



NON-HODGKIN LYMPHOMA: KNOW YOUR SUBTYPE

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LEUKEMIA & LYMPHOMA SOCIETY

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WELCOMING REMARKS


Non-Hodgkin Lymphoma: Know Your Subtype




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The Leukemia & Lymphoma Society

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  **WELCOMING REMARKS**
Non-Hodgkin Lymphoma: Know Your Subtype


 **Lyneshia Johnson- Woodland**
Internet Radio Show Host, Actress and Comedian
NHL Patient since 2020



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  **WELCOMING REMARKS**
Non-Hodgkin Lymphoma: Know Your Subtype

Seattle Genetics: honoraria/consultation fee



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Non-Hodgkin Lymphomas: Know Your Subtype

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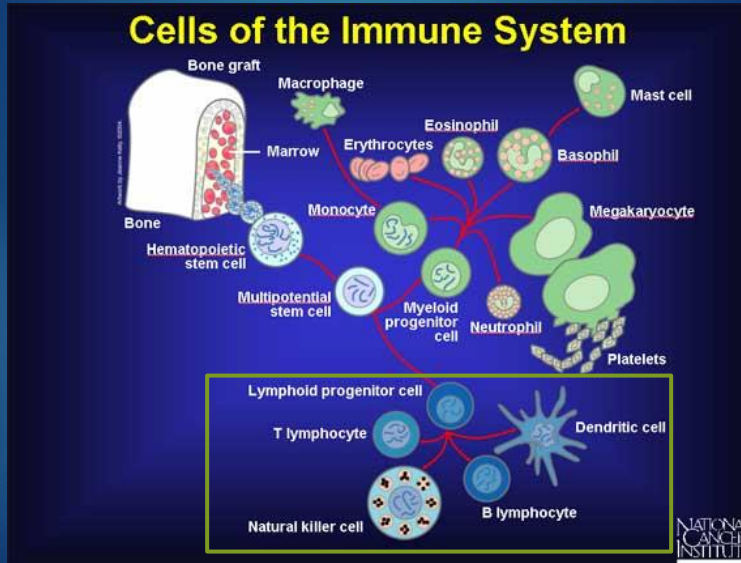
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What are lymphomas?

- Cancers that arise from lymphocytes.
- Lymphocytes are the B-cells, T-cells, and NK cells of your immune system.

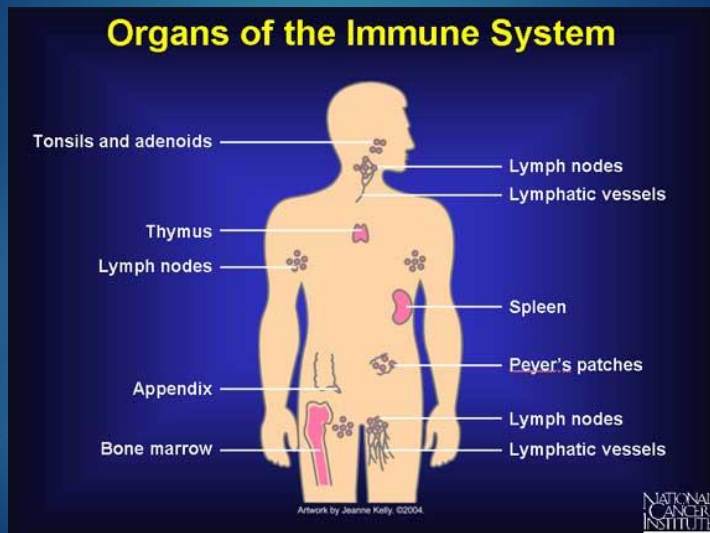
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Lymphocytes



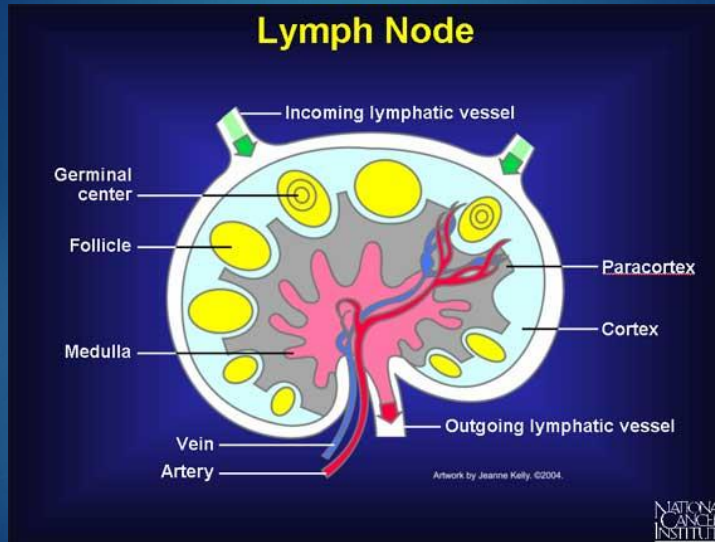
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Immune System



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Lymph Node



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Lymphomas

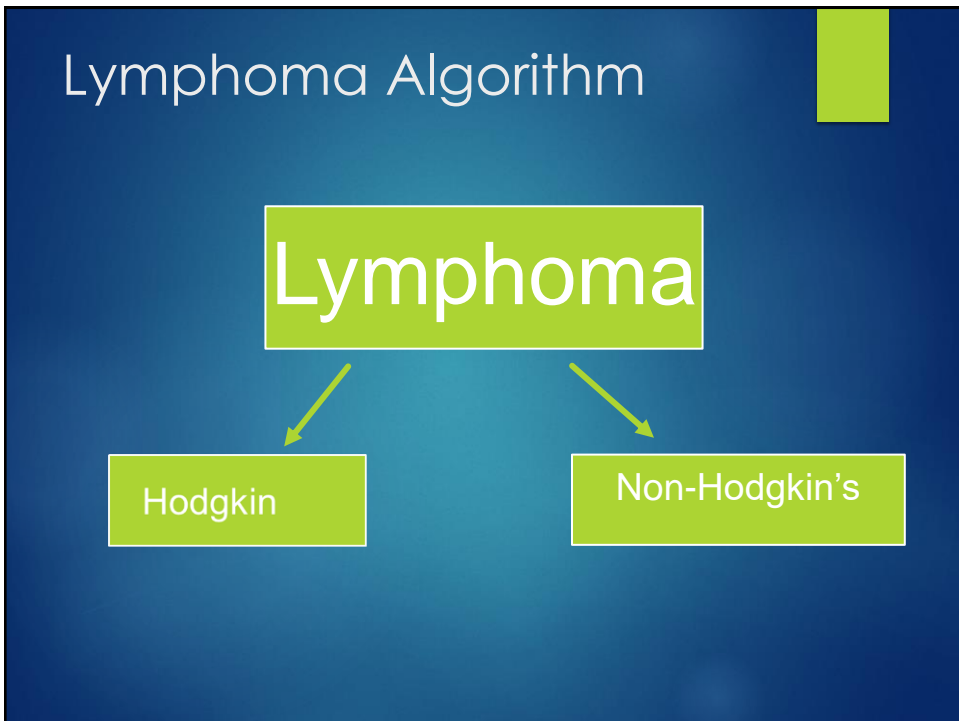
- According to the WHO classification of hematologic malignancies, there are over 50 different types of lymphomas.
- This is due to the variety of cell types that can become a lymphoma.

FOLLICULAR LYMPHOMA GRADE 1-2
Peripheral T cell lymphoma
 Lymphoblastic lymphoma
 Follicular lymphoma grade 3c
 Lymphoplasmacytic lymphoma
 Mantle cell lymphoma
 Marginal zone lymphoma
 Diffuse large B cell lymphoma
Anaplastic large cell lymphoma
BURKITT'S LYMPHOMA
Small lymphocytic lymphoma

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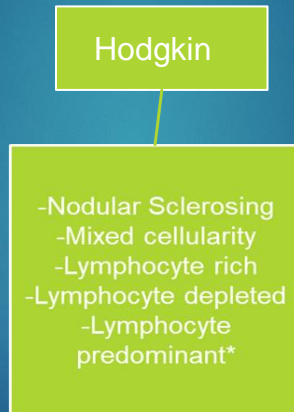


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Lymphoma Algorithm- Hodgkin



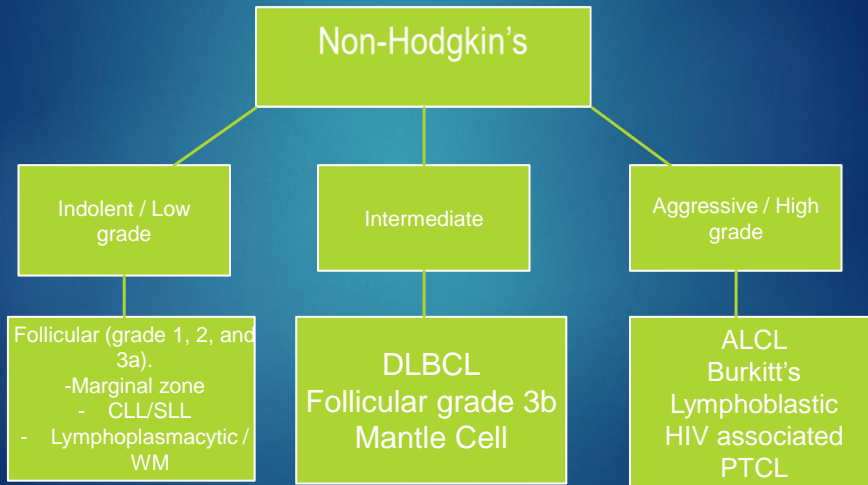
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Hodgkin Lymphoma

- ▶ Cell of origin: B cell
- ▶ Cause: Unknown
- ▶ Distribution:
 - ▶ Accounts for about 10-15% of all lymphomas in the US.
 - ▶ Mainly found in late adolescent / young adults, but a second peak in incidence is seen in people > 55
- ▶ Prognosis: Curable in about 80% of the cases.
- ▶ Treatment: Chemotherapy with a regimen called ABVD

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Lymphoma Algorithm - NHL



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THE GOOD

THE BAD

& THE UGLY

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The Good



- ▶ Low grade follicular lymphomas (grade 1,2, 3A)
- ▶ Marginal zone lymphomas
- ▶ Small lymphocytic lymphoma / CLL
- ▶ Lymphoplasmacytic lymphoma / Waldenstrom's

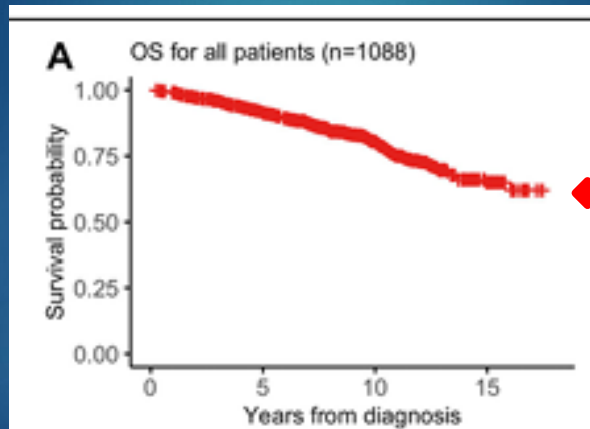
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Why these are good.

- ▶ Very slow growing.
- ▶ People can live with these for years to decades.
- ▶ Some do not require treatment, and they can just be observed.
- ▶ "People die with these, not of these."

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- ▶ Batlevi et al. Blood Cancer Journal 2020.
- ▶ Evaluated 1088 patients with low grade follicular lymphoma.



> 60% still alive at 15 years post diagnosis.

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The Bad

- ▶ Diffuse large B cell lymphoma.
- ▶ Grade 3B follicular lymphoma.
- ▶ Mantle cell lymphoma ***



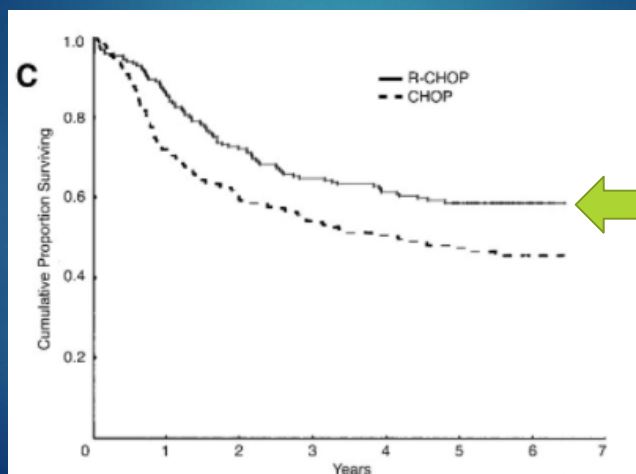
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Why these are bad.

- ▶ Grow quickly
- ▶ Fatal without treatment
- ▶ Can NOT be observed

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- ▶ Some good news: Can be cured in certain cases.
- ▶ Feugier et al. J Clin Oncol. 2005.
- ▶ Results of 399 patients treated with CHOP vs RCHOP. Overall survival.



> 60%
alive at 5
years post
treatment.

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The Ugly

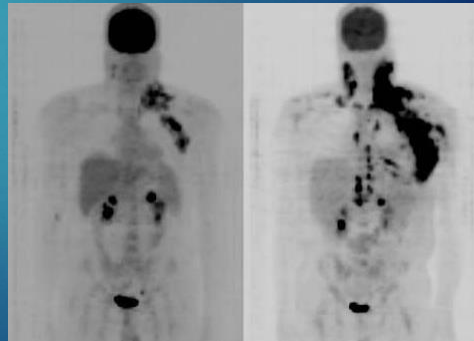
- ▶ Lymphoblastic lymphoma
- ▶ Burkitt's lymphoma
- ▶ Most peripheral T cell lymphomas
- ▶ Anaplastic large cell lymphoma without ALK mutation
- ▶ HIV associated lymphomas
- ▶ Primary central nervous system lymphomas.



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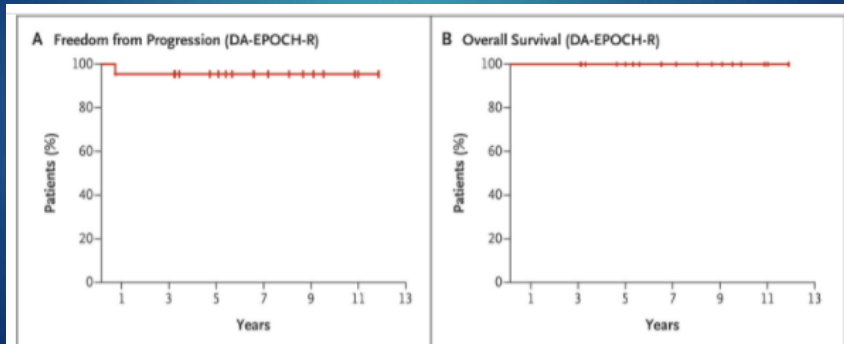
Why these are ugly.

- ▶ Grow extremely quick. Some will double in size within a matter of days.
- ▶ Rapidly fatal without treatment.

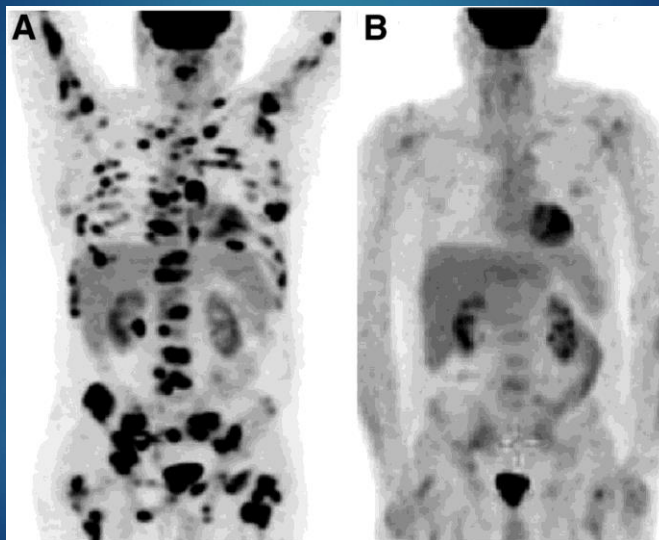


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- ▶ Even though they are extremely aggressive, some can be cured.
- ▶ Dunleavy et al. NEJM. 2013.
- ▶ Evaluated 19 patients with sporadic Burkitt's lymphoma.



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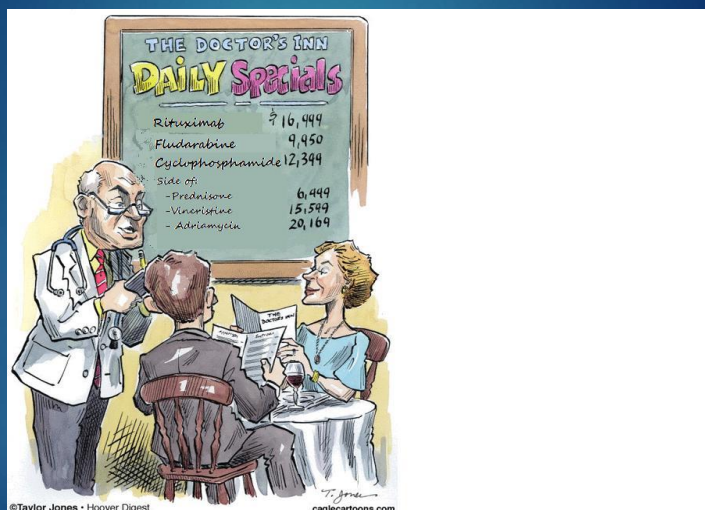


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- Knowing your lymphoma type is important for **prognosis**.
- Knowing your lymphoma type is also important for determining **treatment**.

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Treatment Options



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Chemotherapy

- ▶ Chemicals that kill fast growing cells.
- ▶ Mainly work by attacking some part of the cell process necessary for replication and division (ie copying and splitting of DNA strands).
- ▶ Not specific for any one cell type.

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Chemotherapy

- ▶ Examples:
 - ▶ Cyclophosphamide
 - ▶ Doxorubicin / Daunorubicin
 - ▶ Vincristine
 - ▶ Gemcitabine
 - ▶ Bleomycin
 - ▶ Etoposide
 - ▶ Bendamustine
 - ▶ Etc.

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Chemotherapy

- ▶ Pros:
 - ▶ Very effective at killing cells.
 - ▶ Works well on rapidly growing cells.
- ▶ Cons:
 - ▶ Not specific for cancer cells.
 - ▶ Will also kill other good cells in the body such as blood cells, hair cells, etc.

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Targeted Therapies

- ▶ Monoclonal antibodies
- ▶ Antibody drug conjugates
- ▶ Small molecule inhibitors
 - ▶ Bruton's Tyrosine Kinase (BTK) inhibitors
 - ▶ Phosphatidylinositol 3 kinase (PI3k) inhibitors
 - ▶ BCL2 inhibitors

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Chemotherapy vs Targeted therapy



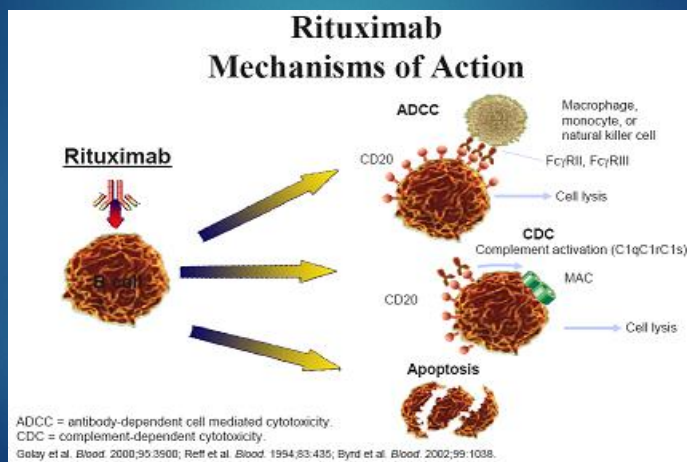
Conventional
Chemotherapy

Targeted
therapy

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Rituximab

- Monoclonal antibody against CD 20.



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Rituximab

- ▶ Only attacks cells that express CD20.
- ▶ If your lymphoma does not express CD20, then this treatment will not work.
- ▶ **Know your type:**
 - ▶ Will not work on T cell lymphomas or Hodgkin lymphomas.
 - ▶ Will work on most B cell lymphomas.

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Tafasitamab (Monjuvi)

- ▶ Monoclonal antibody against a protein called CD19.
- ▶ Will only work on cells that express this protein.
- ▶ CD19 positive lymphomas:
 - ▶ Diffuse large B cell
 - ▶ Follicular lymphoma
 - ▶ Marginal zone lymphoma
 - ▶ Some types of lymphoblastic lymphomas

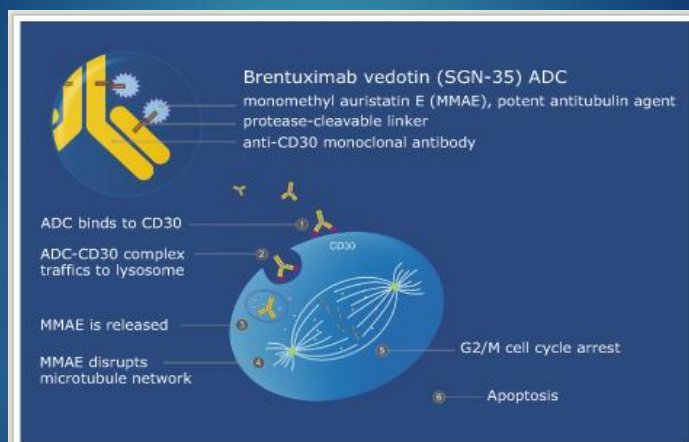
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Antibody Drug Conjugates (ADC)

- ▶ Antibodies that have a poison attached to them.
 - ▶ Brentuximab vedotin
 - ▶ Anti CD30 antibody plus MMAE (poison)
 - ▶ Polatuzumab vedotin
 - ▶ Anti CD79b plus MMAE
 - ▶ Loncastuximab tesirine
 - ▶ Anti CD19 antibody plus SG3199 (poison)

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ADC: Brentuximab vedotin



NCI bulletin December 2014.

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ADCs

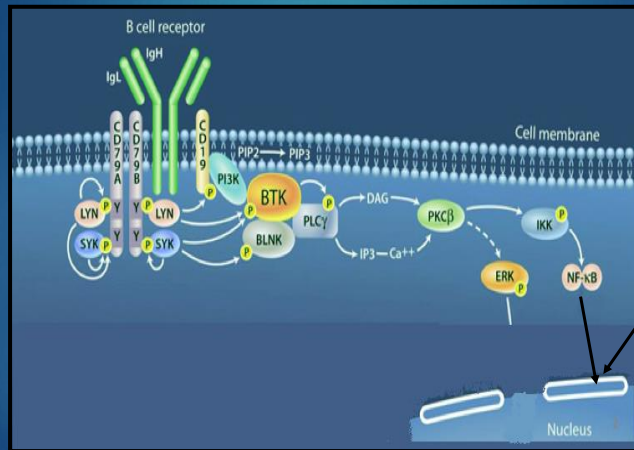
- ▶ Know your lymphoma type!
 - ▶ Brentuximab vedotin
 - ▶ **Only works** on lymphomas that have CD30
 - ▶ Classical Hodgkin Lymphoma
 - ▶ Anaplastic Large Cell Lymphoma
 - ▶ Some types of peripheral and cutaneous T cell lymphomas.
 - ▶ Polatuzumab vedotin
 - ▶ **Only works** on lymphomas that have CD79b
 - ▶ These are mainly your mature B cell lymphomas such as DLBCL and follicular lymphoma.

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Small Molecule Inhibitors/ B-Cell Receptor Inhibitors

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BCR Signaling Pathway



Dr. Susan O'Brien. ASH 2011 oral presentation.

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B cell receptor (BCR) signaling pathway

- BCR signaling is required for lymphoma expansion and proliferation.
- Plays an intricate role in responding to the surrounding supporting cells (microenvironment).
- The BCR signaling pathway is composed of several different elements including kinases.
- Inhibitors of these kinases block signaling which can disrupt cell proliferation and induce cell death.

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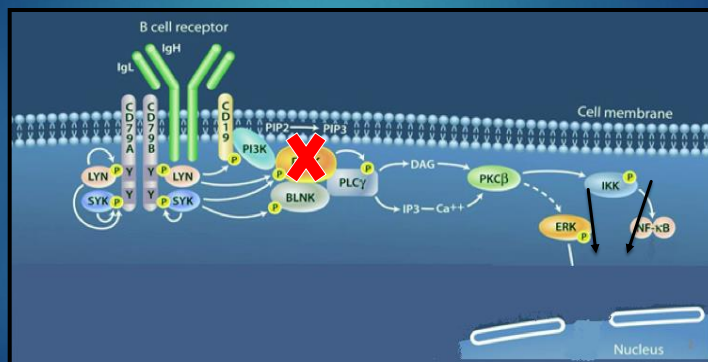
Bruton's Tyrosine Kinase (BTK)

- Primarily expressed in hematopoietic cells.
- Plays a key role in the BCR signaling pathway.
- Thought to also play a role in cell migration.

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Ibrutinib

- Selective BTK inhibitor.



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Ibrutinib

- Commonly used BTK inhibitor in CLL/SLL and mantle cell lymphoma.
- Works in other low grade B cell lymphomas with a specific mutation called MYD88.
- Also works in some types of DLBCL:
 - Study showed results varied based on subtype of DLBCL.
 - Overall response rate of 22% in all patients with DLBCL.
 - Response rate in a subtype called Activated B cell Type (ABC) was around 40%.

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BTK inhibitors

- Other BTKi now available:
 - Acalabrutinib
 - Approved in mantle cell and CLL / SLL.
 - Zanabrutinib
 - Approved for mantle cell, WM, and marginal zone lymphoma.

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Immunotherapy Treatments

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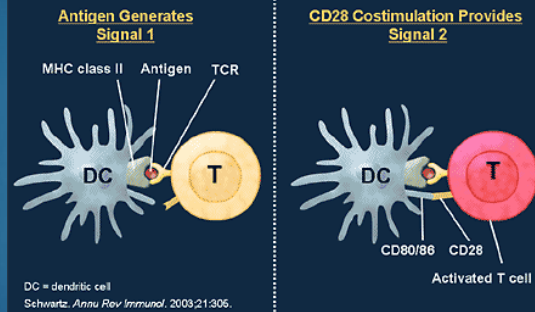
Chimeric Antigen Receptor T cells

- Also known as CAR T-cell therapy.
- They are T cells obtained from the patient that are genetically modified to recognize a specific protein on the lymphoma cells.
- The T cells are also engineered to be more efficient “killers”.

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CAR T cell therapy cont.

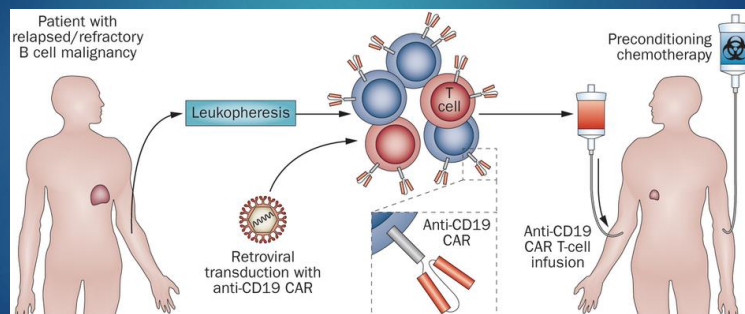
T Cell Activation Requires 2 Signals



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CAR T cell cont.

Treatment regimen done per the following diagram (DLBCL example):



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CAR T cell cont.

- ▶ Current FDA approved CAR T cell products in the US:
 - ▶ Brexucabtagene Autoleucel (Tecartus)
 - ▶ Anti CD19 CAR T cell approved for mantle cell.
 - ▶ Axicabtagene Ciloleucel (Yescarta)
 - ▶ Anti CD19 CAR T cell
 - ▶ Approved for DLBCL and Follicular lymphoma
 - ▶ Tisagenlecleucel (Kymriah)
 - ▶ Anti CD19 CAR T cell
 - ▶ Approved for DLBCL and certain types of lymphoblastic lymphoma / leukemia (ALL)
 - ▶ Lisocabtagene maraleucel (Breyanzi)
 - ▶ Anti CD19 CAR T cell approved for DLBCL

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Summary

- ▶ COMMUNICATION is KEY!
- ▶ Lymphoma is not just one type of cancer.
- ▶ There are over 50 different types of NHL defined in the WHO classification of hematologic malignancies.
- ▶ Diffuse large B cell is the most common type of intermediate / aggressive NHL.
- ▶ The type of lymphoma is important for prognosis and for guiding treatment.

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The Benefits of Discussing Quality of Life Concerns with Your Healthcare Team

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No Two People Are the Same

- ▶ Our likes and dislikes differ.



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Quality of Life Concerns

- ▶ In the aggressive diseases, QoL is not so much an issue.
- ▶ In the slow growing diseases, QoL becomes more of an issue.
 - ▶ Treatment duration
 - ▶ Treatment location
 - ▶ Transportation issues
 - ▶ Cost

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*"Age is an issue of
Mind over Matter.
If you don't mind,
it doesn't matter."
~Mark Twain*

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WELCOMING REMARKS

Non-Hodgkin Lymphoma: Know Your Subtype

- **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.



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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



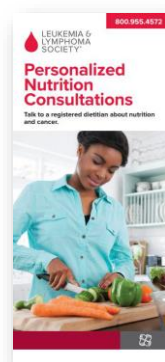
Email: www.LLS.org/ContactUs
All email messages are answered within one business day.



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




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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.

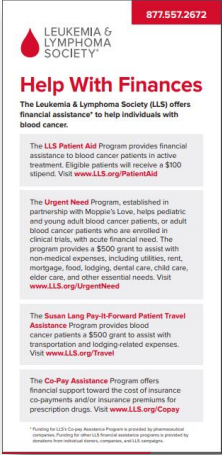


Patient Podcast

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.



LLS EDUCATION & SUPPORT RESOURCES




Help With Finances

The Leukemia & Lymphoma Society (LLS) offers financial assistance* to help individuals with blood cancer:

- The LLS Patient Aid Program** provides financial assistance to blood cancer patients in active treatment. Eligible patients will receive a \$100 stipend. Visit www.LLS.org/PatientAid
- The Urgent Need Program**, established in partnership with Maggie's Lives, helps pediatric and young adult blood cancer patients, or adult blood cancer patients who are enrolled in clinical trials, with acute financial need. The program provides a \$500 grant to assist with non-medical expenses, including utilities, rent, mortgage, food, lodging, dental care, child care, elder care, and other essential needs. Visit www.LLS.org/UrgentNeed
- The Susan Lang Pay-It-Forward Patient Travel Assistance Program** provides blood cancer patients a \$500 grant to assist with transportation and lodging related expenses. Visit www.LLS.org/Travel
- The Co-Pay Assistance Program** offers financial support toward the cost of insurance co-payments and/or insurance premiums for prescription drugs. Visit www.LLS.org/Copay

*Funding for LLS Co-pay Assistance Program is provided by pharmaceutical companies. Funding for other LLS financial assistance programs is provided by donations from individual donors, companies, and LLS campaigns.

The Leukemia & Lymphoma Society (LLS) offers the following financial assistance programs to help individuals with blood cancer: www.LLS.org/Finances



To order free materials: www.LLS.org/Booklets

