

Lymphoma

Updates and Treatment Options

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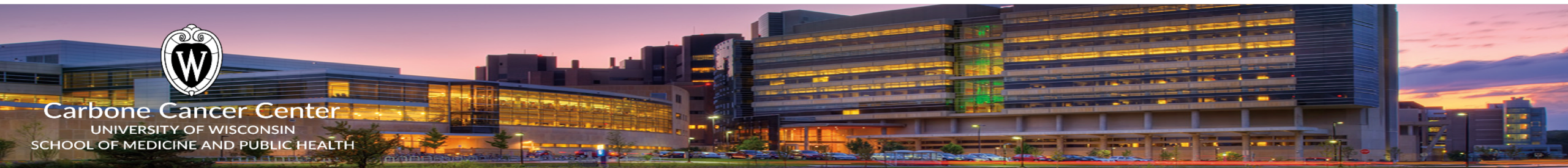
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Disclosures

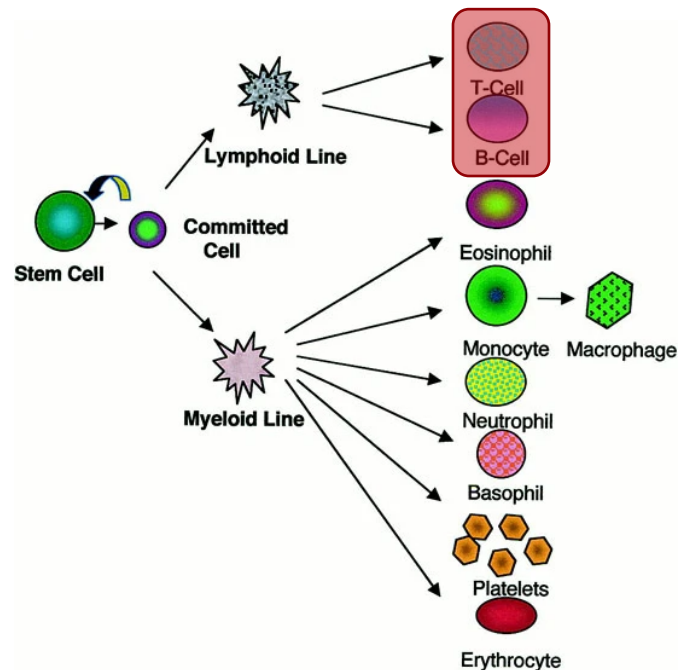
- I have no conflicts of interest to disclose

Outline

- Lymphoma Overview
- Treatment options
- Research updates
- Question & Answer session

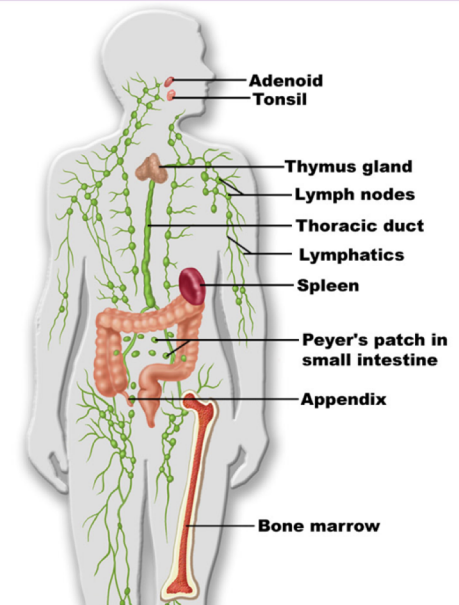
What is lymphoma?

- 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.

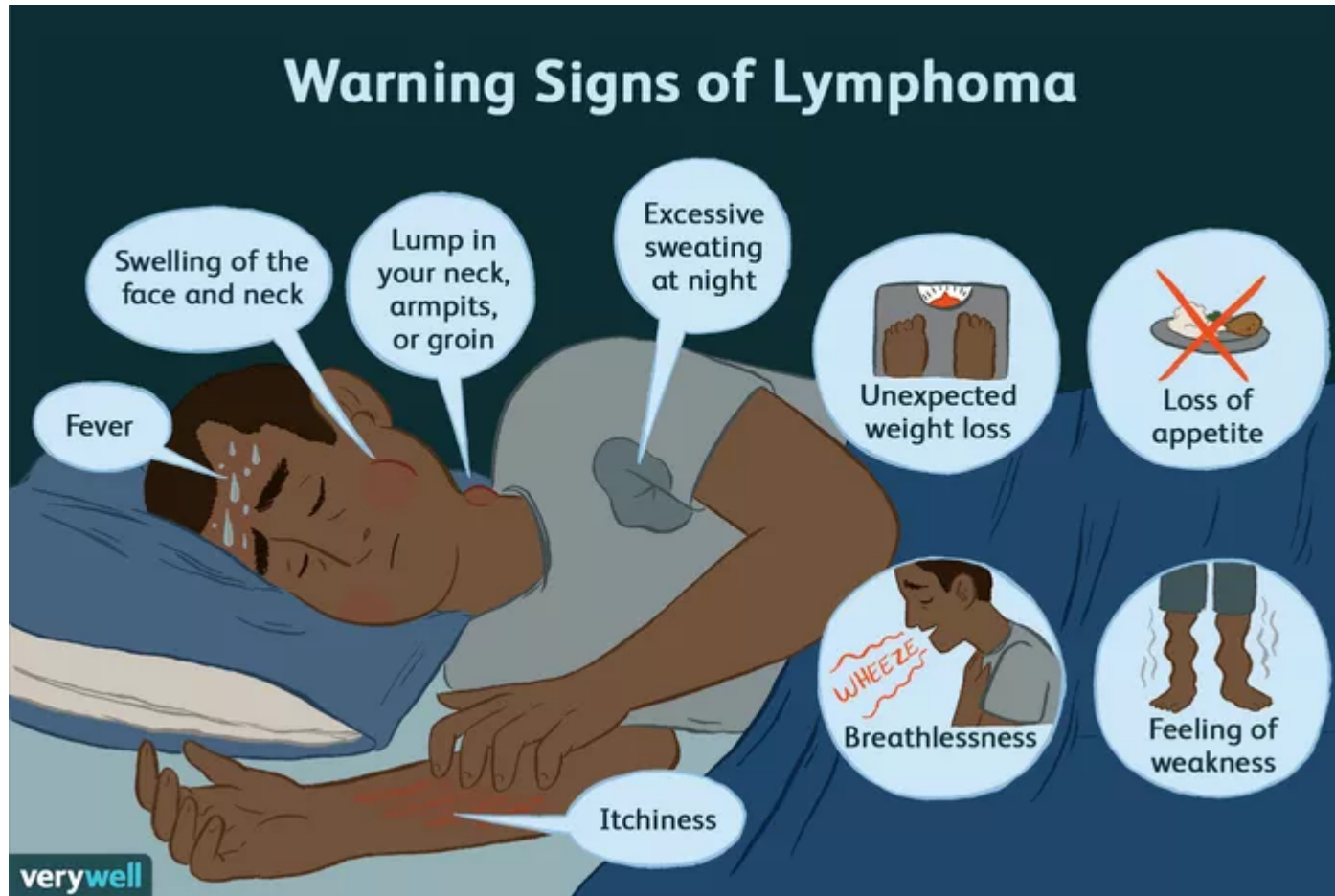


Lymphatic System

- **Lymphocytes**
- **Lymphoid organs**
 - Primary
 - Bone marrow
 - Thymus
 - Secondary
 - Lymph nodes
 - Spleen
 - Tonsils, adenoids, (Waldeyer's ring)
 - GI and respiratory tract (MALT)



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*

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

2016 WHO classification includes >70 types of 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

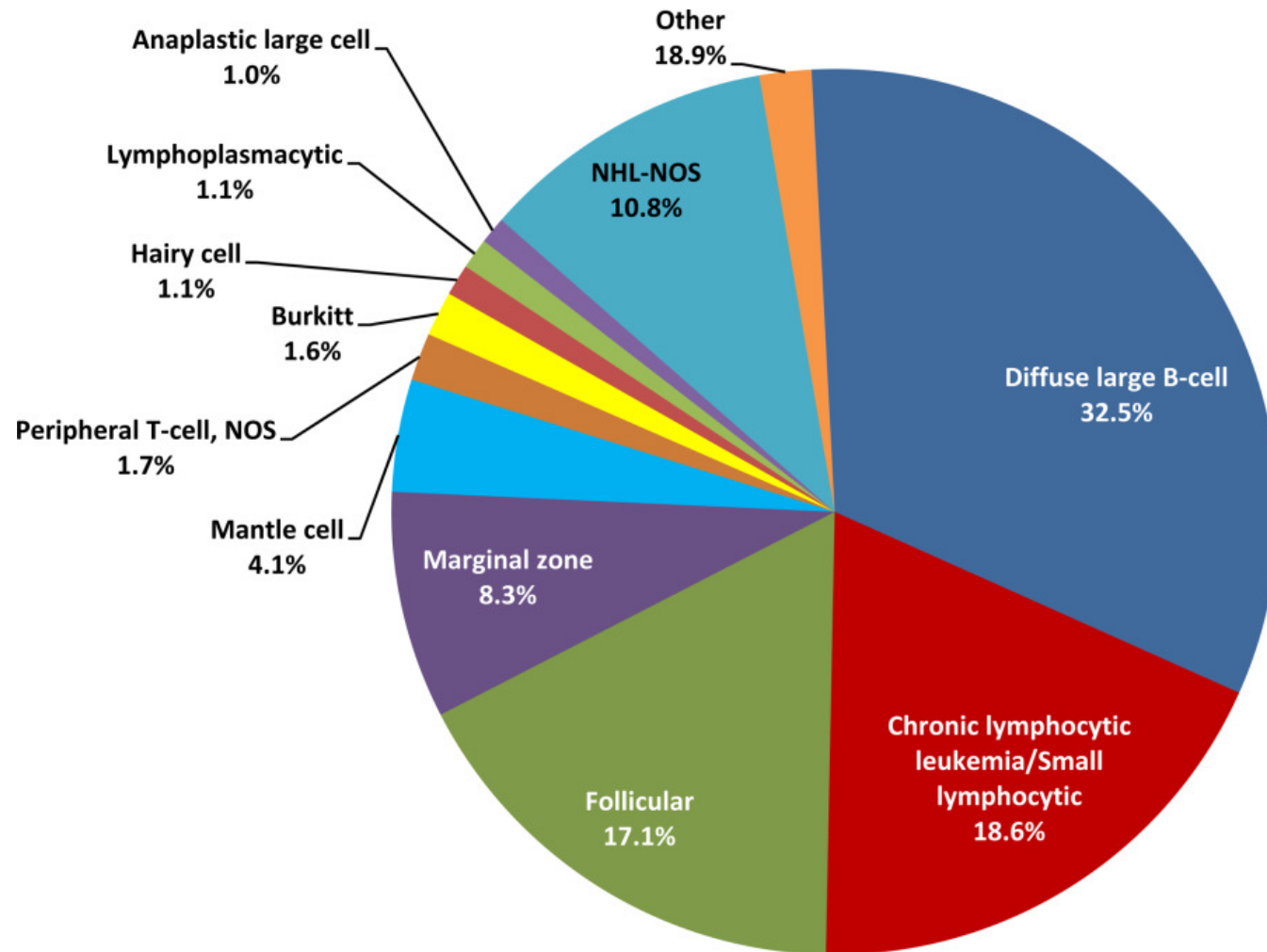
Nodular sclerosis classical Hodgkin lymphoma

Lymphocyte-rich classical Hodgkin lymphoma

Mixed cellularity classical Hodgkin lymphoma

Lymphocyte-depleted classical Hodgkin lymphoma

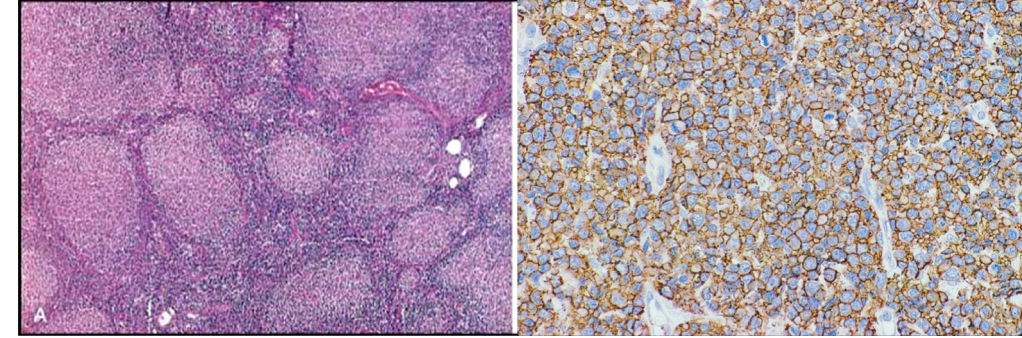
Non-Hodgkin lymphoma subtype distribution in the US: 1998 to 2011



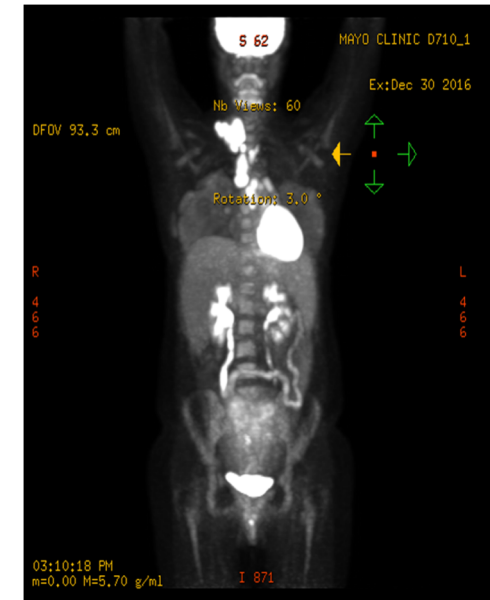
What do *you* need to know about *your lymphoma*?

- 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?

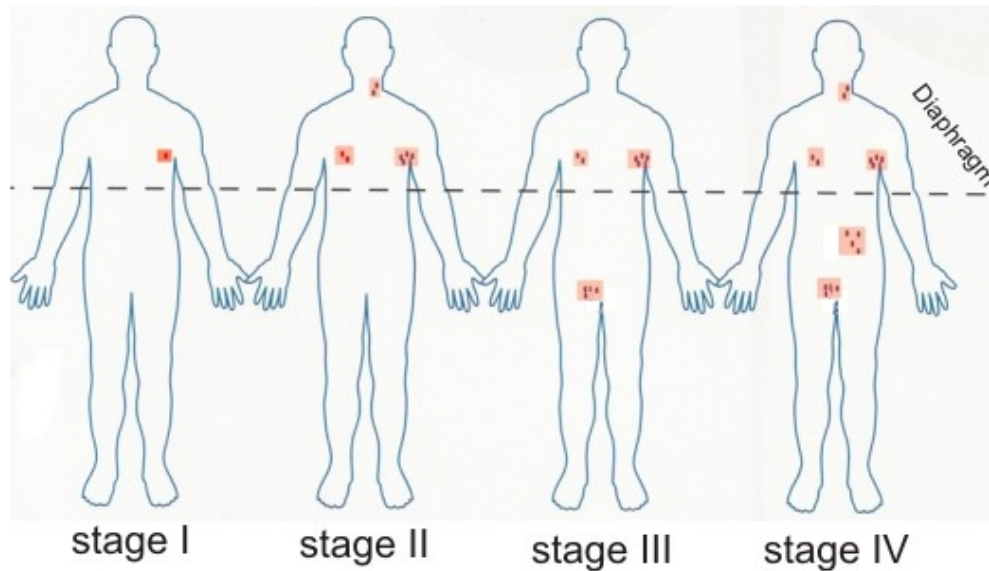
Lymphoma diagnostic work up



- **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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- Pre-treatment testing may include: ECHO, PFT (lung function), fertility preservation
- 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

Chemo-immunotherapy	Chemotherapy combined with a monoclonal antibody e.g. Rituximab
Targeted agents	Newer drugs that work differently than traditional chemotherapy by blocking/modulating a specific target on the cancer cell

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Remission	Response to treatment, can be complete (CR) or partial (PR)
Relapse	Disease comes back after achieving remission
Refractory	Disease did not respond adequately to treatment

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

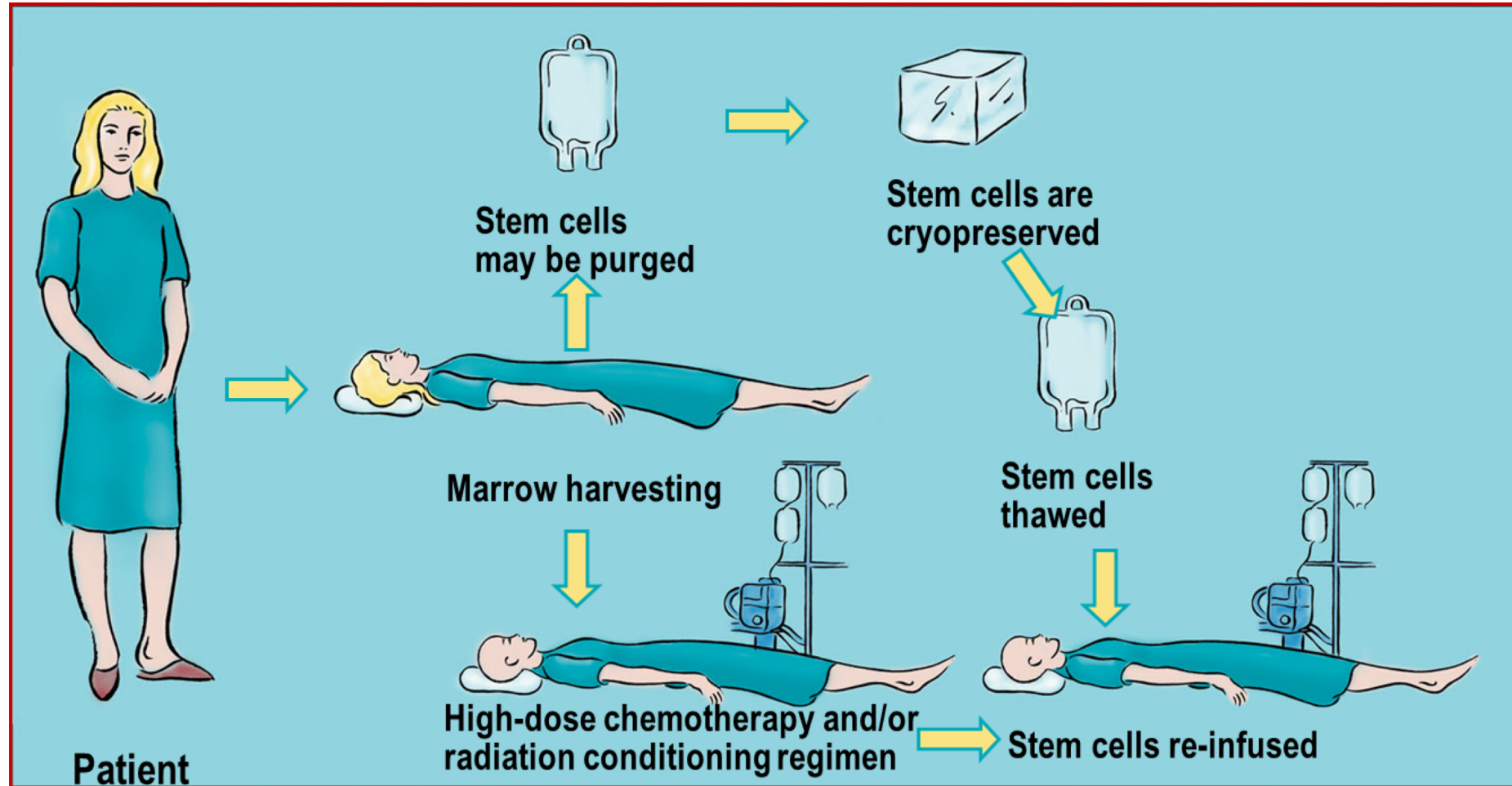
What to expect during and after treatment?

- 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

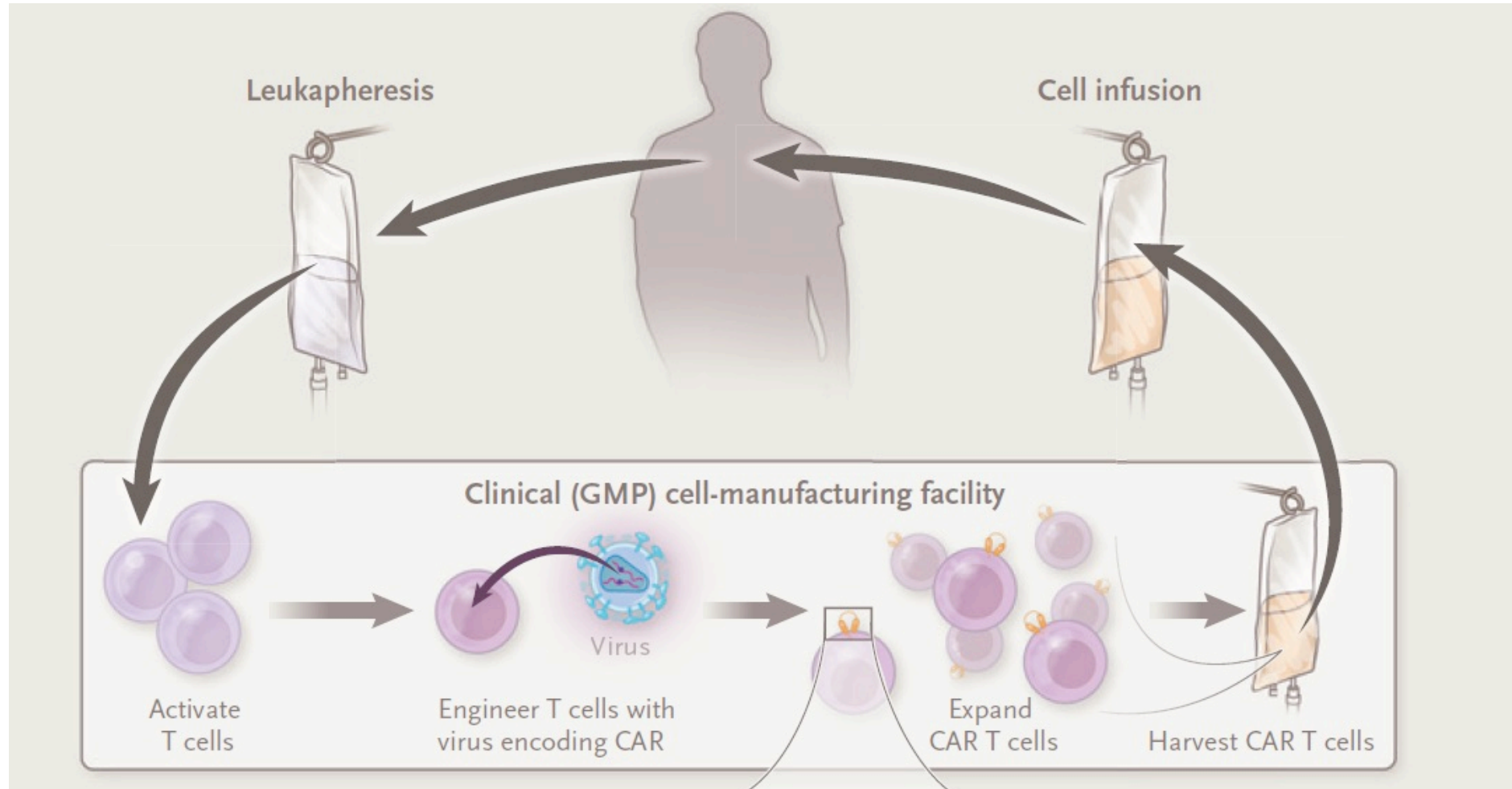
Relapsed/Refractory lymphoma: What are the options?

- **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



Chimeric Antigen Receptor T cells (CAR-T)

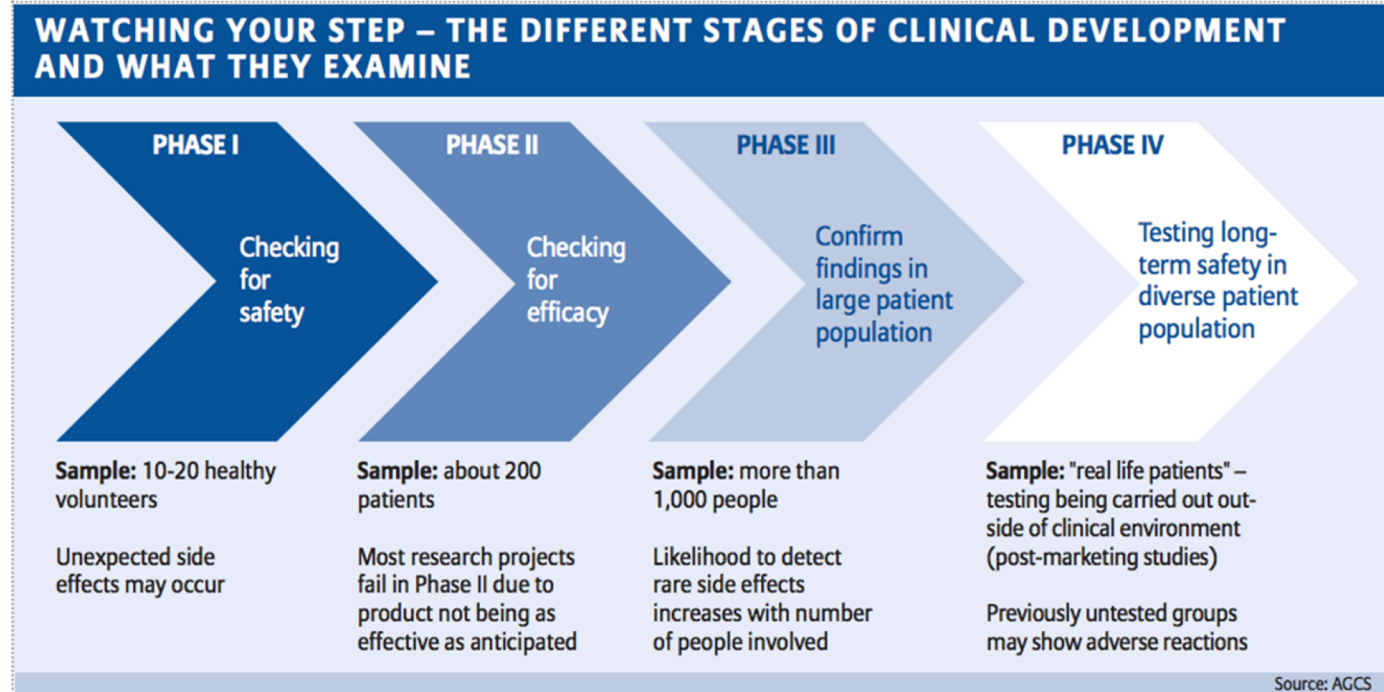


Are clinical trials an option? Always ask your doctor!

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!

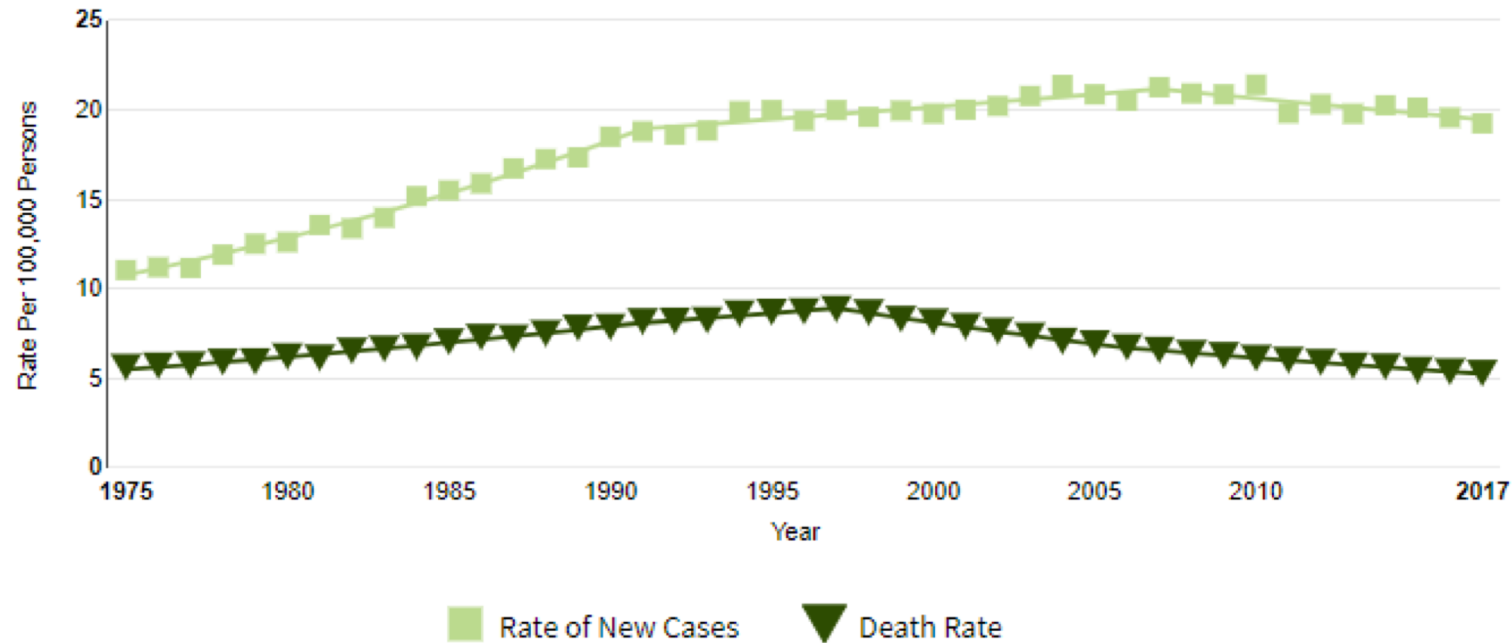
CLL/SLL	Ibrutinib, Acalabrutinib, Venetoclax, Obinutuzumab, Duvelisib
DLBCL	CAR-T, Polatuzumab vedotin, Tafasitamab+lenalidomide, selinexor
Hodgkin	Brentuximab vedotin, Nivolumab, Pembrolizumab
Follicular	Tazemetostat, lenalidomide, duvelisib
Mantle cell	CAR-T, Zanubrutinib, Acalabrutinib, Ibrutinib
Marginal zone	Lenalidomide
T-cell lymphoma	Brentuximab vedotin, Mogamulizumab

Clinical trials available at UWCCC Madison WI

For more information call UW Carbone Cancer Connect at (608) 262-5223 or (800) 622-8922

	First line treatment	Relapsed/refractory disease
CLL	Ibrutinib plus Obinutuzumab versus Ibrutinib plus Venetoclax and Obinutuzmab in <ul style="list-style-type: none"> 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] Ibrutinib during and following Autologous Stem Cell Transplantation versus Placebo in Patients with Relapsed or Refractory DLBCL of the ABC subtype Many Phase 1 studies with novel agents
Follicular lymphoma	Venetoclax in Combination with Obinutuzumab and Bendamustine in Patient with High Tumor Burden FL [PrE0403]	Randomized Phase II Trial in Early Relapsing or Refractory Follicular Lymphoma [S1826] Many Phase 1 studies with novel agents
Mantle cell lymphoma	Bendamustine, Rituximab and High Dose Cytarabine (BR/CR) vs BR/CR- Acalabrutinib vs BR-Acalabrutinib in Patients ≤ 70 yrs [EA4181] Consolidation with ASCT Followed by Maintenance Cell Rituximab vs. Maintenance Rituximab Alone for Patients in MRD negative CR1 [EA4151] Bendamustine + Obinutuzumab Induction Chemoimmunotherapy with Risk-Adapted Obinutuzumab Maintenance Therapy	A Phase I/II Study of Ixazomib and Ibrutinib in Relapsed/Refractory Mantle Cell Lymphoma Many Phase 1 studies with novel agents
Hodgkin lymphoma	Nivolumab Plus AVD or Brentuximab Vedotin Plus AVD in Patients (Age ≥/ 12 Years) with Advanced Stage Classical Hodgkin Lymphoma [S1826] Brentuximab Vedotin in Front-line Therapy of HL and CD30-expressing Peripheral T-cell Lymphoma (PTCL) in Adults Age 60 and Above	Phase I Study of Nivolumab in Combination with Ruxolitinib in Relapsed or Refractory Classical Hodgkin Lymphoma
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 its 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

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

An aerial photograph of a city harbor at sunset. The sun is low on the horizon, casting a warm, golden glow over the water and the city skyline. Numerous sailboats are anchored in the harbor. The city buildings are visible along the waterfront, and a large body of water occupies the foreground and middle ground.

Thank you!

Questions/Comments



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