

Aggressive B- and T-cell Lymphoma: a primer

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August 14, 2020



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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

How common is lymphoma?

	Male			Female		
Estimated New Cases	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	62,300	7%	Urinary bladder	65,620	7%
	Melanoma of the skin	60,300	7%	Melanoma of the skin	40,170	4%
	Kidney & renal pelvis	45,300	5%	Kidney & renal pelvis	40,160	4%
	Non-Hodgkin lymphoma	42,300	5%	Non-Hodgkin lymphoma	34,860	4%
	Oral cavity & pharynx	38,380	4%	Oral cavity & pharynx	28,230	3%
	Leukemia	35,300	4%	Leukemia	27,200	3%
	Pancreas	30,400	3%	Pancreas	25,060	3%
	All sites	893,600		All sites	912,930	

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

662,789 people living with lymphoma

	Male			Female		
Estimated Deaths	Lung & bronchus	72,500	22%	Lung & bronchus	63,220	22%
	Prostate	33,330	10%	Prostate	42,170	15%
	Colon & rectum	28,630	9%	Colon & rectum	24,570	9%
	Pancreas	24,640	8%	Pancreas	22,410	8%
	Liver & intrahepatic bile duct	20,020	6%	Liver & intrahepatic bile duct	13,940	5%
	Leukemia	13,420	4%	Leukemia	12,590	4%
	Esophagus	13,100	4%	Esophagus	10,140	4%
	Urinary bladder	13,050	4%	Urinary bladder	9,680	3%
	Non-Hodgkin lymphoma	11,460	4%	Non-Hodgkin lymphoma	8,480	3%
	Brain & other nervous system	10,190	3%	Brain & other nervous system	7,830	3%
	All sites	321,160		All sites	285,360	

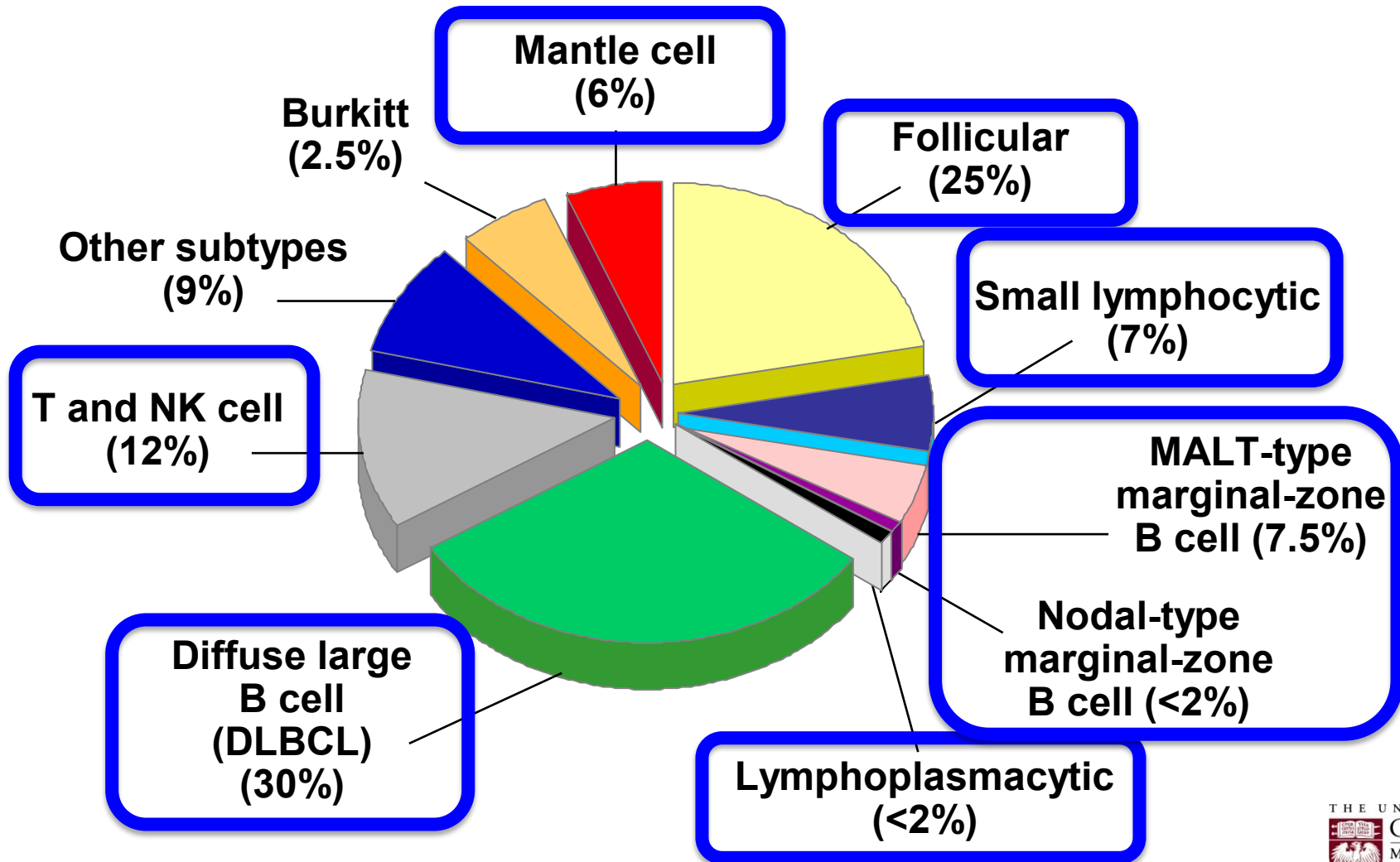
Hodgkin and non-Hodgkin lymphoma affect both genders, all ages, all races

What causes lymphoma?

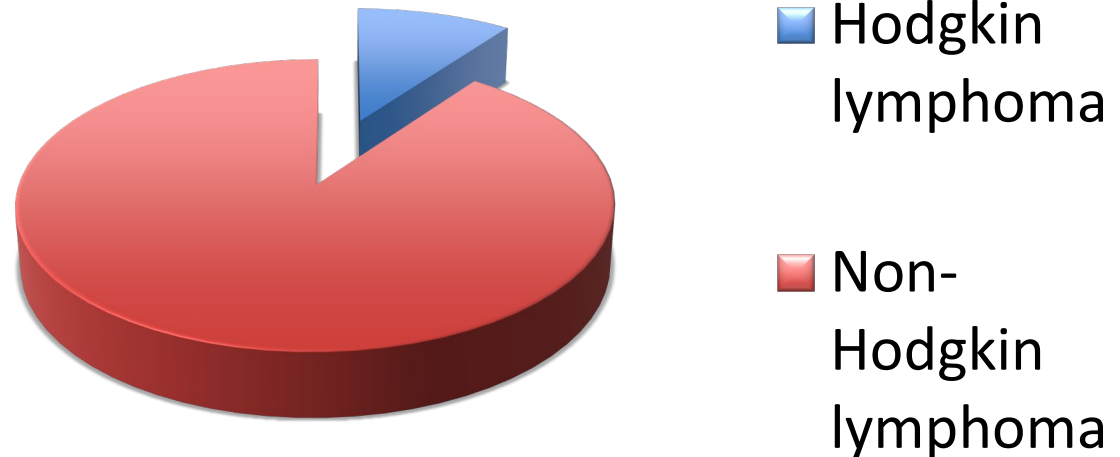
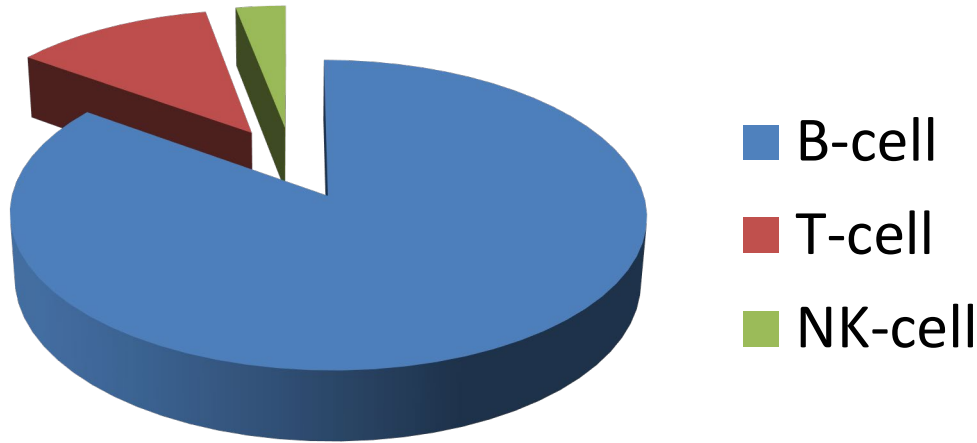
- Increasing age
- Abnormalities of the immune system
 - Inherited
 - Related to treatment of another condition
 - Acquired (HIV)
- Viruses
 - Hepatitis B and C
 - Human herpes virus 6
- Exposure to certain chemicals
- Bacteria
 - *Helicobacter pylori*

Genetics?
Environment?
Diet/lifestyle?

There are more than 80 types of lymphoma



There are many ways to slice the “lymphoma pie”



What is an aggressive lymphoma?

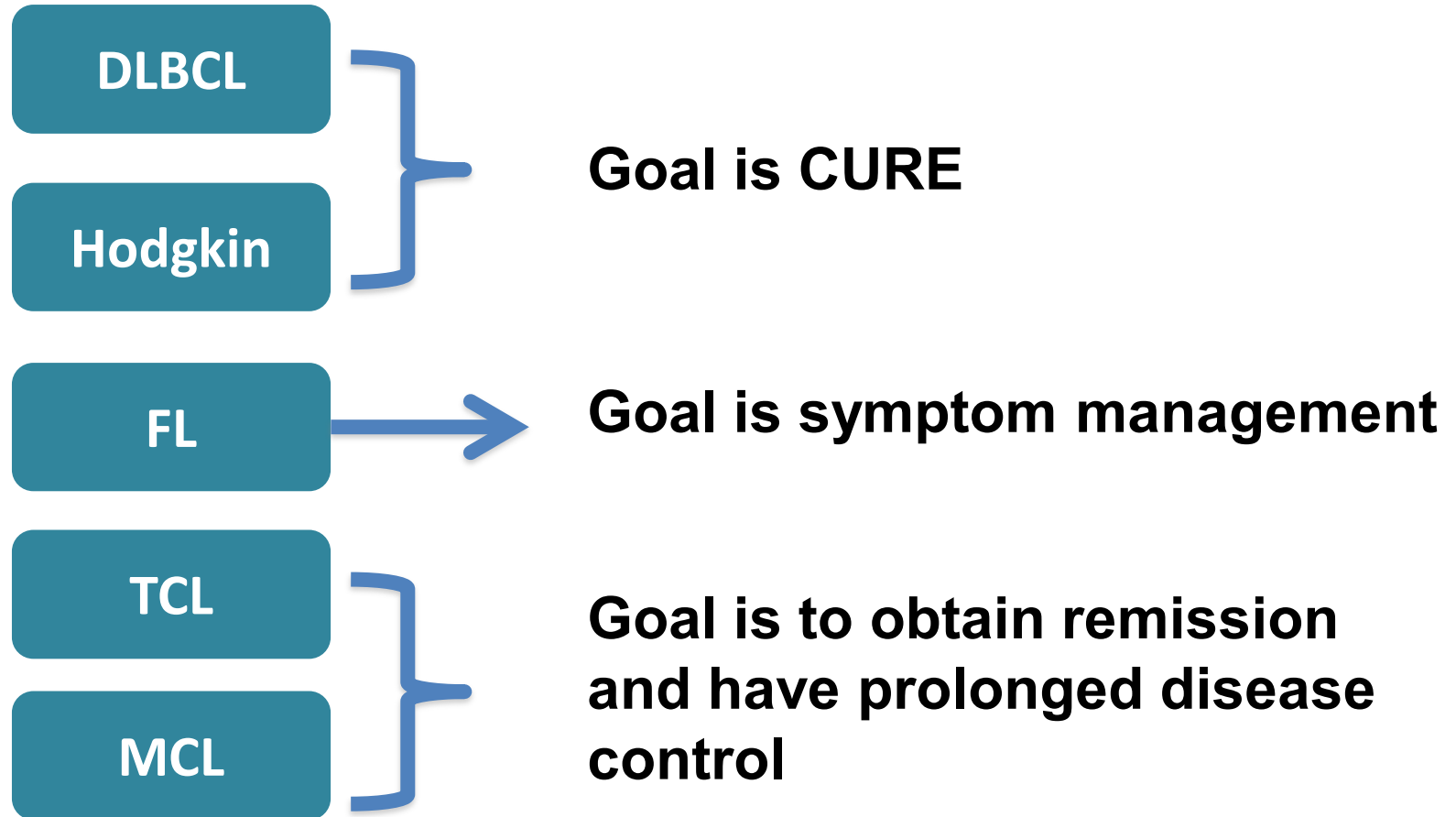
- Generally used to describe a lymphoma that grows quickly and needs treatment either urgently or emergently
- Many faster growing lymphomas respond to chemotherapy-based treatment
- **Examples:**
 - Diffuse large B-cell lymphoma and high-grade B-cell lymphomas
 - Includes “double hit” and “triple hit”
 - Burkitt lymphoma
 - Mantle cell lymphoma
 - Peripheral T-cell lymphomas

TREATMENT APPROACH TO LYMPHOMAS

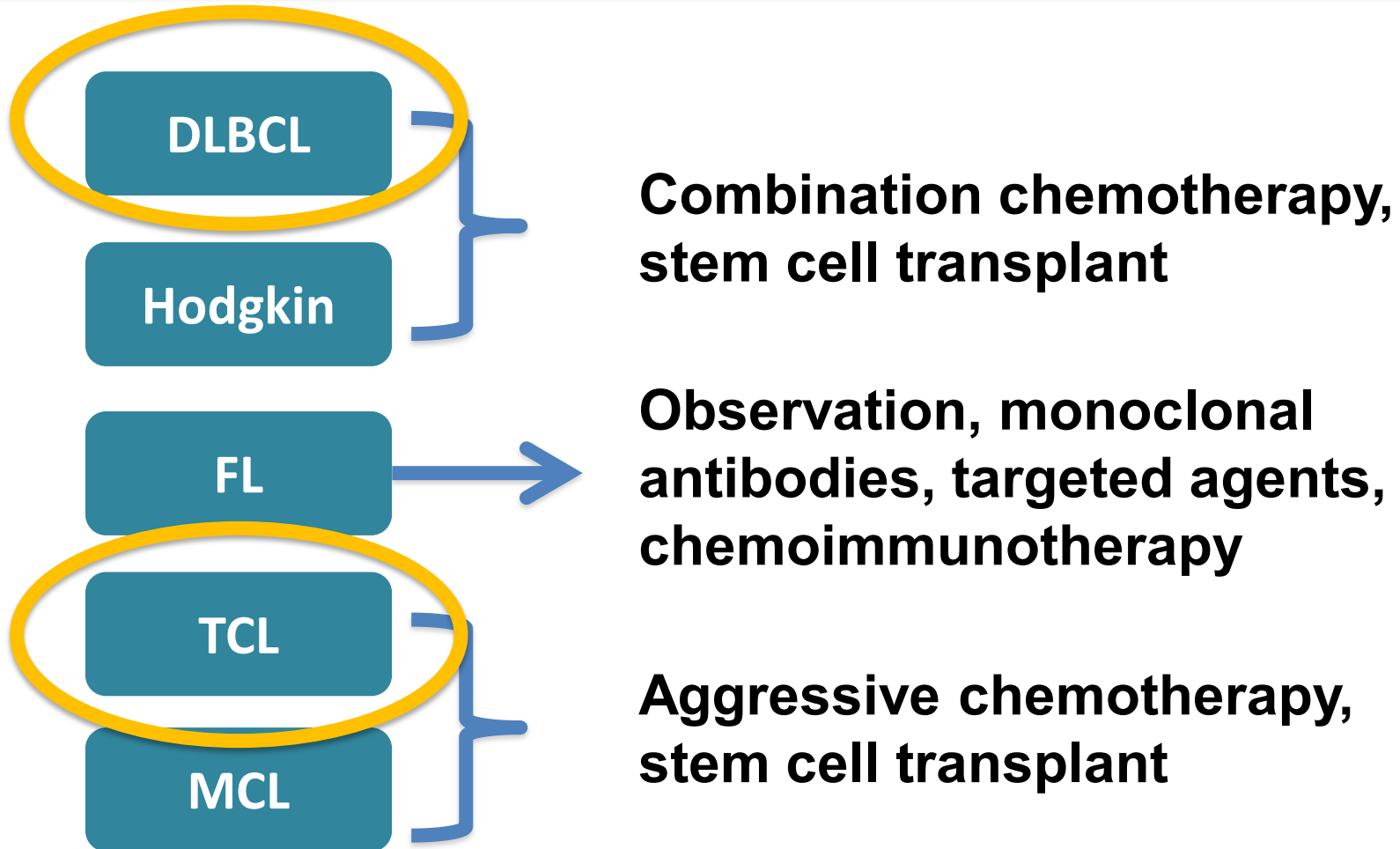
Treatment: General Principles

- 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



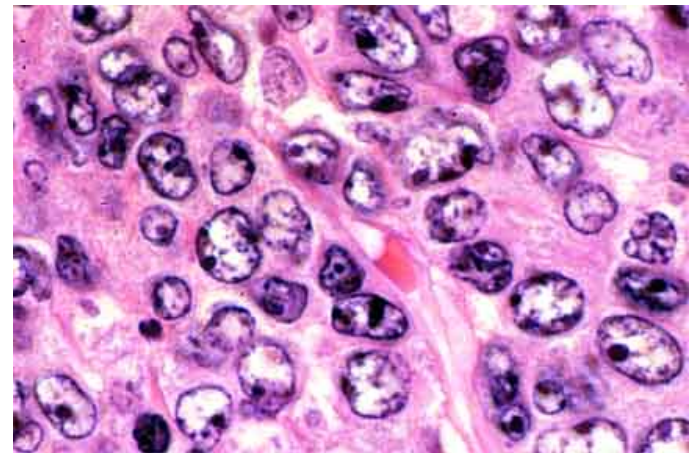
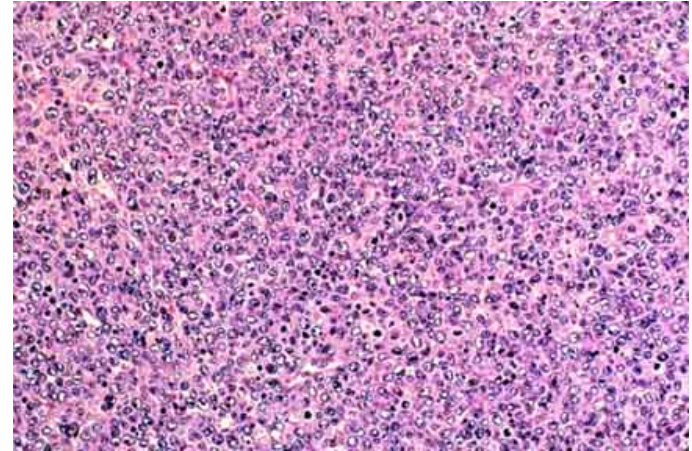
Type of treatment depends on the disease



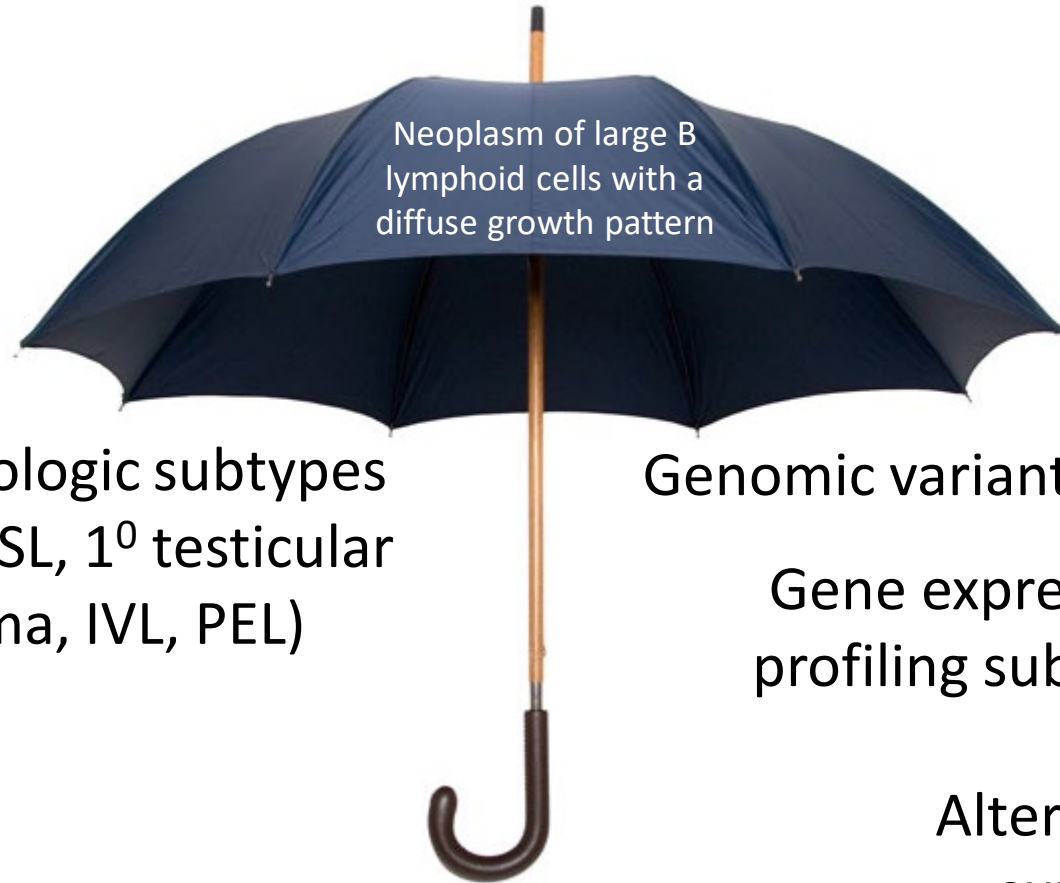
TREATMENT OF DIFFUSE LARGE B-CELL LYMPHOMA

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



Neoplasm of large B lymphoid cells with a diffuse growth pattern

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

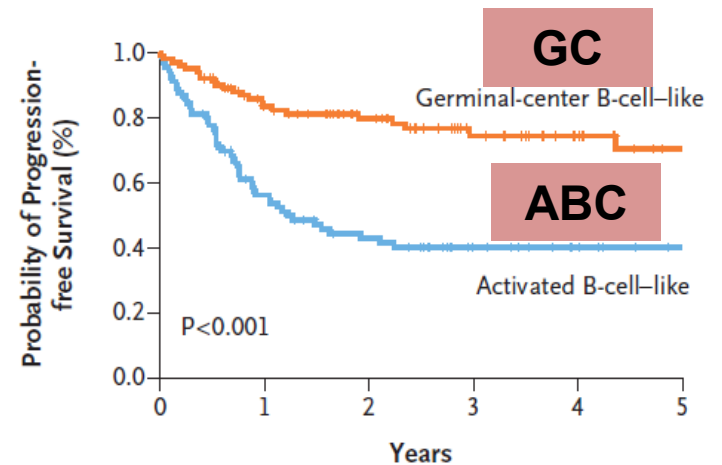
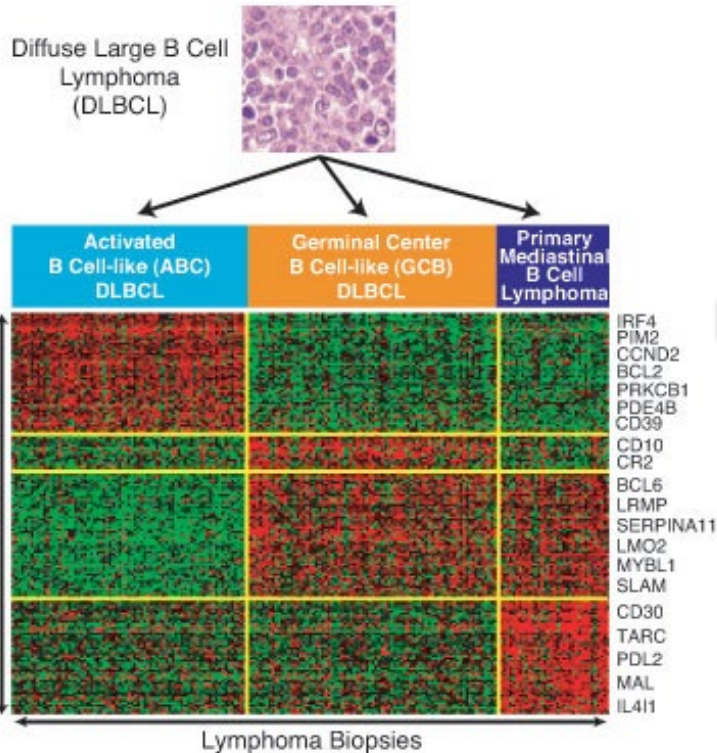
Genomic variants

Gene expression
profiling subtypes

Altered protein
expression

Morphologic variants

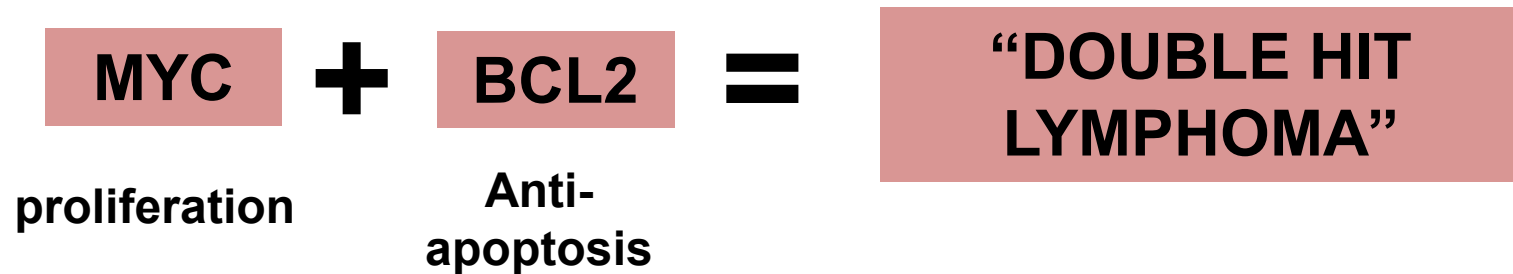
DLBCL is more than one disease



Two molecular subtypes with disparate outcomes

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

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



- ❑ 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"

Initial treatment of aggressive B-cell lymphomas

Diffuse large B-cell lymphoma



R-CHOP x 4-6 cycles

High grade B-cell lymphoma with double/triple hit biology



Intensive chemotherapy (i.e. DA-EPOCH-R)

Burkitt lymphoma

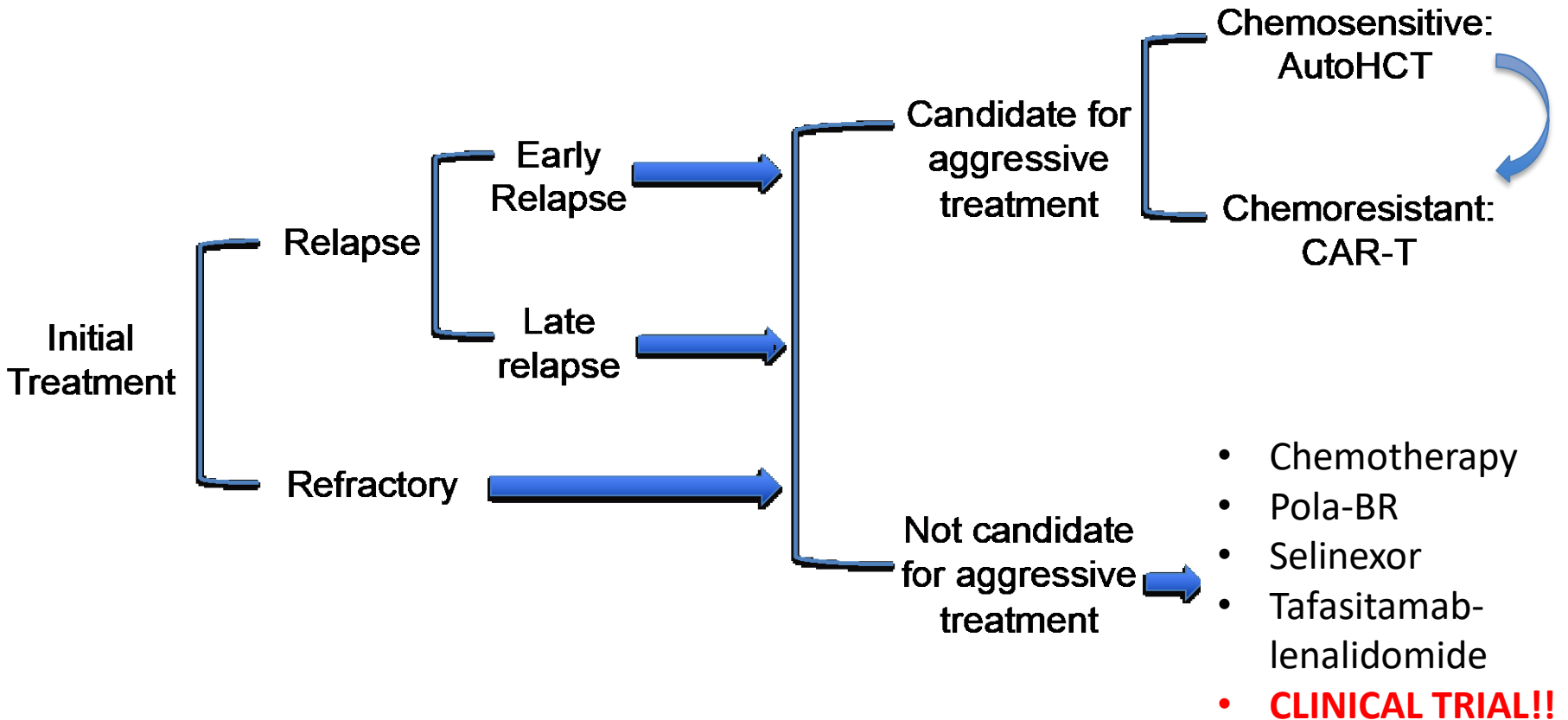


Intensive chemotherapy

Radiation and surgery do not have a role

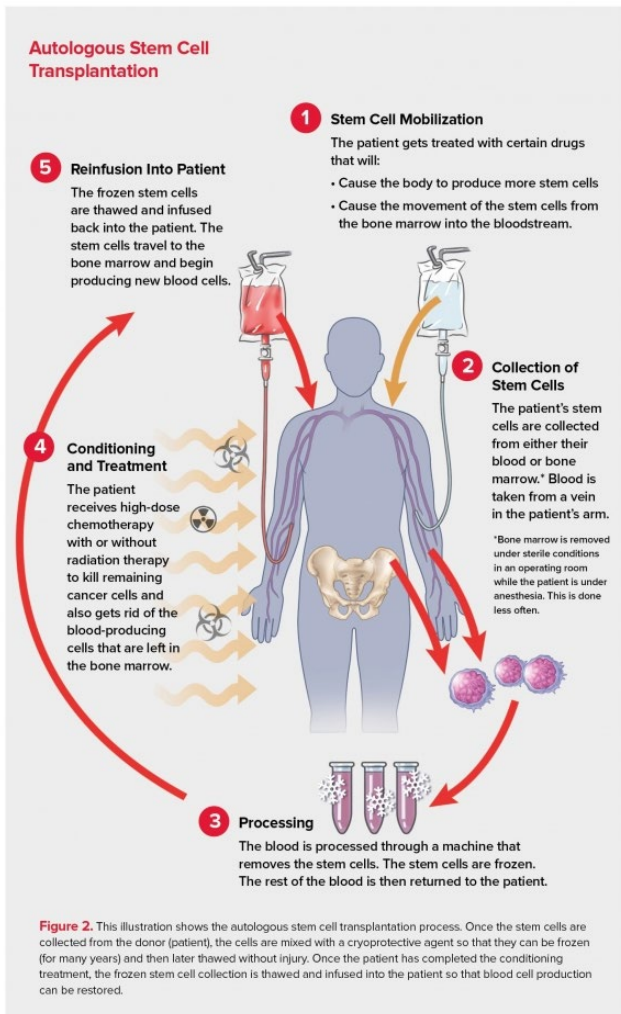
**WHAT IF THE DISEASE DOES NOT
RESPOND OR COMES BACK?**

Treatment considerations in relapsed aggressive B-cell lymphomas



*not FDA-approved

Autologous stem cell transplant



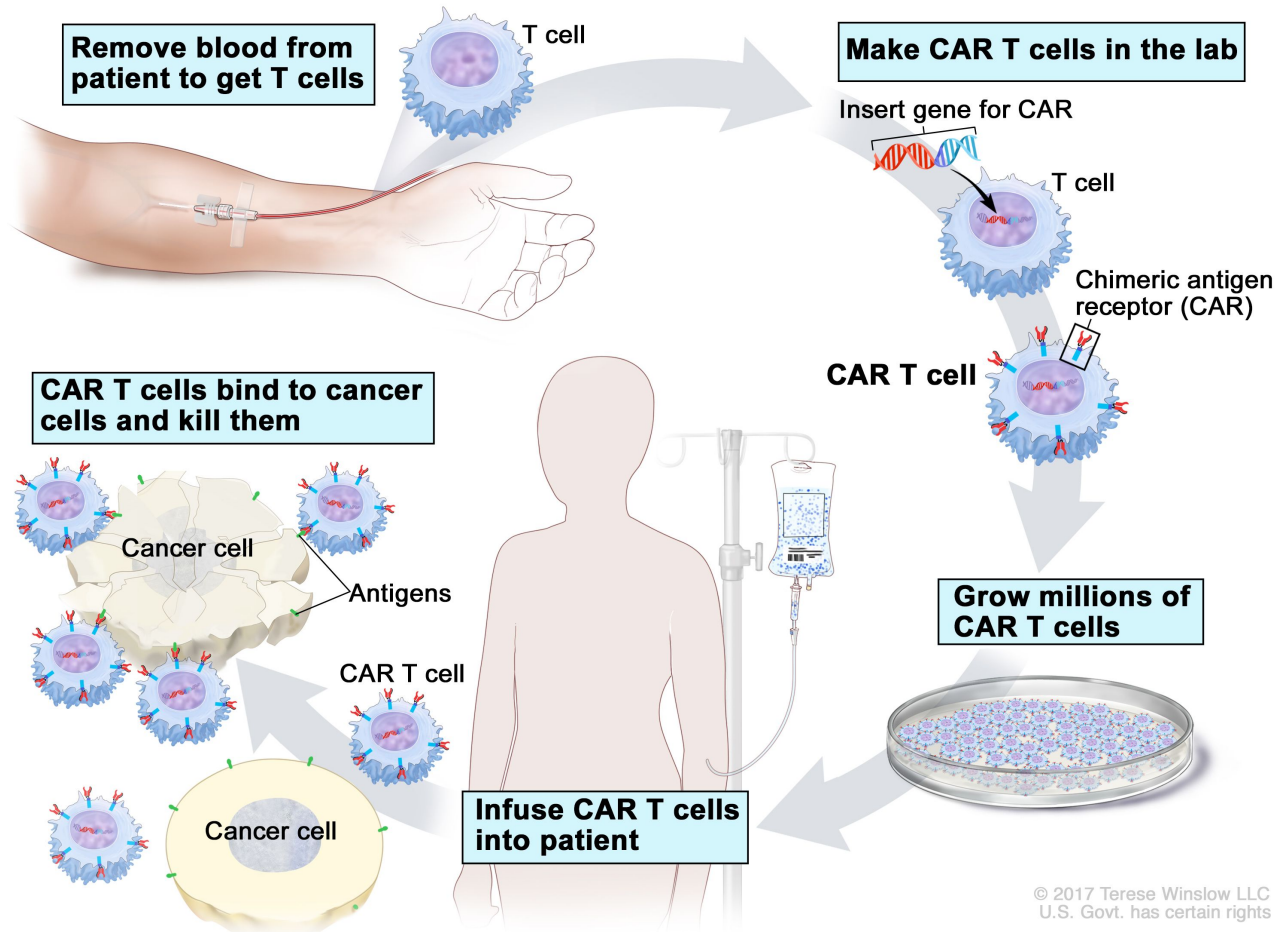
- Autologous stem cell transplant is based on the concept that “more is better”
- There are 4 main parts:
 - “Salvage” chemotherapy
 - Stem cell collection (“mobilization”)
 - Delivery of high dose chemotherapy with autologous stem cell rescue
 - Post transplant recovery and immunizations
- It works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

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

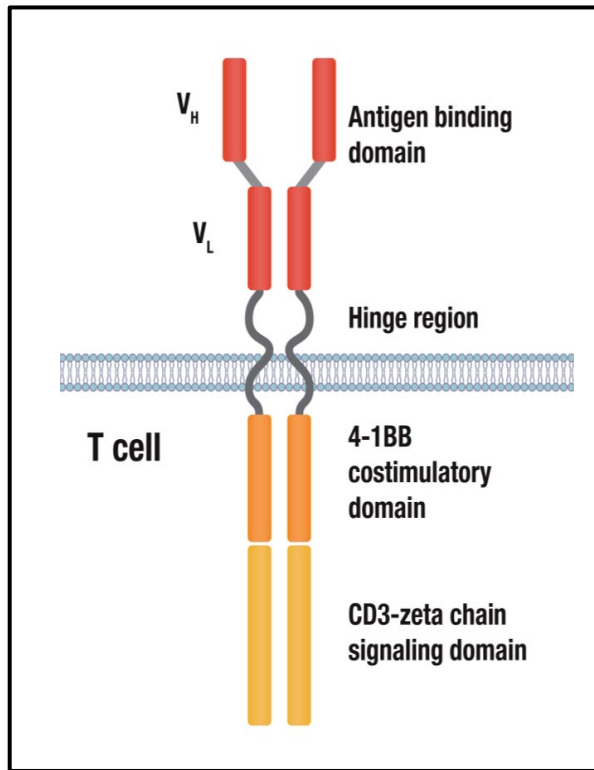
CAR-T cell process

CAR T-cell Therapy

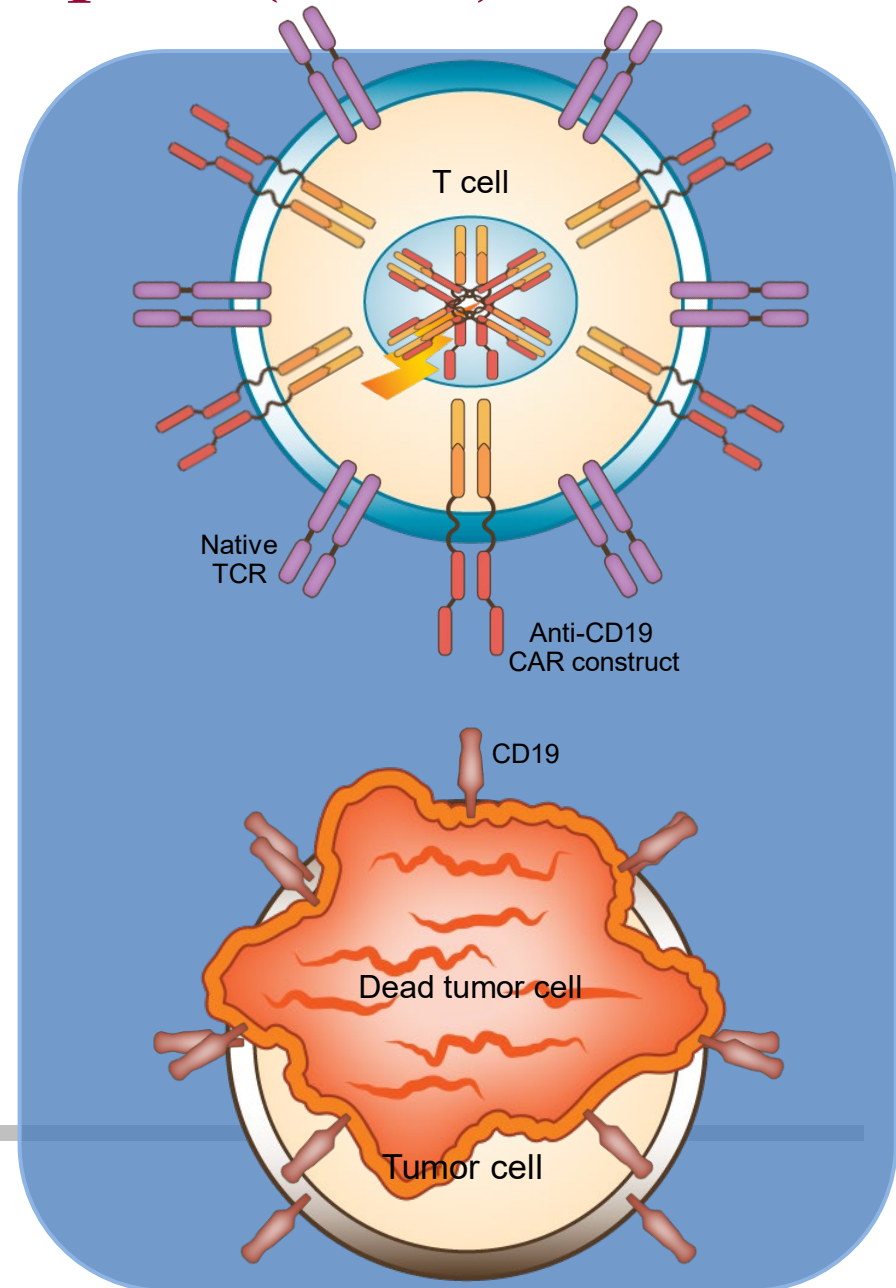


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Chimeric Antigen Receptor (CAR) T-cells



- Uses patients own cells
- Tumor specific
- Can be applied to multiple malignancies



T-CELL LYMPHOMAS

T-cell lymphomas are rare and come in many different flavors

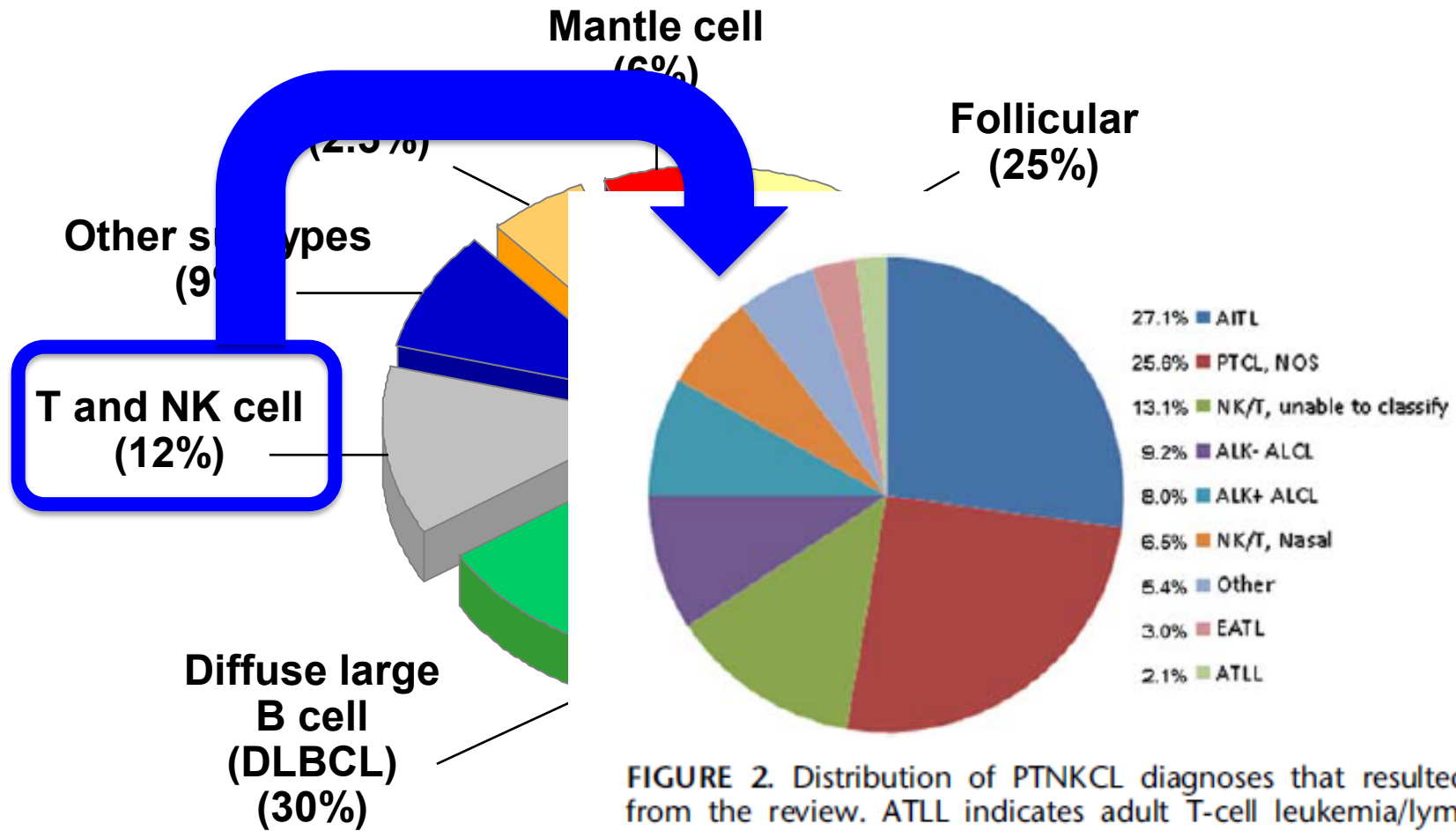


FIGURE 2. Distribution of PTNKCL diagnoses that resulted from the review. ATLL indicates adult T-cell leukemia/lymphoma; EATL, enteropathy-associated T-cell lymphoma.

Initial treatment approach for T-cell lymphomas

CHEMO



Consolidation

*CHOP,
CHOEP,
BV-CHP*



*Autologous
stem cell
transplant*

What if the disease comes back?

- Re-consider stem cell transplant
- Second-line treatment options:
 - CLINICAL TRIAL!!!
 - More chemo (ICE, GVD, Gem-ox)
 - Non-chemo
 - Brentuximab vedotin
 - Romidepsin
 - Pralatrexate
 - Belinostat

Summary: Aggressive Lymphomas

- Lymphomas are a complex family of blood cancers
- A good biopsy is CRITICAL for management
- Treatment usually needs to start quickly
- Many fast growing lymphomas respond to chemotherapy
- There are MANY new treatments that are based on better science

Thank you!



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