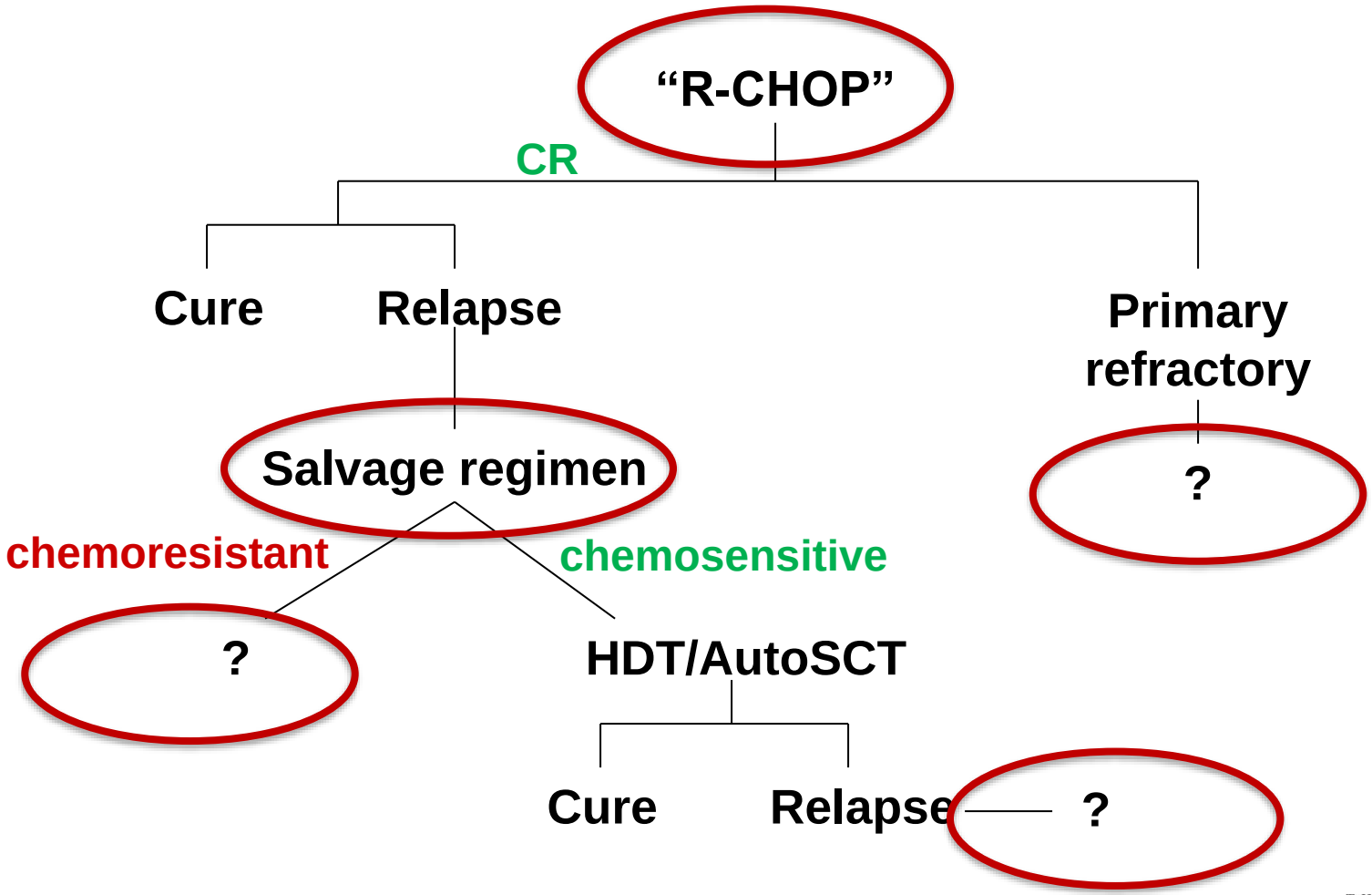
→ **R-CHOP**

→
- ❑ **Intensive therapy**
- ❑ **Consider CNS prophylaxis**

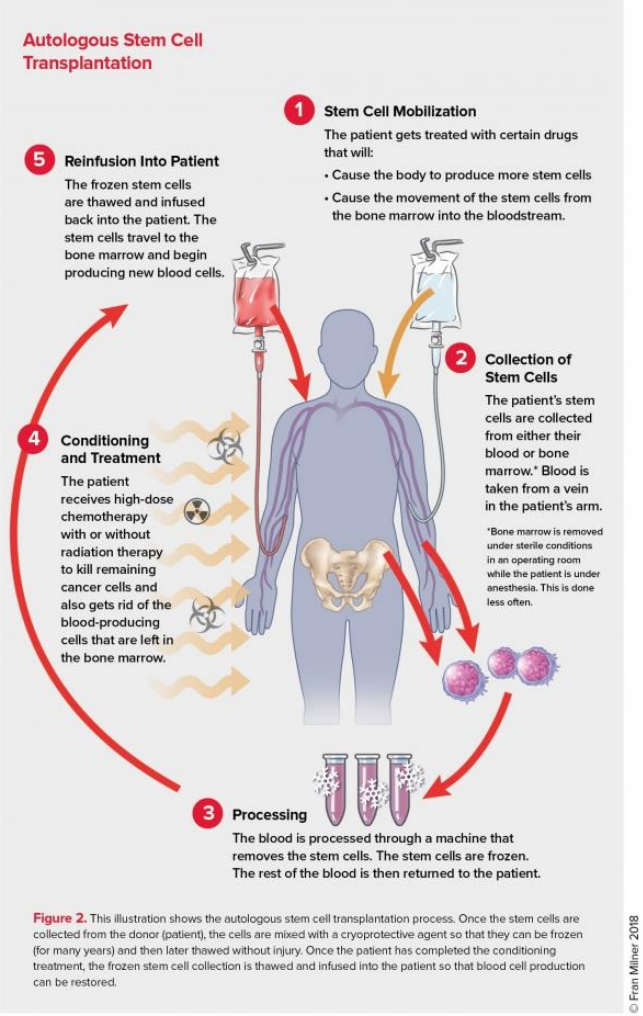
Slide courtesy of Paul Barr

WHAT IF THE DISEASE DOES NOT RESPOND OR COMES BACK?

“Treatment Algorithm” for DLBCL



Autologous stem cell transplant



- Autologous stem cell transplant is based on the concept that “more is better”
- There are 4 main parts:
  - “Salvage” chemotherapy
  - Stem cell collection (“mobilization”)
  - Delivery of high dose chemotherapy with autologous stem cell rescue
  - Post transplant recovery and immunizations
- It works best if:
  - Disease responds to salvage chemotherapy
  - There is no bone marrow involvement
  - Patient is in good condition to receive high doses of chemotherapy

https://www.lls.org/treatment/types-of-treatment/stem-cell-transplantation/autologous-stem-cell-transplantation

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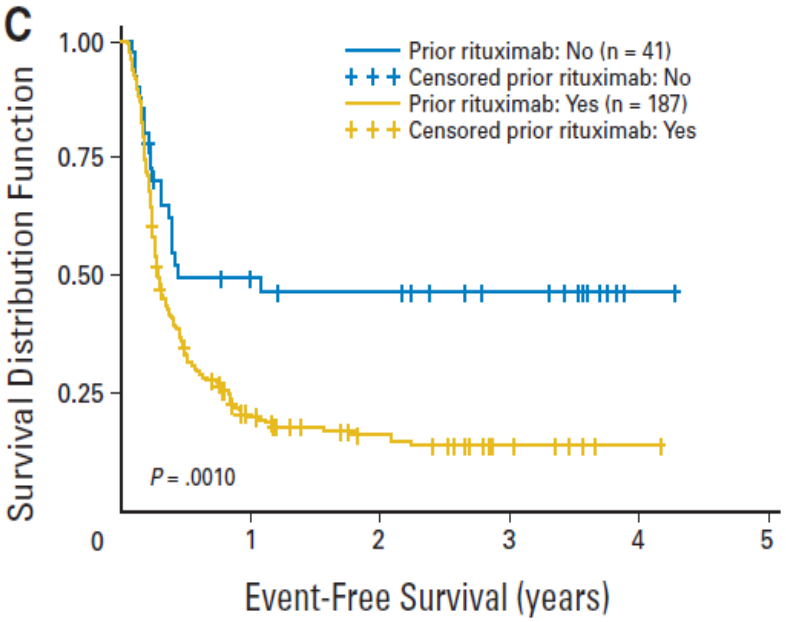
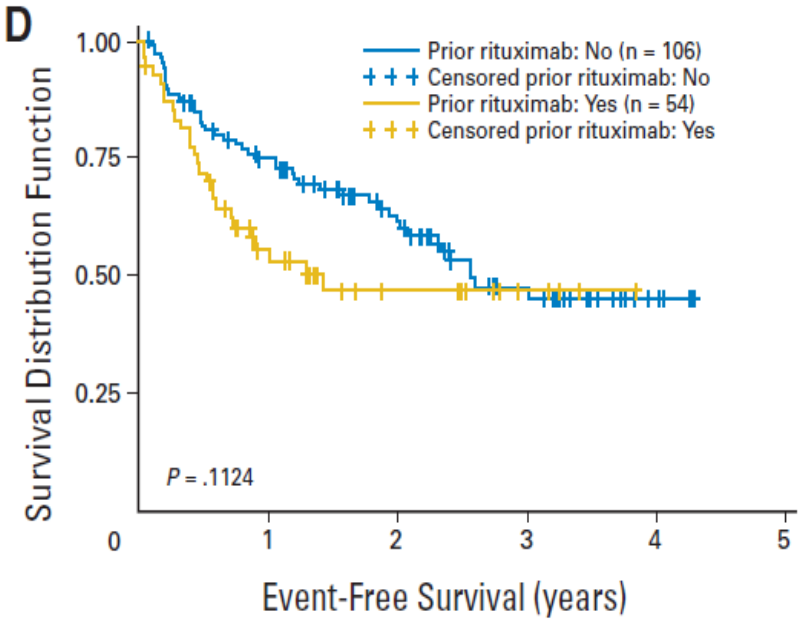
CORAL: outcome by prior rituximab exposure and time to relapse





Outcome by prior rituximab AND relapse < 12 months

Outcome by prior rituximab AND relapse > 12 months

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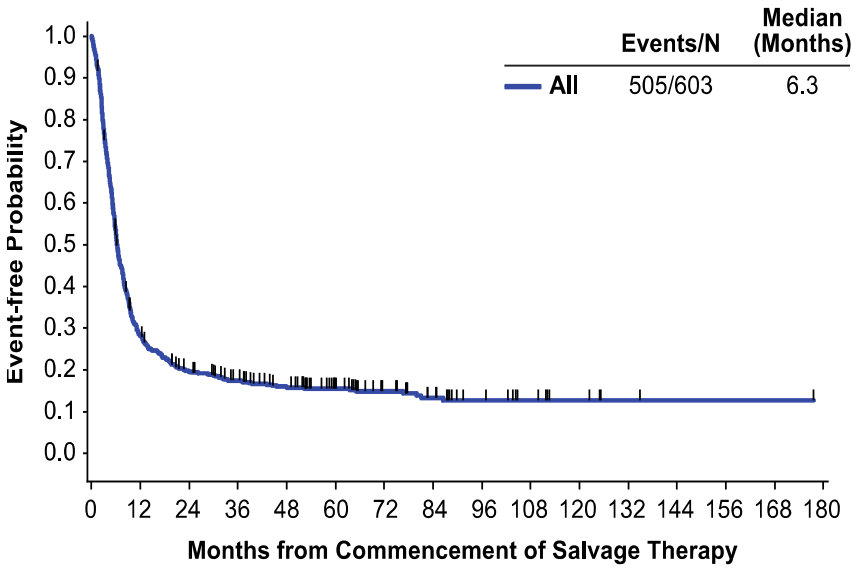
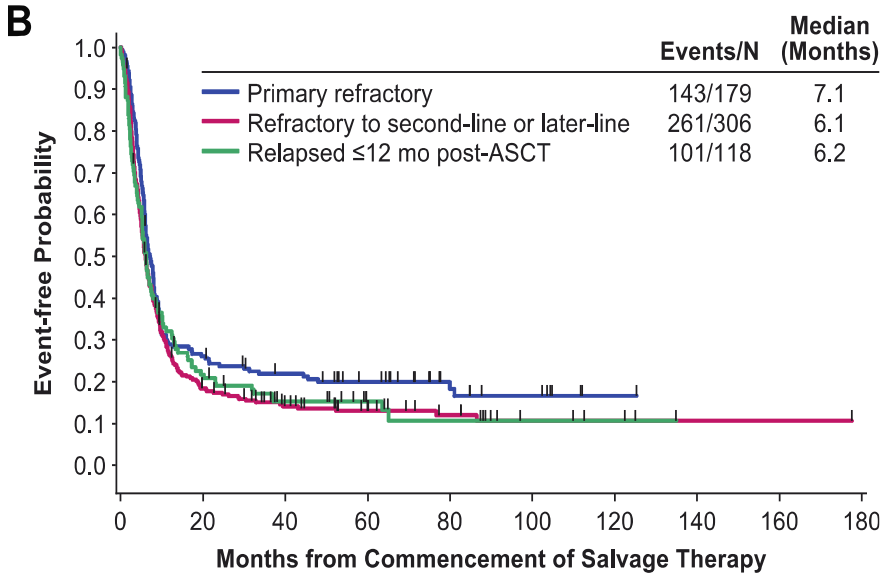
Expected survival for rel/ref DLBCL





Patients unable to undergo autologous stem cell transplant have median survivals < 1 year

Crump Blood Aug 3, 2017, pre-pub

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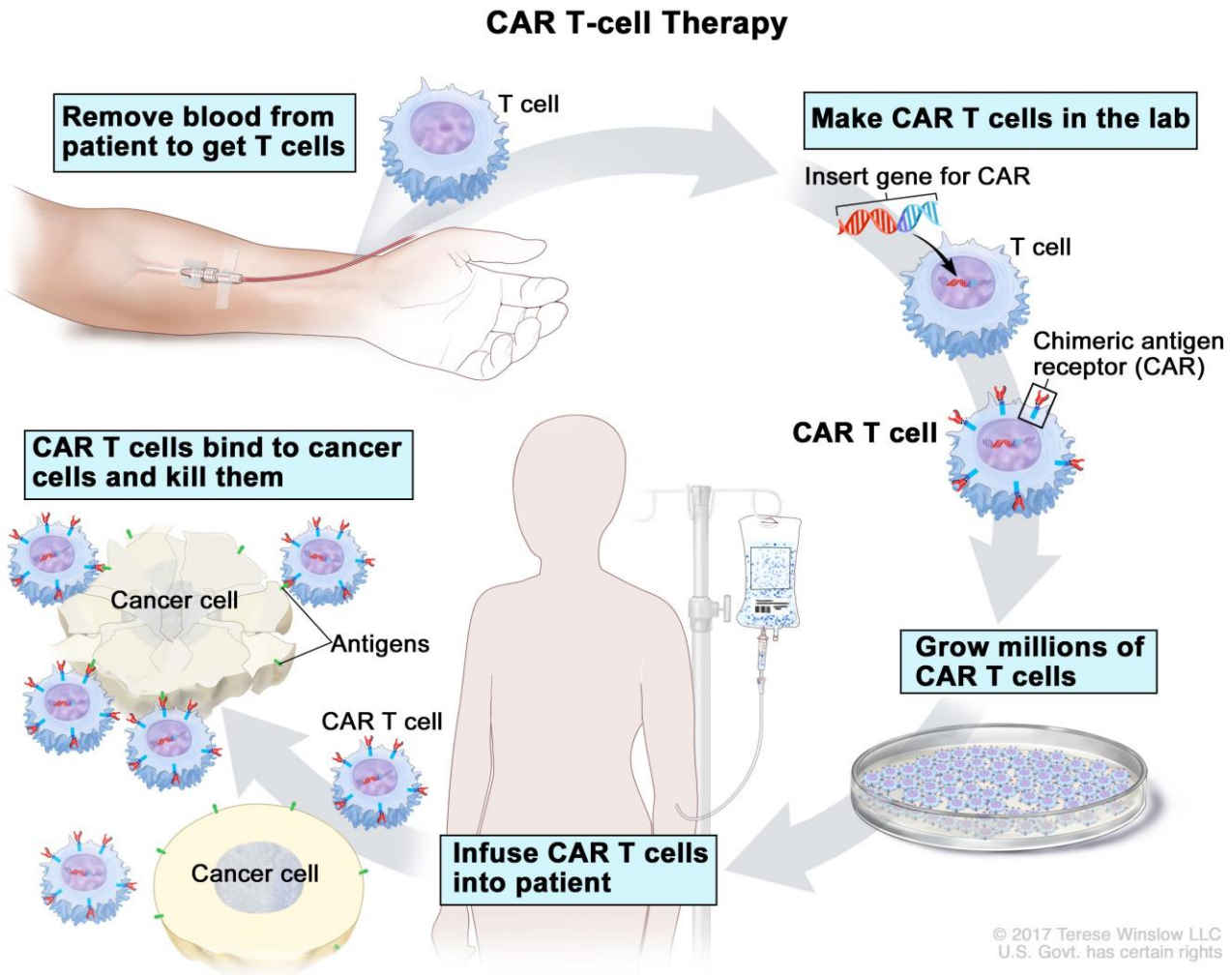
CAR-T cell therapy

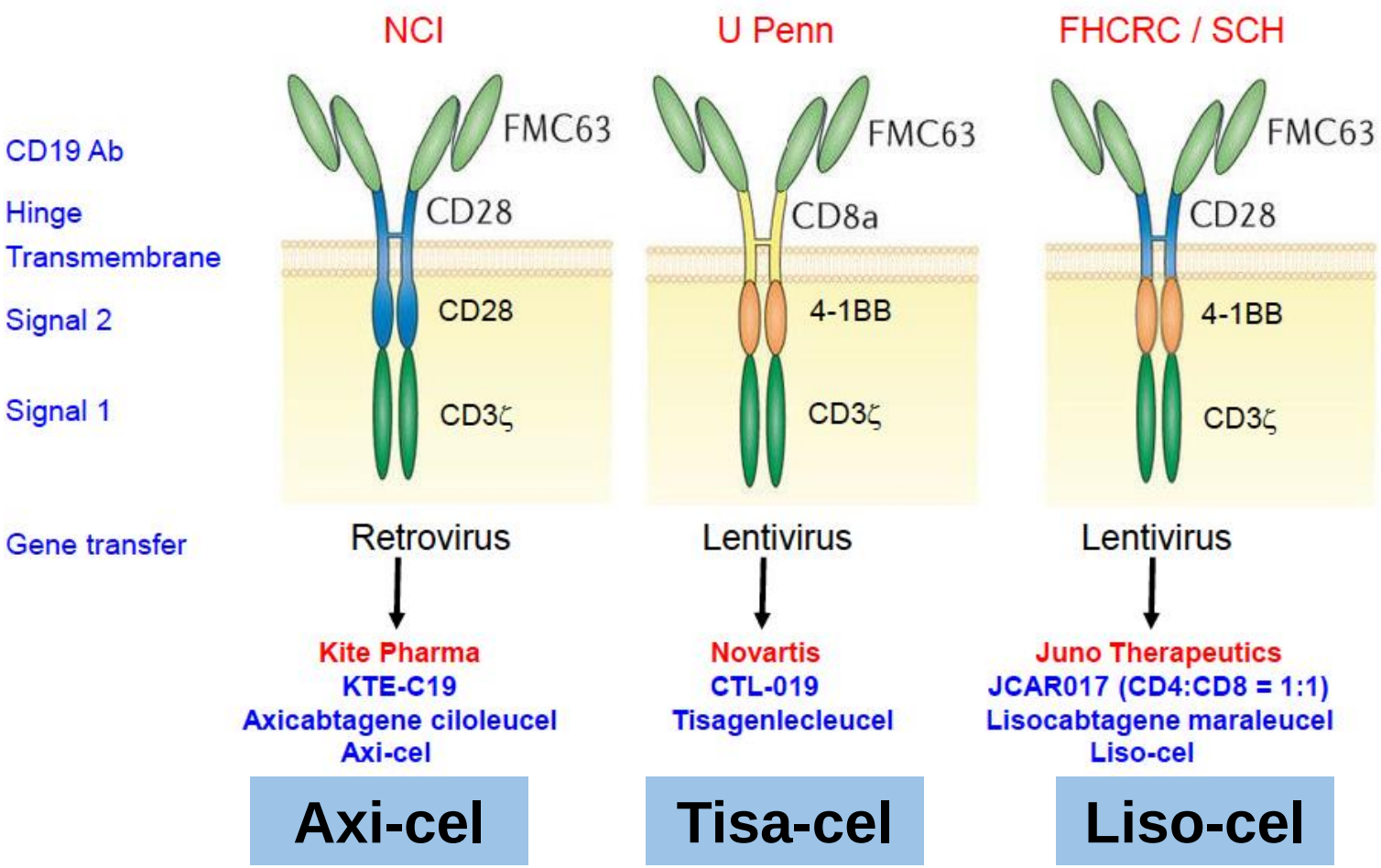
- Uses a patient's own T-cells instead of stem cells
- Does not require the disease to be in remission
- Uses less chemotherapy than an autologous stem cell transplant
- A "living drug"
- Has different risks:
  - Cytokine release syndrome (CRS)
  - Neurotoxicity

CAR-T cell process



https://www.cancer.gov/publications/dictionaries/cancer-terms/def/car-t-cell-therapy

CD19 Directed CAR T Cell Products in Clinical Development

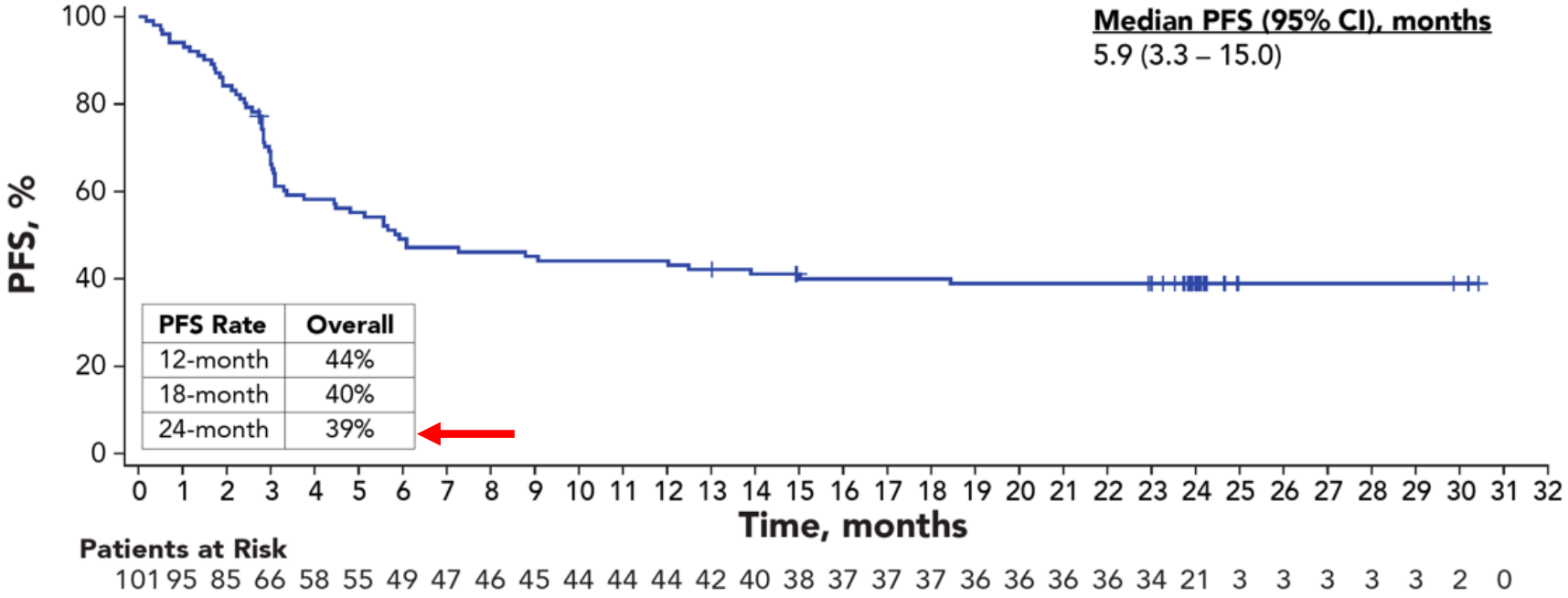


Adapted from van der Steegan et al. Nat Rev Drug Discov, 2015

2-year follow up of ZUMA-1

Axi-cel

Progression-Free Survival



- The 6-month plateau was largely maintained, with only 10 patients progressing beyond the 6-month follow-up

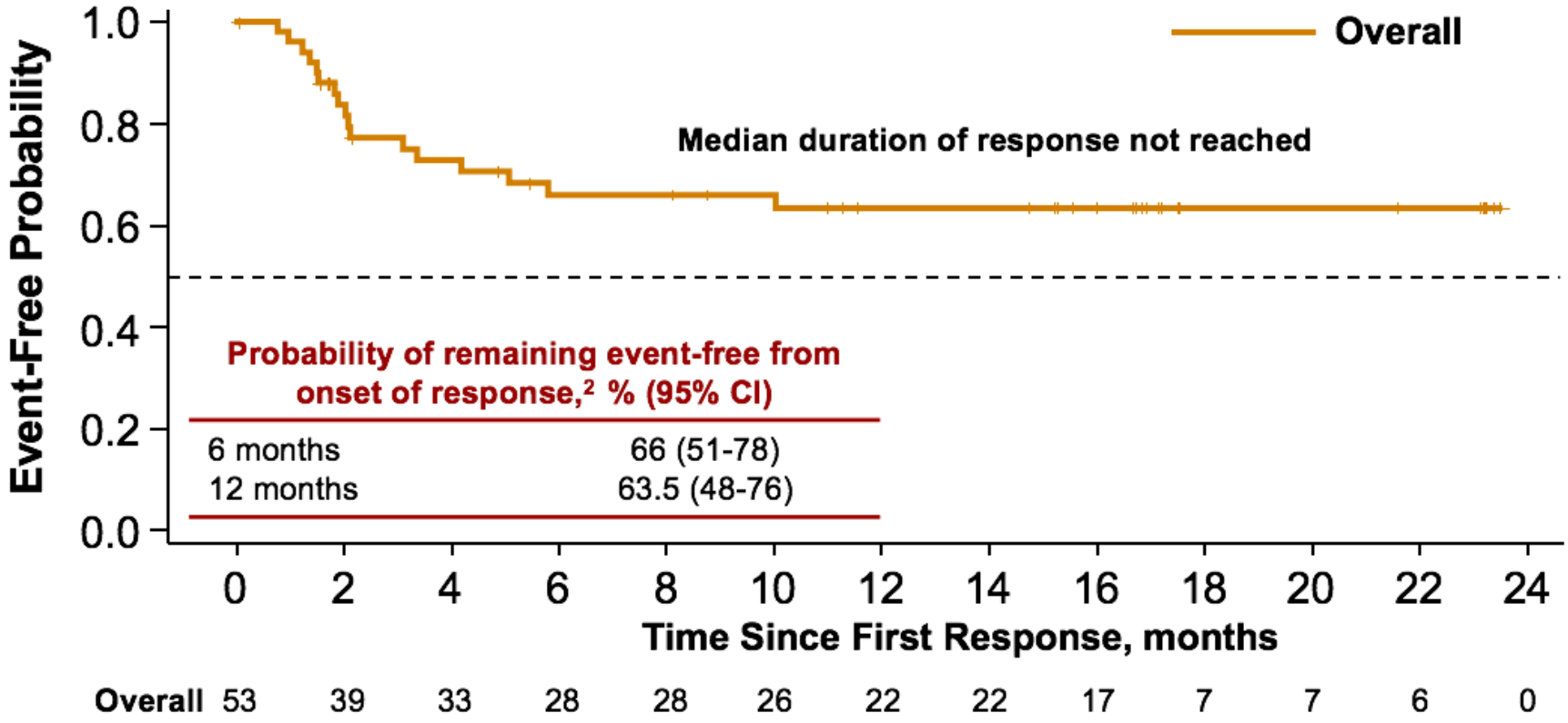
NR, not reached; PFS, progression-free survival.

Neelapu et al ASH 2018 2967

From Neelapu SS, et al. Presented at 60th American Society of Hematology Annual Meeting; December 1-4, 2018; San Diego, CA. Abstract 2967.

JULIET: Median Duration of Response

(Tisa-cel)



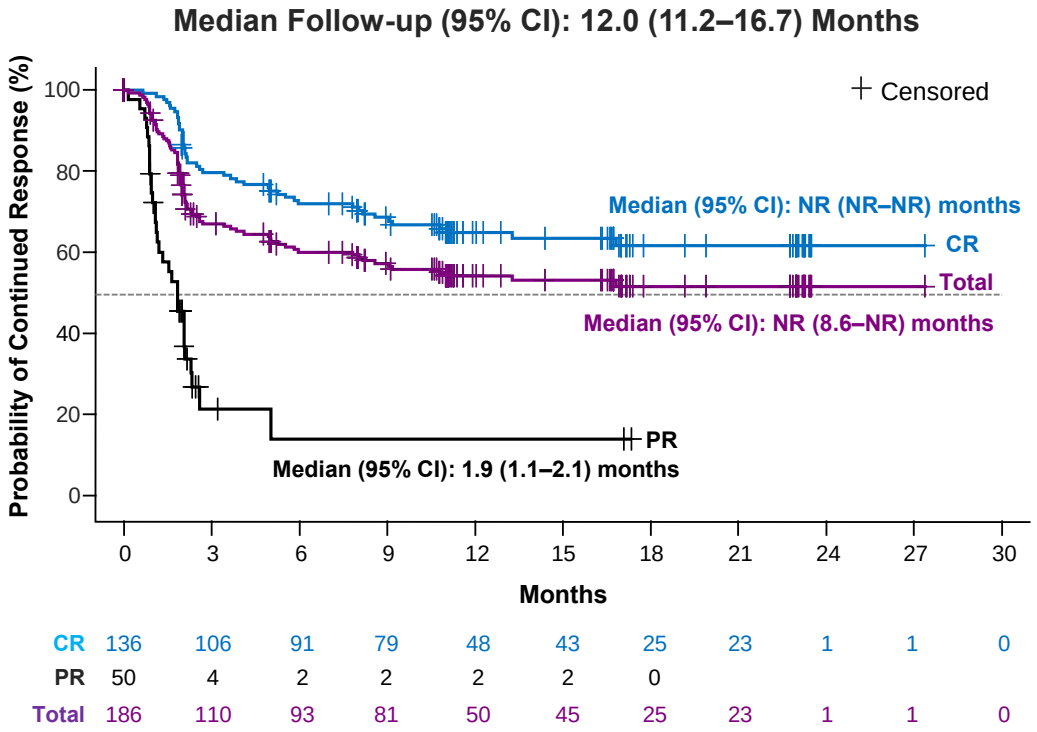
- No relapses were observed beyond 11 months after infusion
- 54% (15/28) of patients who had achieved a PR converted to CR

From Schuster SJ, et al. Presented at 60th American Society of Hematology Annual Meeting; December 1-4, 2018; San Diego, CA. Abstract 1684.

(Liso-cel)

Response and Durability by IRC Assessment

Efficacy-Evaluable Patients (N=256)	
ORR (95% CI)	73% (67–78)
CR rate (95% CI)	53% (47–59)
Time to first CR or PR, median (range), months	1.0 (0.7–8.9)
DOR at 6 months (95% CI), %	60.4 (52.6–67.3)
DOR at 12 months (95% CI), %	54.7 (46.7–62.0)



Efficacy among patients who received nonconforming product (n=25) was similar to those who received liso-cel

CI, confidence interval; CR, complete response; DOR, duration of response; IRC, independent review committee; NR, not reached; ORR, objective response rate; PR, partial response.

11

Efficacy of CAR T-Cell Therapy in B-NHL

	Axicabtagene Ciloleucel	Tisagenlecleucel	Lisocabtagene Maraleucel
Median follow-up	24 months	18 months	12 months
Best ORR	74%	50%	80%
Best CR Rate	54%	32%	59%
Median PFS	5.9 months	2.9 months	_____
Median OS	NR	12 months	NR
Durable ORR	36%	34%	49%
Durable CR Rate	35%	29%	46%

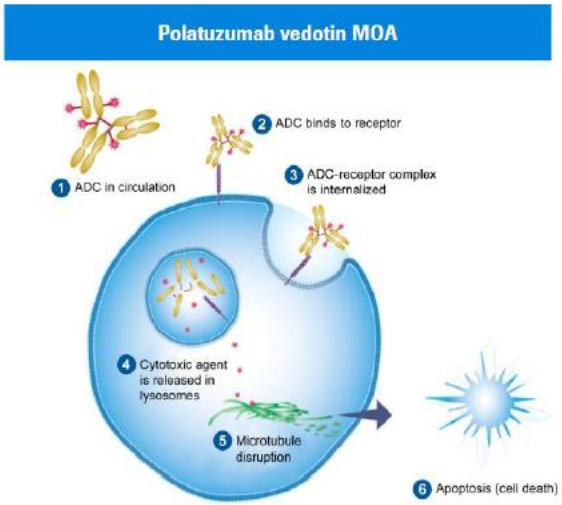
KYMRIAH [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; 2017/2018
YESCARTA [package insert]. Santa Monica, CA: Kite Pharma, Inc.; 2017
Neelapu SS, et al. Presented at 59th American Society of Hematology Annual Meeting; December 9-12, 2017; Atlanta, GA. Abstract 578.
Schuster SJ, et al. Presented at 60th American Society of Hematology Annual Meeting; December 1-4, 2018; San Diego, CA. Abstract 1684.
Abramson JS, et al. Presented at 2018 American Society of Clinical Oncology Annual Meeting; June 1-5, 2018; Chicago, IL. Abstract 7505.

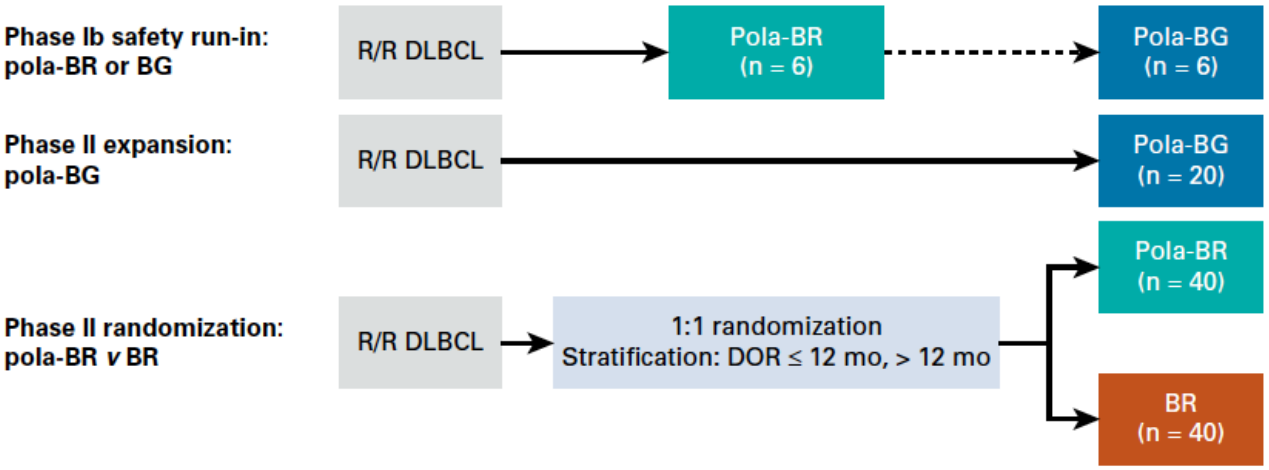
No standard of care—goal is palliation

- ***Clinical trials***
- Chemoimmunotherapy
  - Gemcitabine-based regimens
  - Pola-BR
- Non-chemotherapy options
  - Selinexor
  - Tafasitamab-lenalidomide (FDA-approved 7/31/2020)
  - *Ibrutinib (preferential activity in non-GC DLBCL)**
  - *Len/rituximab (preferential activity in non-GC DLBCL)**
- Best supportive care

**not FDA-approved*

Pola-BR: anti CD79b ADC plus BR





- Primary endpoint CR rate at EOT
- Med f/u 22.3 months

Sehn *Journal of Clinical Oncology* 36, no. 15_suppl (May 20, 2018) 7507-7507.
Figure courtesy of Roche.com

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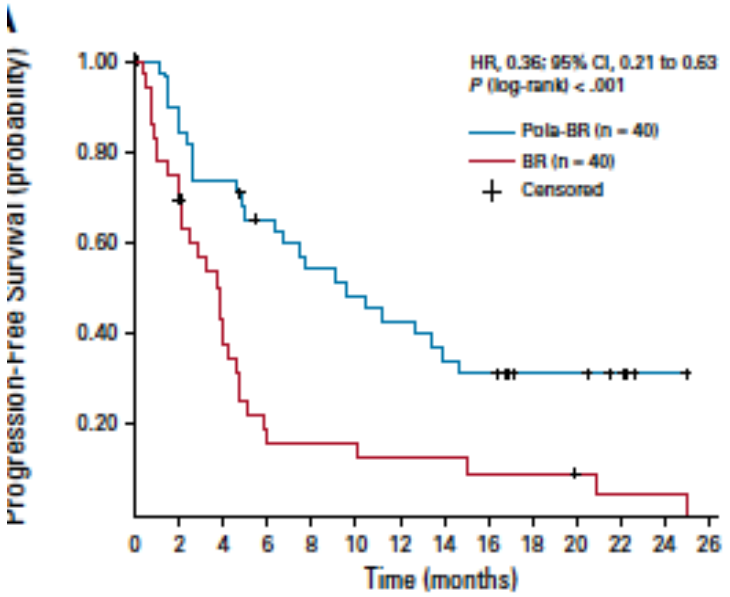
RP2: Pola-BR vs. BR

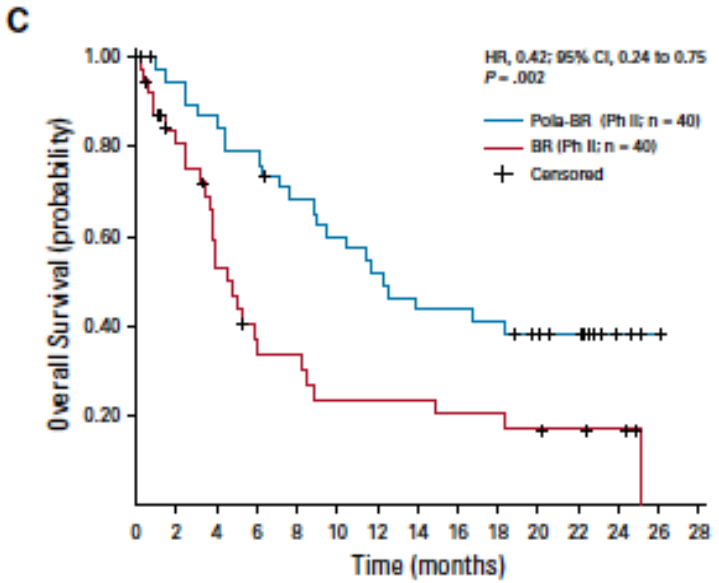
	Pola-BR (n=40)	BR (n=40)
Median age	67y (33-86)	71y (30-84)
Male	70%	62.5%
PS 0-1	83%	78%
ABC-DLBCL	48%	48%
GCB-DLBCL	38%	43%
Med prior Rx	2 (1-7)	2 (1-5)
Ref to last Rx	75%	85%
DOR to last Rx $\leq$ 12 m	45%	48%

Main reasons for transplant ineligibility include advanced age and insufficient response to prior salvage therapy

Sehn *Journal of Clinical Oncology* 36, no. 15_suppl (May 20, 2018) 7507-7507.

Pola-BR vs. BR Results





	Pola-BR (n=40)	BR (n=40)
EOT Response % (ORR/CR)	45/40	18/18
Best response % (ORR/CR)	63/50	25/23
Med DR	12.6	7.7m
Med PFS	9.5m	3.7m
Med OS	12.4m	4.7m

Sehn *Journal of Clinical Oncology* 36, no. 15_suppl (May 20, 2018) 7507-7507.

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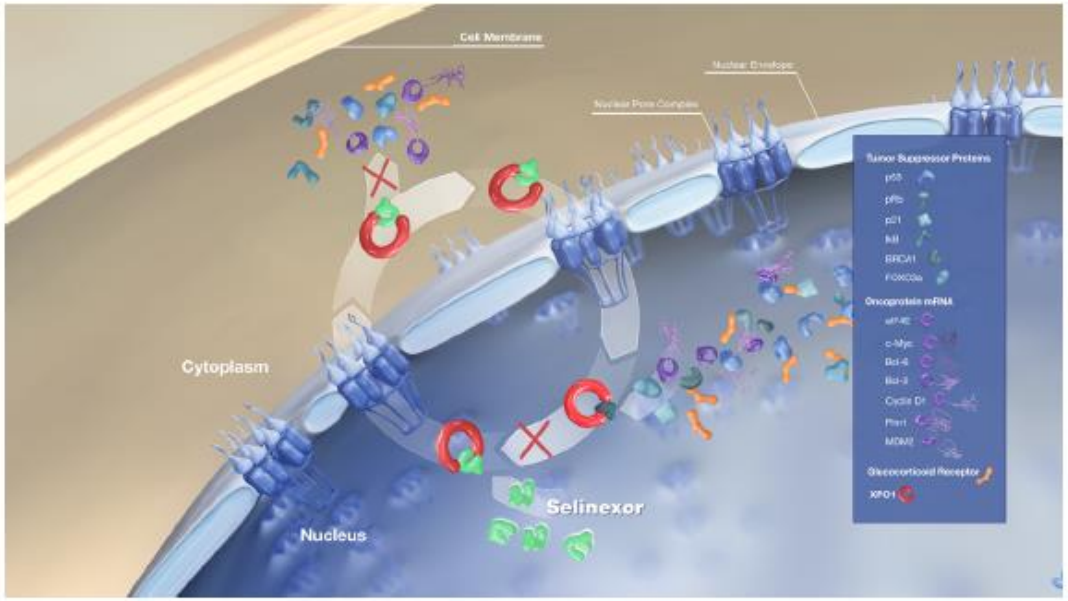
Selinexor: oral XPO1 inhibitor

Selinexor: Mechanism of Action



Exportin 1 (XPO1 or CRM1) mediates the nuclear export of proteins, mRNAs, rRNAs, snRNAs and impacts

- **Tumor suppressor proteins** (p53, IκB, FOXO etc.)
- **eIF4E** (Translational initiation factor) bound oncogenic mRNAs (c-Myc, Bcl-xL, cyclins etc.)

Selinexor is an oral selective **XPO1** inhibitor; preclinical data support that XPO1 inhibition:

- Reactivates multiple TSPs relevant to NHL, (p53, p21, IκB, FOXO etc.)
- Disrupts localization of eIF4e (overexpressed in most B-cell lymphomas[1]
- Reduces c-Myc, Bcl-2, and Bcl-6 levels[2-3]

1. Kodali 2011 2. Kuruvilla 2014 3. Schmidt 2013

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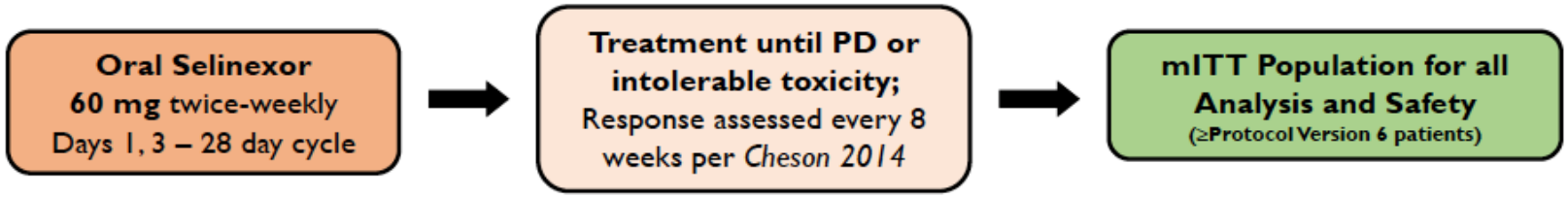
SADAL: Phase 2b trial of selinexor monotherapy



Objectives:

- **Primary Endpoint**: Overall response rate (ORR): Independent Central Radiological Review (ICRR); Lugano Classification (2014)
- **Secondary Endpoints**: Duration of response (DOR), Overall survival (OS), Safety

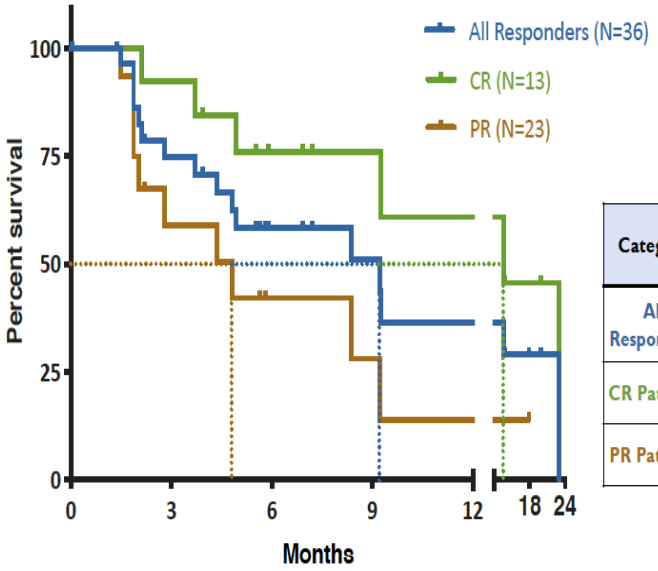
Modified Intent to Treat (mITT) Population: All patients who were randomized to the **60 mg Arm**

Characteristic	N
Enrolled* as of April 3, 2019	**127**
Median Age, Years (Range)	**67** (35–87)
Males (%) : Females (%)	**75** (59%) : **52** (41%)
Median Years from DLBCL Diagnosis (Range)	**2.6 yrs** (<1–26.2)
De novo DLBCL : Transformed DLBCL : Unknown	**96** (76%) : **30** (24%) : **1** (<1%)
GCB Subtype : Non-GCB Subtype : Unclassified	**59** GCB : **63** Non-GCB : **5** Unclassified
Median Prior Treatment Regimens (Range)	**2 (1–6)**
Prior Transplantation	39 (31%)

Kalakonda ICML 2019

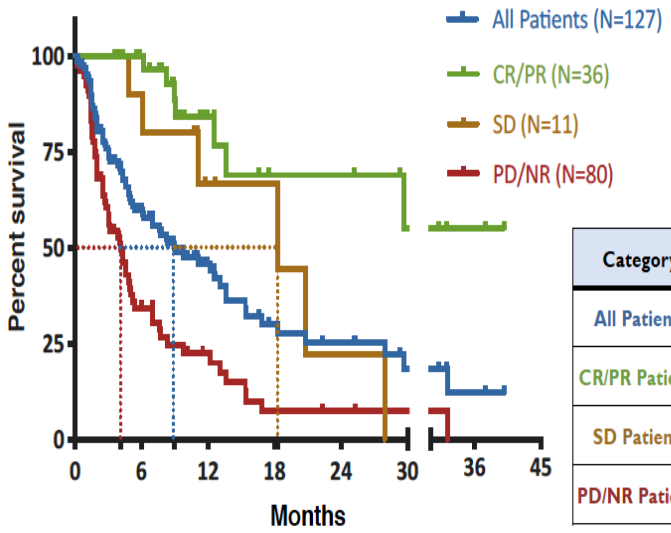
SADAL: Results

Duration of response



Category	Median DOR (months)	95% CI
All Responders	9.2	(4.8 – 23.0)
CR Patients	13.5	(9.3 – 23.0)
PR Patients	4.8	(2.0 – NE)

Overall survival



Category	Median OS (months)	95% CI
All Patients	9.0	(6.2 – 13.7)
CR/PR Patients	Not Reached	(13.7 – NE)
SD Patients	18.3	(11.1 – 28.0)
PD/NR Patients	4.1	(3.0 – 5.2)

Median follow-up of 11 months

- Selinexor dosing is 60mg BIW with 17% stopping due to A/Es
- ORR 29% (CR 13%)
- Median DOR 9.3 months and for CR 23 months
- Main toxicities: asthenia, nausea, weight loss, cytopenias

Kalakonda ICML 2019

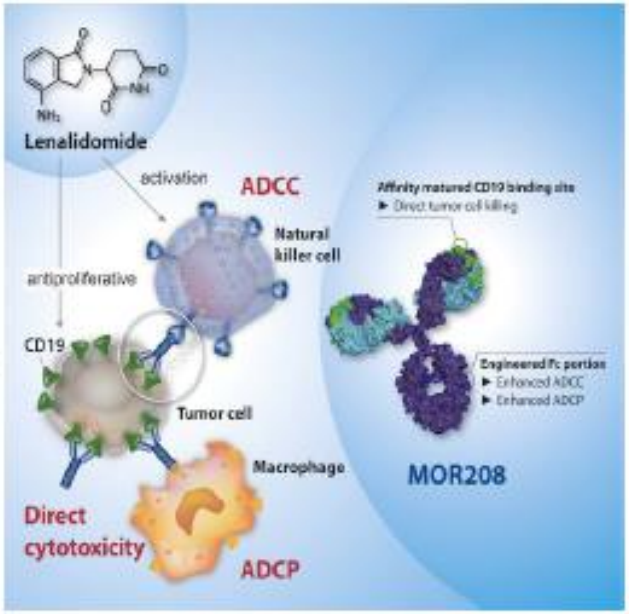
Tafasitamab MOA

MOR208
Fc-enhanced, anti-CD19 mAb

+

Lenalidomide

- ADCC ↑
- ADCP ↑
- Direct Cell Death
- Encouraging single agent activity in NHL patients with long DoR in R/R DLBCL



- T and NK Cell Activation/Expansion
- Direct Cell Death
- Demonstrated activity as an anti-lymphoma agent, alone or in combination
- Approved for treatment of MCL and FL/MZL

Potentiation of activity by combining Tafasitamab & LEN in vivo and in vitro

Salles et al. ICML 2019. #124.
Hortonet al., 2008; Awanet al., 2010; Richter et al., 2013; MorphoSys data on file; Wu et al., 2008; Lapalombella et al., 2008; Zhang et al., 2013, Wiernik et al., 2008; Witzig et al., 2011; Czuczman et al., 2017; Jurczak et al, 2018

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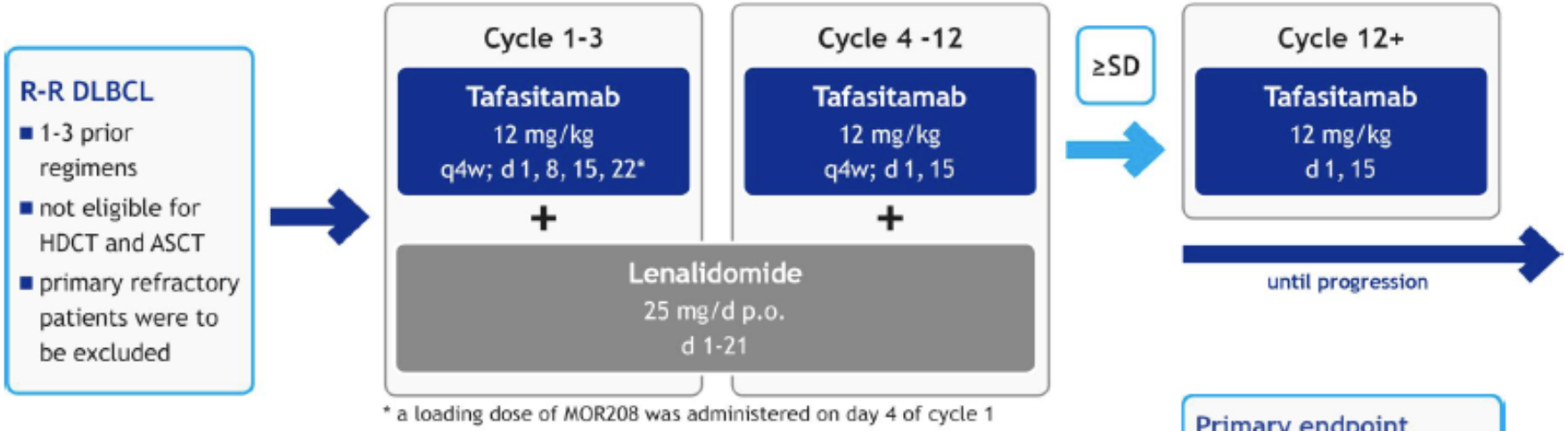
L-MIND: Study Design



* a loading dose of MOR208 was administered on day 4 of cycle 1

- Sample size suitable to detect ≥15% absolute increase in ORR for Tafasitamab/LEN combination vs. LEN monotherapy at 85% power, 2-sided alpha of 5%
- Mature Data: Primary Endpoint Analysis with data cut-off 30 Nov 2018; minimum Follow-Up 12 months, median Follow-Up 17.3 months

-Primary refractory DLBCL was defined as no response to or progression/relapse during or within 6 months of frontline therapy.
-Response assessment (Cheson 2007 Criteria) was after cycles 2, 4, 6, 9 and 12, thereafter every 3 cycles.
-ASCT, autologous stem cell transplant; HDCT, high-dose chemotherapy; SD, stable disease, p.o., per os.

Primary endpoint
- ORR (Central read)

Secondary endpoints
- PFS
- DoR
- OS
- Safety of the Tafasitamab + LEN combination
- Exploratory and biomarker-based analyses

- Salles et al. ICML 2019. #124.

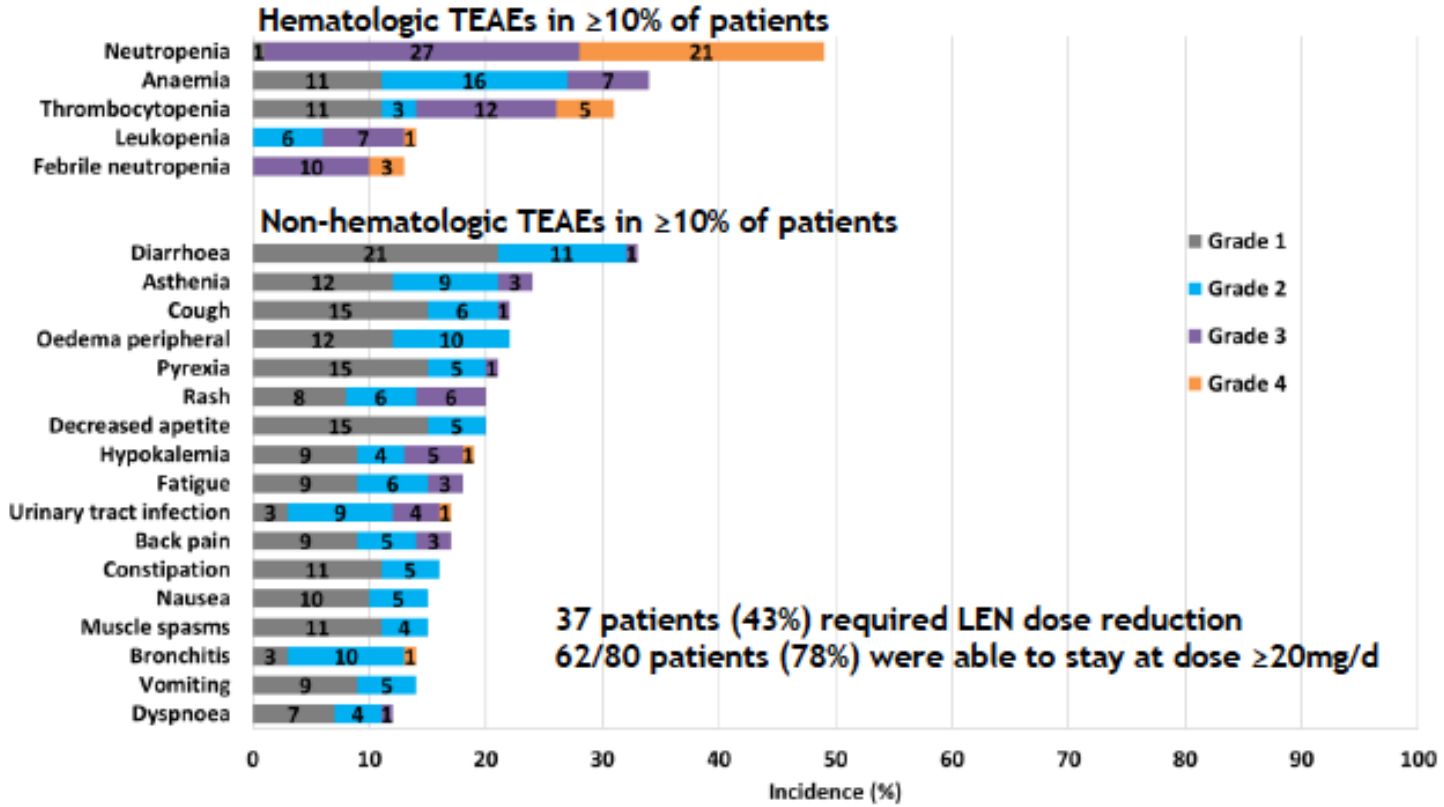
L-MIND: Baseline Characteristics

Characteristic	Specification	n=81 (%)
Sex	Male Female	44 (54) 37 (46)
Age [years]*	median (range)	72 (41-86)
Risk (IPI)*	0-2 3-5	40 (49) 41 (51)
Ann Arbor Stage*	I-II III-IV	20 (25) 61 (75)
Elevated LDH*	Yes No	45 (56) 36 (44)
Prior Lines*	median 1 2 3 4	2 40 (49) 35 (43) 5 (6) 1(1)
Primary Refractory	Yes No	15 (18) 66 (82)
Refractory to last prior therapy*	Yes No	36 (44) 45 (56)
Prior SCT	Yes No	9 (11) 72 (89)
Cell of Origin (Centrally assessed - Hans algorithm)	GCB Non-GCB Unknown	37 (46) 20 (25) 24 (30)

*at study entry

- Salles et al. ICML 2019. #124.

L-MIND: Treatment-Emergent AEs



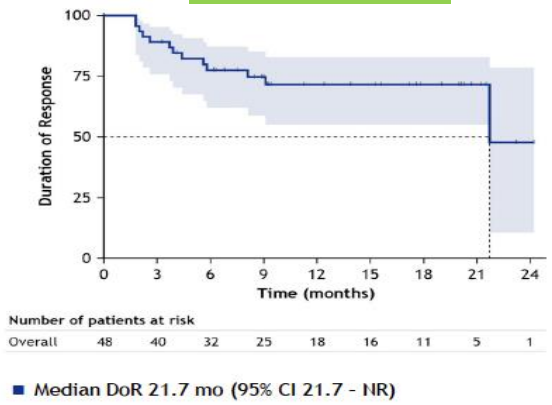
- 5 infusion-related reactions in 5 patients (6%) were reported for Tafasitamab (all grade 1)
- Treatment-related SAEs occurred in 15 (18.5%) patients (primarily infections [10%] or neutropenic fever [5%])
- 4 treatment-emergent deaths (sudden death, respiratory failure, cerebrovascular accident, PML) were reported as unrelated to study drugs

N=81. TEAEs, treatment-emergent adverse events, numbers represent % patients

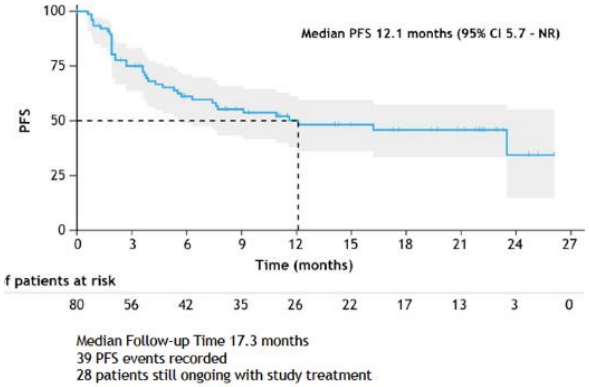
- Salles et al. ICML 2019. #124.

L-MIND: Efficacy

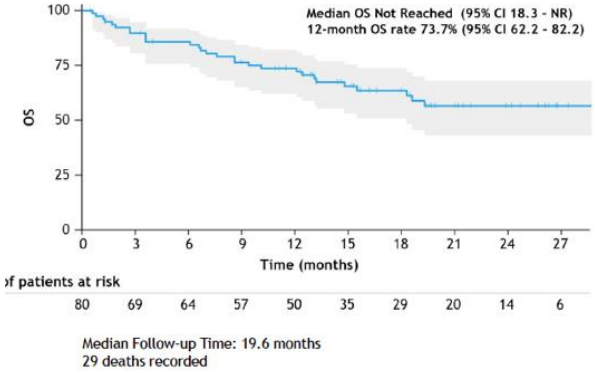
DR



PFS



OS



<u>Key Outcomes</u>:

ORR 60%**

CR 42.9%

Med DR 21.7m

Med PFS 12.1m

12m OS 73.7%

Salles et al. ICML 2019. #124; Lancet Oncology 2020.

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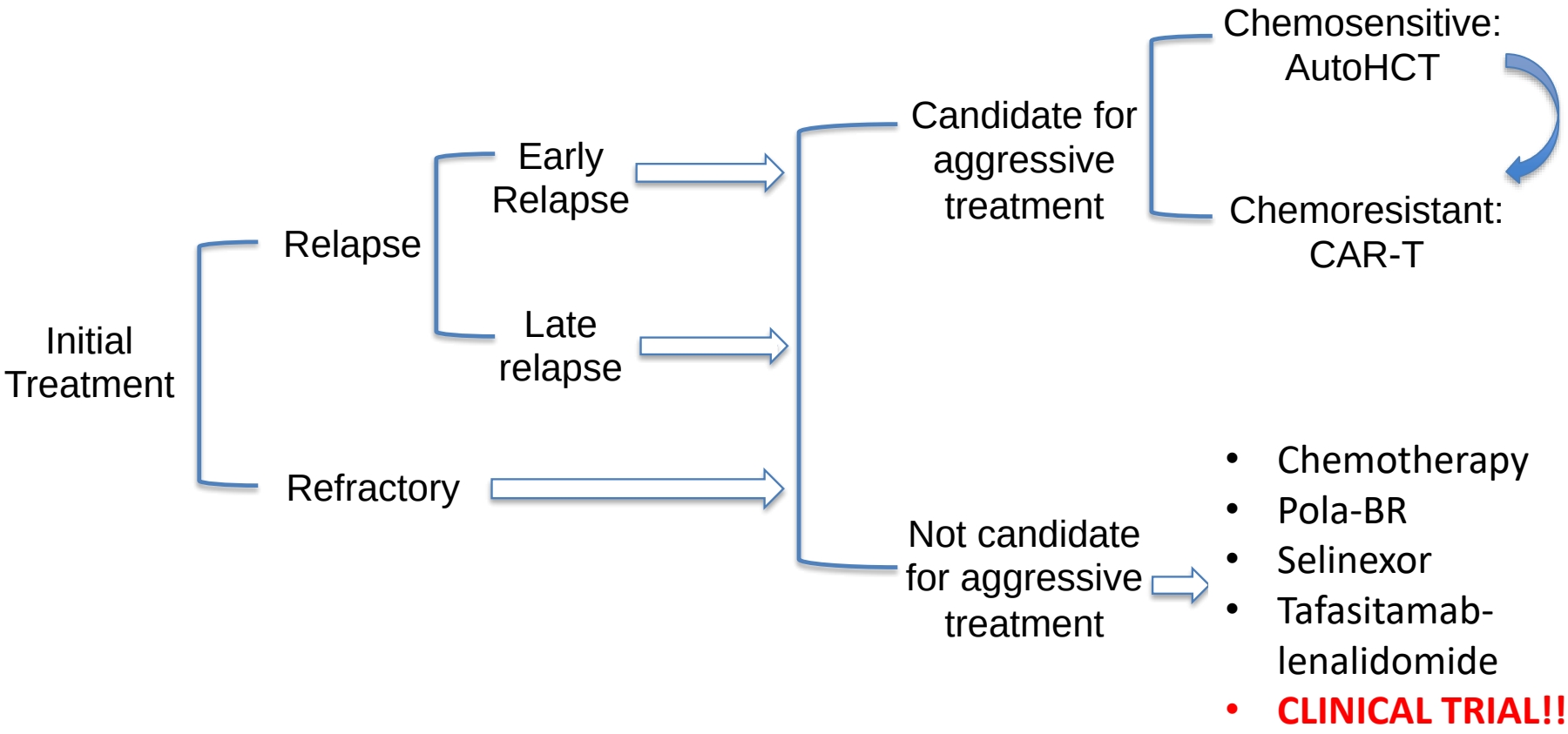
Treatment considerations in relapsed aggressive B-cell lymphomas



*not FDA-approved

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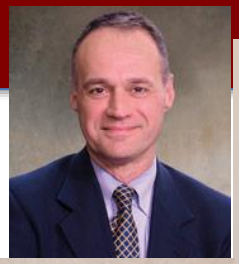
The University of Chicago Lymphoma Program













Not pictured: Rachel Kraft, Michelle Rainer, Amy Wang

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Questions?

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