Disclosures

• I have no conflicts of interest to disclose
Outline

• Lymphoma Overview

• Treatment options

• Research updates

• Question & Answer session
What is lymphoma?

• Lymphomas are cancers of cells called lymphocytes.

• Cancer is uncontrolled growth of clones of one type of cell.

• Lymphocytes are blood cells that are a part of the immune system.
How do patients present with lymphoma?

Abnormal labs such as blood counts
Abnormal scans
How/why do patients get lymphoma?

• NHL is the most common blood-related cancer and the 7th most common cancer in the US
• Most frequently diagnosed among ages 65-74

• Most patients have no clear risk factor or known cause of lymphoma

• Possible risk factors:
  • Viruses like EBV, HTLV-I, hepatitis C
  • Bacteria like H. pylori, Campylobacter, Chlamydia psittaci
  • Immunodeficiency induced or acquired (organ transplant, HIV), or congenital
  • Immune dysregulation like lupus, rheumatoid arthritis
  • Exposure to chemicals
  • Usually not transmitted genetically (in families)
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
  - Heavy-chain disease
  - Heavy-chain disease
- Monoclonal gammopathy of undetermined significance (MGUS), IgG/A
- Plasma cell myeloma
- Solitary plasmacytoma of bone
- Extramedullary plasmacytoma
- Monoclonal immunoglobulin deposition diseases
- Extramedullary 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
- B-cell-type follicular lymphoma
- Large B-cell lymphoma with t(14;18) 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/Hodgkin-type 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 t(15;17) rearrangement
- 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
- Hydoa vaiceformae-like lymphoproliferative disorder
- Adult T-cell leukemia/lymphoma
- Extramedullary 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 panlicular-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 alveolar CD8+ “T-cell lymphoma”
- Primary cutaneous CD4+ small/multinucleated 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

2016 WHO classification includes >70 types of lymphoma
What do you need to know about your lymphoma?

• Is it a Non-Hodgkin or Hodgkin lymphoma?

• Is it a B-cell or T-cell lymphoma?

• Is it aggressive (fast growing) or indolent (slow growing)?

• It may be helpful to know:
  What is the stage?
  Do I need treatment?
    If yes:
    • What is the goal of treatment?
    • What are the treatment options?
    If no:
    What symptoms do I need to watch for?
Lymphoma diagnostic work up

- **Biopsy:** Surgical excision, Core needle biopsy
- **Pathology:** Immunohistochemistry (stains), flow cytometry, gene rearrangements, FISH, PCR
- **Labs:** CBC, electrolytes, kidney and liver function, lactate dehydrogenase (LDH)
- **Procedures:** Bone marrow biopsy, lumbar puncture (in specific cases)
- **Imaging:** PET scans or CT scans or MRI (brain)
Staging of lymphoma: different from other cancers

Ann Arbor staging further classifies patients with lymphoma into A or B categories:
- **A** = without symptoms
- **B** = with symptoms including unexplained weight loss (10% in 6 months prior to diagnosis, unexplained fever, and drenching night sweats.)

**Stage I** - disease in single lymph node or lymph node region.

**Stage II** - disease in two or more lymph node regions on same side of diaphragm.

*Note*: Stage II contiguous means two or more lymph nodes in close proximity (side by side)

**Stage III** - disease in lymph node regions on both sides of the diaphragm are affected.

**Stage IV** - disease is wide spread, including multiple involvement at one or more extranodal (beyond the lymph node) sites, such as the bone marrow.
Lymphoma: Treatment planning

• Factors that determine treatment choice and goal:
  • Type of lymphoma
  • Grade or expected growth rate
  • Stage
  • Specific features of the lymphoma
  • Previous therapies and their outcomes
  • Age and other medical problems

• Pre-treatment testing may include: ECHO, PFT (lung function), fertility preservation
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• Can you predict disease course or treatment outcome?
  • Using above factors, discuss risk vs benefit from treatment
  • May use tools called prognostic calculators (IPI, FLIPI, IPS, CLL-IPI and many others) to categorize your disease as high, intermediate or low risk
Lymphoma: Treatment options

- **Surgery**: Used primarily for diagnosis

- **Radiation**: For “local” control

- **Systemic therapy is the mainstay**: single agent or combination of immuno-chemotherapy or targeted agents
  - Most commonly used chemo: RCHOP for DLBCL; BR for FL/indolent; ABVD for HL

- Observation or “watchful waiting” may be appropriate in indolent lymphomas
**Commonly used medical terminology**

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<td>Remission</td>
<td>Response to treatment, can be complete (CR) or partial (PR)</td>
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<td>Relapse</td>
<td>Disease comes back after achieving remission</td>
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<tr>
<td>Refractory</td>
<td>Disease did not respond adequately to treatment</td>
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Potential side-effects of treatment

Short-term:

• Low blood counts - transfusions
• Infection risk due to low neutrophils - growth factors, antibiotics
• Hair loss
• Nausea - antiemetics
• Neuropathy - tingling or numbness of fingers or toes
• Fatigue

Long-term:

• Fertility issues
• Risk of heart and lung disease (specific drugs)
• Risk of secondary cancers
What to expect during and after treatment?

• Regular visits to see your treatment team to assess and treat side-effects
• PET or CT scans to assess response 6-8 weeks after the end of treatment

• If you’re in complete remission:
  • Visit/labs every 3 months x 2 years then less frequent to assess for signs of disease and long term side effects
  • Scans are usually NOT done for surveillance in aggressive lymphomas
  • Maintenance therapy could be recommended for some lymphoma types
Relapsed/Refractory lymphoma: What are the options?

• **Next line of therapy**: different chemo, targeted agent

• **Clinical trial**

• **Autologous stem cell transplant** using patient’s *own* stem cells

• **Chimeric-antigen T-cell therapy (CAR-T)** for DLBCL, PMBCL, mantle cell

• **Allogeneic stem cell transplant** using another person’s *(donor)* stem cells (less common for lymphomas)
Autologous Stem Cell Transplant: Procedure Overview

- Stem cells may be purged
- Stem cells are cryopreserved
- Marrow harvesting
- High-dose chemotherapy and/or radiation conditioning regimen
- Stem cells thawed
- Stem cells re-infused
Chimeric Antigen Receptor T cells (CAR-T)

Tran E, Longo DL, Urba WJ. NEJM, 2017
**Are clinical trials an option?** Always ask your doctor!

A clinical trial is carefully controlled research study conducted by doctors to

- Improve treatment options
- Increase survival
- Improve quality of life

Designed to give patients the safest, potentially most effective therapies
New treatment options FDA approved after clinical trials!

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<th>Type</th>
<th>Treatments</th>
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<td>CLL/SLL</td>
<td>Ibrutinib, Acalabrutinib, Venetoclax, Obinutuzumab, Duvelisib</td>
</tr>
<tr>
<td>DLBCL</td>
<td>CAR-T, Polatuzumab vedotin, Tafasitamab+lenalidomide, selinexor</td>
</tr>
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<td>Hodgkin</td>
<td>Brentuximab vedotin, Nivolumab, Pembrolizumab</td>
</tr>
<tr>
<td>Follicular</td>
<td>Tazemetostat, lenalidomide, duvelisib</td>
</tr>
<tr>
<td>Mantle cell</td>
<td>CAR-T, Zanubrutinib, Acalabrutinib, Ibrutinib</td>
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<tr>
<td>Marginal zone</td>
<td>Lenalidomide</td>
</tr>
<tr>
<td>T-cell lymphoma</td>
<td>Brentuximab vedotin, Mogamulizumab</td>
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Clinical trials available at UWCCC Madison WI
For more information call UW Carbone Cancer Connect at (608) 262-5223 or (800) 622-8922

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<th>Relapsed/refractory disease</th>
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<tr>
<td><strong>CLL</strong></td>
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<td>Ibrutinib plus Obinutuzumab versus Ibrutinib plus Venetoclax and Obinutuzumab in</td>
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</table>
  • Untreated Older Patients (≥70) with CLL [A041702] |
  • Untreated Younger patients with CLL [EA9161] | Many Phase 1 studies with novel agents |
| **DLBCL**            |                             |
| Enzastaurin Plus R-CHOP Versus R-CHOP in High-Risk Diffuse Large B-Cell Lymphoma | Tisagenlecleucel (CART) versus standard of care in adult patients with relapsed or refractory aggressive B-cell non-Hodgkin lymphoma [BELINDA] |
| **Follicular lymphoma** |                             |
| Venetoclax in Combination with Obinutuzumab and Bendamustine in Patient with High Tumor Burden FL [FrE0403] | Randomized Phase II Trial in Early Relapsing or Refractory Follicular Lymphoma [S1826] |
| **Mantle cell lymphoma** |                             |
| Bendamustine, Rituximab and High Dose Cytarabine (BR/CR) vs BR/CR-Acalabrutinib vs BR-Acalabrutinib in Patients ≤70 yrs [EA4181] | A Phase I/II Study of Ixazomib and Ibrutinib in Relapsed/Refractory Mantle Cell Lymphoma |
| Consolidation with ASCT Followed by Maintenance Cell Rituximab vs. Maintenance Rituximab Alone for Patients in MRD negative CR1 [EA4151] | Many Phase 1 studies with novel agents |
| Bendamustine + Obinutuzumab Induction Chemoimmunotherapy with Risk-Adapted Obinutuzumab Maintenance Therapy |                             |
| **Hodgkin lymphoma** |                             |
| Nivolumab Plus AVD or Brentuximab Vedotin Plus AVD in Patients (Age ≥12 Years) with Advanced Stage Classical Hodgkin Lymphoma [S1826] | Phase I Study of Nivolumab in Combination with Ruxolitinib in Relapsed or Refractory Classical Hodgkin Lymphoma |
| Brentuximab Vedotin in Front-line Therapy of HL and CD30-expressing Peripheral T-cell Lymphoma (PTCL) in Adults Age 60 and Above |                             |
| **T-cell lymphoma** |                             |
| Brentuximab Vedotin in Front-line Therapy of HL and CD30-expressing Peripheral T-cell Lymphoma (PTCL) in Adults Age 60 and Above | Phase 1 studies with novel agents |
Lymphoma patients are living longer! 😊

New cases come from SEER 9. Deaths come from U.S. Mortality. All Races, Both Sexes. Rates are Age-Adjusted.
Survivorship: Living with and beyond lymphoma

• Be aware that lymphoma and it’s treatments can cause long term complications

• What can I do to prevent my lymphoma from coming back/progressing?
  • There are some things you cannot control like disease biology

• There are some things you can!
  • Eat healthy balanced diet, try to maintain a healthy weight (BMI)
  • Stop smoking
  • Minimize alcohol use

• Exercise! [www.exerciseismedicine.org/movethruca](http://www.exerciseismedicine.org/movethruca)

  Moderate-intensity aerobic activity at least 3 times per week, for at least 30 min
  + Resistance training at least 2 times per week, using at least 2 sets of 8 - 15 repetitions
Lymphoma and COVID19

• Am I at a higher risk of getting sick?
  • Limited data suggest that cancer patients MAY be at higher risk but no specific data in lymphoma.

• What can I do to prevent illness?
  • Practice social distancing, hand washing, wear a mask in public spaces

• Should I start/continue my lymphoma treatment?
  • Please DO NOT make changes to your treatment without discussing with your treating physician
  • Discuss your specific concerns with your lymphoma provider- each circumstance may be different
  • DO NOT delay emergency care or if you are directed to a ED or clinic

• How is care different in the COVID era?
  • Telemedicine
  • Most lymphoma care is necessary and ongoing
Thank you!

Questions/Comments

@priyankapophali