

WELCOME AND INTRODUCTIONS

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SPEAKERS

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DISCLOSURES

Jonas Paludo, MD has a financial interest/relationship or affiliation in the form of:

Advisory Board/Consultant: AbbVie- Lymphoma Research Grant: Karyopharm- Lymphoma; Biofourmis- CAR T-Cell Therapy

Darci L. Zblewski, APRN, CNP, has nothing to disclose.

All relevant financial relationships have been mitigated.





LEUKEMIA & LYMPHOMA SOCIETY°

TARGET AUDIENCE

This activity is intended for hematologist/oncologists, oncology nurses, and other healthcare professionals involved in the care of patients with lymphoma.

EDUCATIONAL OBJECTIVES

After completing this CE activity, the participant should be better able to:

- Identify indolent lymphoma subtypes and explain the importance of an accurate diagnosis
- Explain new and emerging treatments for follicular lymphoma, marginal zone, and Waldenstrom macroglobulinemia (WM)
- Identify the interprofessional healthcare team's role in managing a patient with a chronic blood cancer
- Describe common treatment side effects and patient management
- Review patient education and support resources



CE DESIGNATION

Accreditation, Credit and Supp



In support of improving patient care, this activity has been planned and implemented by Medical Learning Institute, Inc. and The Leukemia & Lymphoma Society. Medical Learning Institute, Inc. is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

Physician Continuing Medical Education

Medical Learning Institute, Inc. (MLI) designates this live activity for a maximum of 1.0 AMA PRA Category 1 Credits **. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

ursing Continuing Professional Development Approval for nurses has been obtained by the National Office of The Leukemia & Lymphoma Society under Provider Number CEP 5832 to award 1.0 continuing education contact hour through the California Board of Registered Nursing. $\{cc\}$

Nurse Practitioner Credit Designation

This activity is approved for 1.00 contact hour(s) of continuing education (which includes 0.50 hour(s) of pharmacology) by the American Association of Nurse Practitioners. Activity ID# 23086272. This activity was planned in accordance with AANP Accreditation Standards and Policies.

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This activity was planned by and for the healthcare team, and learners will receive 1.0 Interprofessional Continuing Education (IPCE) credit for learning and change

A IPCE CREDIT

ILNA Recertification Points

The program content has been reviewed by the Oncology Nursing Certification Corporation (ONCC) and is acceptable for recertification points in the following ILNA subject areas: Care Continuum (ONC, CBCN, CPHON, AOCNP), Oncology Nursing Practice (OCN), Professional Practice/Performance (BMTCN, AOCNP), Psychosocial Dimensions of Care (AOCNP, CPHON, ONC, CBCN), Symptom Management, Pallative Care, Supportive Care (OCN, CPHON, AOCNP), Treatment (OCN, CBCN, AOCNP), CPHON). Total points: 1.0*

Note that the course content applies to multiple subject areas across multiple credentials. The numerical value indicated above is the maximum number of points that can be claimed in each subject area. The total amount of points claimed may not exceed the total amount of nursing continuing professional development (NCPD) or CME awarded from this course and may only apply to the credential you are renewing.

There is no commercial support associated with this CE activity.

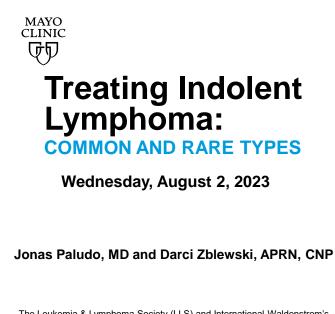
Providers

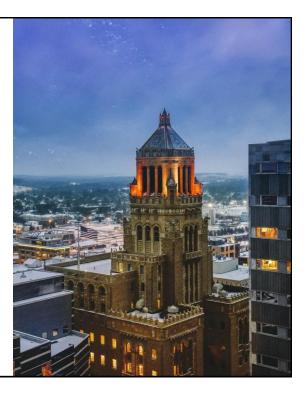
This activity is provided by The Leukemia & Lymphoma Society and Medical Learning Institute, Inc., in collaboration with the International Waldenstrom's Macroglobulinemia Foundation.



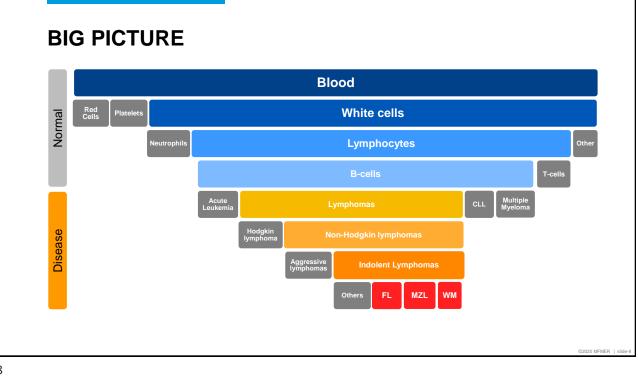


LEUKEMIA & LYMPHOMA OCIETY

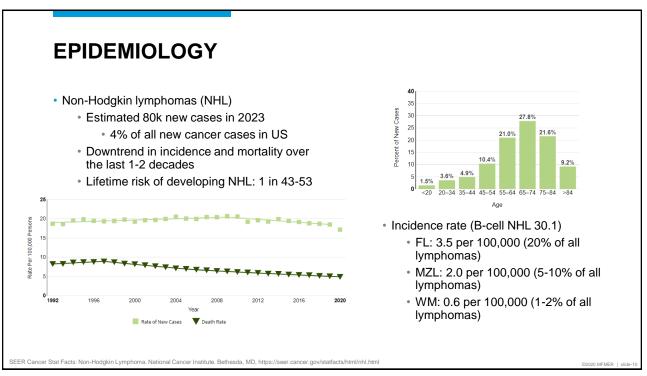


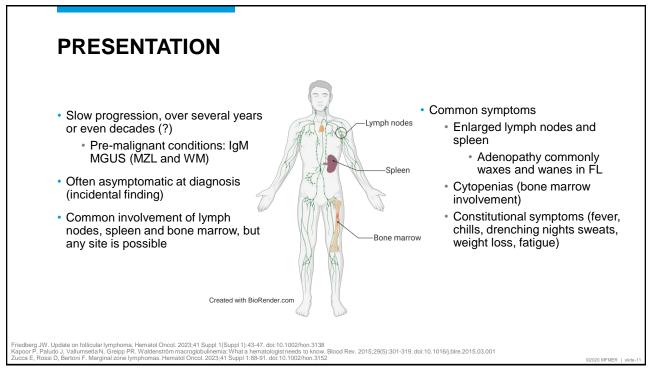


The Leukemia & Lymphoma Society (LLS) and International Waldenstrom's Macroglobulinemia Foundation (IWMF).

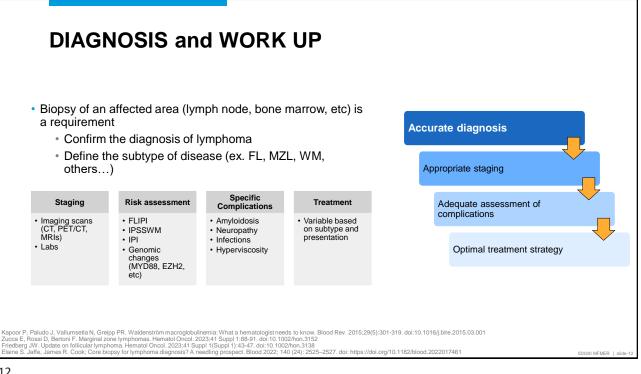


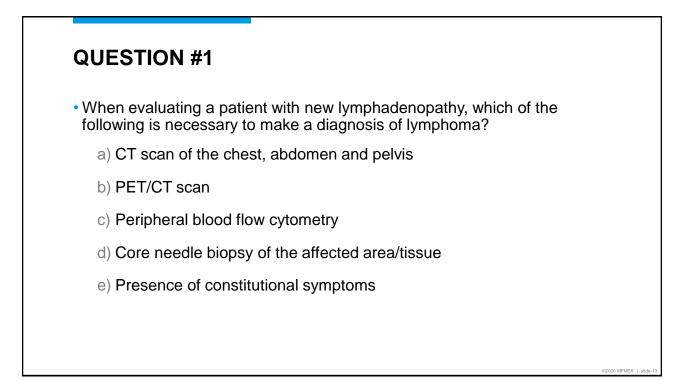
| B-cell, Non-Hodgkin Lymphomas Indolent Aggressive WM Marginal Zone Follicular Mantle Cell Diffuse Large B-cell Double Hit Burkitt's Highly responsive to treatment Less responsive to treatment Incurable Potentially curable | EHAVIOR | |
|--|--------------------------------|------------------------------|
| WM Marginal Zone Follicular Mantle Cell Diffuse Large B-cell Double Hit Burkit's Highly responsive to treatment Less responsive to treatment | B-cell, Non-Hodgki | n Lymphomas |
| With Zone Political Cell B-cell Double Hit Durktes Highly responsive to treatment Less responsive to treatment | Indolent | Aggressive |
| | | |
| Incurable Potentially curable | Highly responsive to treatment | Less responsive to treatment |
| | Incurable | Potentially curable |
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| | | |



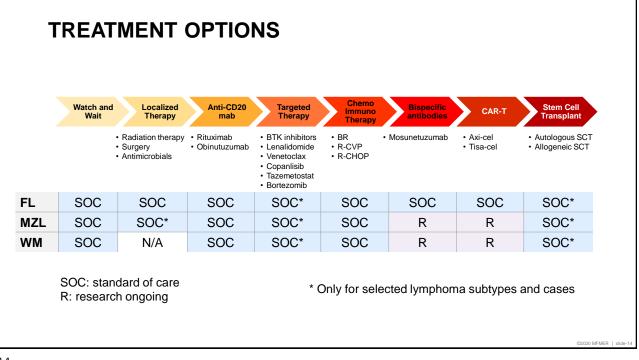


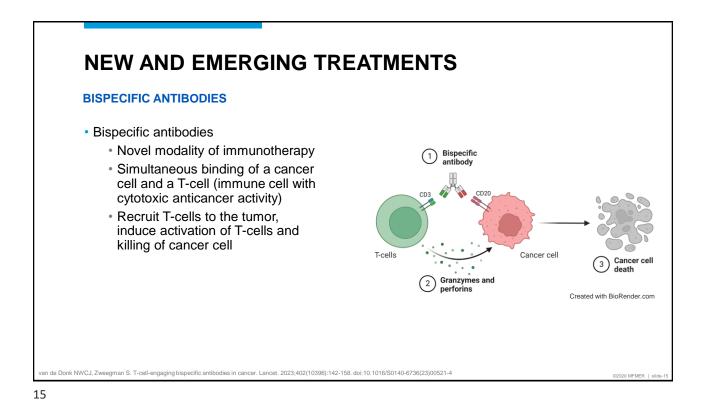










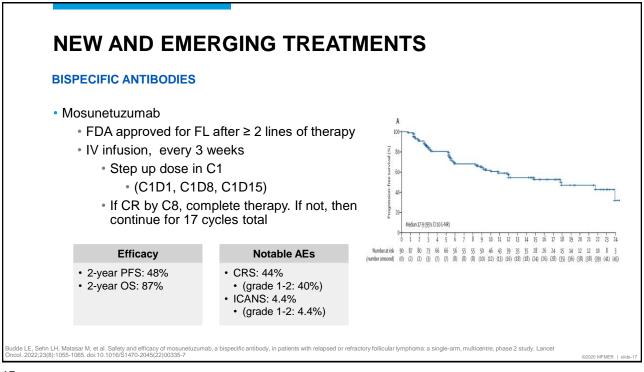


NEW AND EMERGING TREATMENTS

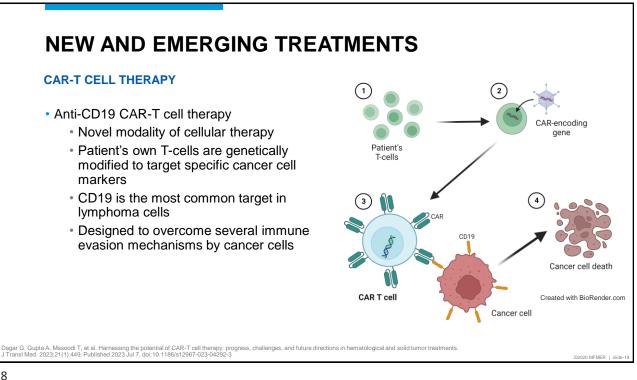
BISPECIFIC ANTIBODIES

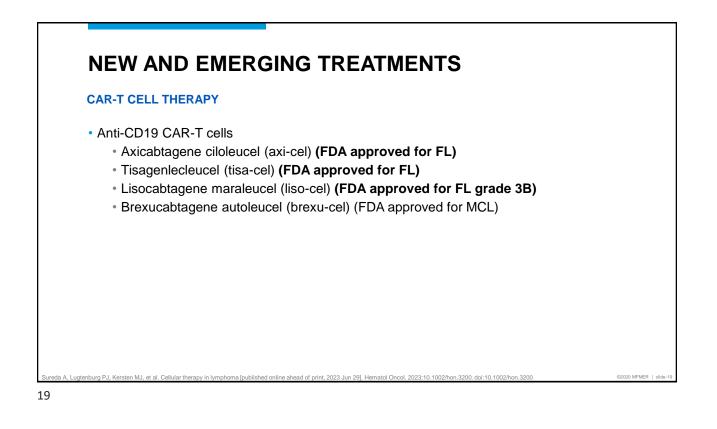
CD20 x CD3 Bispecific antibodies

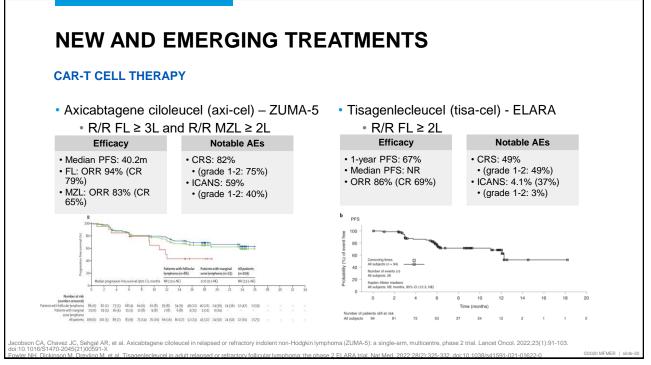
- · Clinical trials: single agent, or in combination therapy:
- Mosunetuzumab (FDA approved: FL)
- Epcoritamab (FDA approved for DLBCL)
- Glofitamab (FDA approved for DLBCL)
- Odronextamab
- Plamotamab

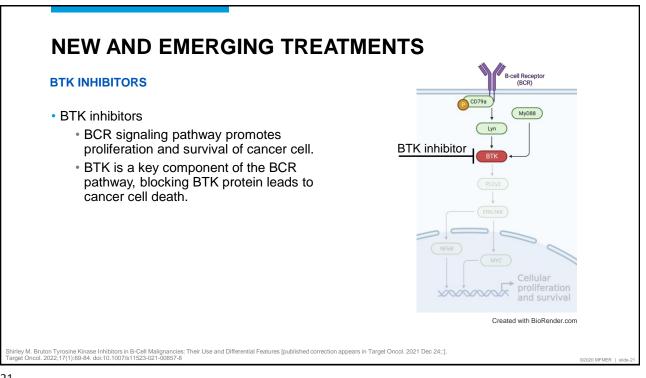












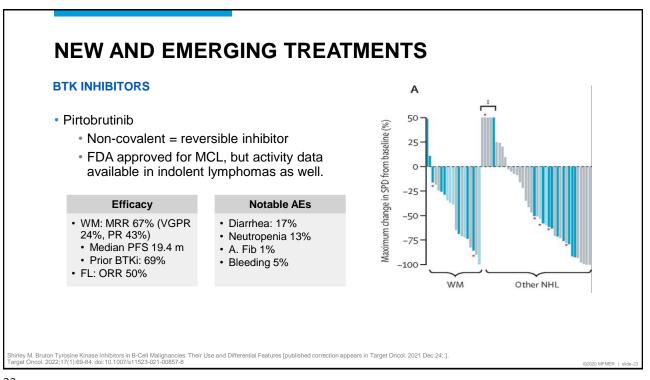
21

NEW AND EMERGING TREATMENTS

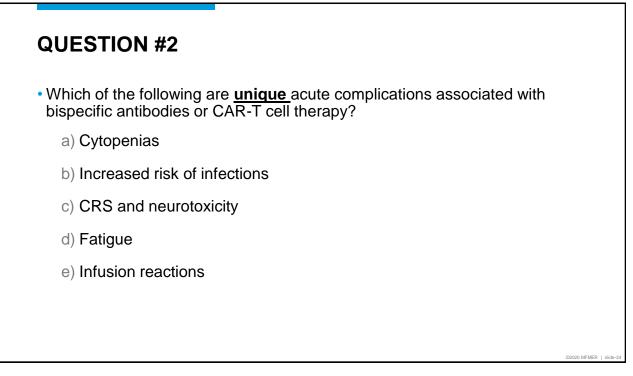
BTK INHIBITORS

- BTK inhibitors
 - 1st generation: ibrutinib (MZL, WM)
 - 2nd generation: acalabrutinib, zanubrutinib (MZL, WM), tirabrutinib and orelabrutinib
 - 3rd generation (non-covalent): pirtobrutinib and nemtabrutinib
 - · Continuous oral regimen

Shirley M. Bruton Tyrosine Kinase Inhibitors in B-Cell Malignancies: Their Use and Differential Features [published correction appears in Target Oncol. 2021 Dec 24;;]. Target Oncol. 2022;17(1):69-84. doi:10.1007/s11523-021-00857-8







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25

Mosunetuzumab

- Cytokine Release Syndrome (CRS)
- Neurologic Toxicity (Includes ICANS)
- Cytopenias
- Infections
- Tumor Flare

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| Mosunetuzumab- Management of CRS |
|----------------------------------|
|----------------------------------|

| CRS Grade | Symptoms | Actions |
|--------------------|---|---|
| Grade 1 | Temperature ≥38°C (≥100.4°F)a, attributed to CRS | Stop infusion and manage per practice guidelines. If symptoms resolve, restart infusion at the same rate. Ensure CRS symptoms are resolved for at least 72 hours prior to the next mosunetuzumab dose. Administer premedication prior to the next mosunetuzumab dose and monitor more frequently. |
| Grade 2 | Temperature ≥38°C (≥100.4°F)a with: hypotension not requiring vasopressors and/or hypoxia requiring low-flow oxygen (<6 L/minute) via nasal cannula | Stop infusion and manage per practice guidelines. If symptoms resolve, restart infusion at the 50% rate. Ensure CRS symptoms are resolved for at least 72 hours prior to the next mosunetuzumab dose. Administer premedication prior to the next mosunetuzumab dose and consider infusing the next dose at 50% rate. For the next dose, monitor more frequently and consider hospitalization. |
| Grade 2, recurrent | | Manage per grade 3 CRS |

27

Mosunetuzumab-Management of CRS

| Grade | Symptoms | Actions | |
|--------------------|---|--|--|
| Grade 3 | Temperature ≥38°C (≥100.4°F)a with: hypotension requiring a vasopressor (with or without vasopressin) and/or hypoxia requiring high-flow oxygen (≥6 L/minute) via nasal cannula, face mask, non-rebreather mask, or Venturi mask | Stop infusion and manage per practice guidelines and provide supportive therapy, which may include intensive care. Ensure CRS symptoms are resolved for at least 72 hours prior to the next mosunetuzumab dose. Administer premedication prior to the next mosunetuzumab dose and infuse the next dose at 50% rate. Hospitalize for the next mosunetuzumab dose. | |
| Grade 3, recurrent | | Permanently discontinue mosunetuzumab. Manage CRS per practice guidelines and provide supportive therapy, which may include ICU care | |
| Grade 4 | Temperature ≥38°C (≥100.4°F)a with: hypotension requiring multiple vasopressors (excluding vasopressin) and/or hypoxia requiring oxygen via positive pressure (eg, continuous positive airway pressure [CPAP], bilevel positive airway pressure [BiPAP], intubation, and mechanical ventilation) | Permanently discontinue mosunetuzumab. Manage CRS per practice guidelines and provide supportive therapy, which may include ICU care. | |

Mosunetuzumab-Management of Neurotoxicity

| Adverse reaction | Severity | Actions |
|---------------------------------------|----------|---|
| Neurologic toxicity (including ICANS) | Grade 2 | Withhold mosunetuzumab until neurologic toxicities/symptoms improve to grade 1 or baseline for at least 72 hours. Provide supportive therapy. If ICANS, manage per practice guidelines. |
| | Grade 3 | Withhold mosunetuzumab until neurologic toxicities/symptoms improve to grade 1 or baseline for at least 72 hours. Provide supportive therapy, which may include ICL care; consider neurology evaluation. If ICANS, manage per practice guidelines. If grade 3 neurologic toxicity recurs, permanently discontinue mosunetuzumab. |
| | Grade 4 | Permanently discontinue mosunetuzumab. Provide supportive therapy, which may include intensive care; consider neurology evaluation. If ICANS, manage per practice guidelines. |

29

Other Toxicities

- Infections
 - Prophylaxis per guidelines
- Cytopenias
 - · Severe cytopenias particularly grade 3 or 4 neutrophil count current in 30% of patients
 - monitor blood counts and treat as appropriate.
- Tumor flare
 - In 4% of patients a tumor flare occurred
 - new or worsening pleural effusion
 - · localized pain and swelling at the site of the lymphoma
 - tumor inflammation
 - · signs or symptoms of compression or obstruction based on organ

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CAR-T

- Cytokine Release Syndrome (CRS)
- Neurotoxicity (ICANS)
- Cytopenias
- Hypogammaglobulinemias
- Infections

ASTCT ICANS Consensus Grading for Adults

| Neurotoxicity | Grade 1 | Grade 2 | Grade 3 | Grade 4 |
|--|-----------------------|------------------|--|---|
| CE score | 7-9 | 3-6 | 0-2 | 0 (patient is unarousable and unable to perform ICE) |
| Depressed level of consciousness | Awakens spontaneously | Awakens to voice | Awakens only to tactile stimulus | Patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse. Stupor or coma |
| Seizure | N/A | N/A | Any clinical seizure focal or generalized that resolves rapidly or nonconvulsive seizures on EEG that resolve with intervention | Life-threatening prolonged seizure (>5 min); or Repetitive clinical or electrical seizures without return to baseline in between |
| Motor findings [‡] | N/A | N/A | N/A | Deep focal motor weakness such as hemiparesis or paraparesis |
| Elevated ICP/cerebral edema | N/A | N/A | Focal/local edema on neuroimaging [®] | Diffuse cerebral edema on neuroimaging; decerebrate or decorticate posturing; or cranial nerve VI palsy; or papilledema; or Cushing's triad |

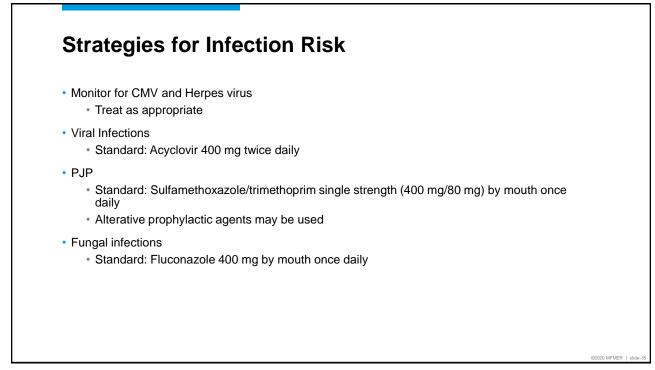
Cytopenias Prolonged Cytopenias can occur 30-90 days post CAR-T and can persist or occur >90 days post CAR-T. · Early onset cause: · Lymphodepletion, possibly infection or HLH like syndrome · Often correlates with severity of CRS or ICANS Prolonged/Late onset: A bone marrow biopsy is important to evaluate for both primary disease and secondary neoplasm as causes Treatment strategies: · Growth factors, thrombopoietin-receptor agonist, stem cell boost, transfusion support

33

Infections

- Viral Infections
- PJP
- Fungal Infections
- CMV
- Herpes Reactivation

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35

Hypogammaglobulinemias

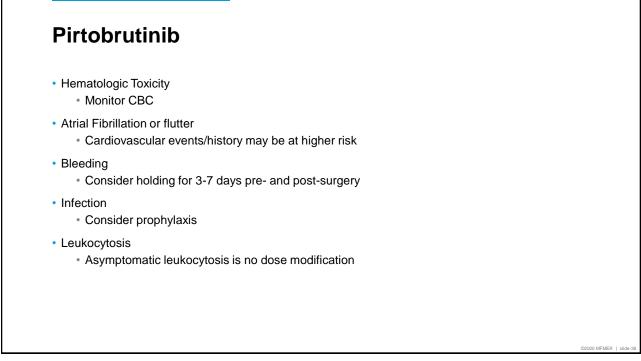
- Hypogammaglobulinemia is defined as IgG < 400 mg/dL.
- 90 days post CAR-T, 67% of patients had hypogammaglobulinemia at some point.
- · Hypogammaglobulinemia has been reported to last up to 4 years.
- IVIG replacement recommendations vary. Recommend IVIG replacement for levels <400.

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Question #3

- What test would be the standard to rule out secondary myeloid malignancies in CAR-T patients with prolonged cytopenias?
 - A) CBC with Differential
 - B) CT Scan
 - C) Bone Marrow Biopsy
 - D) All the Above

37



Healthcare Team

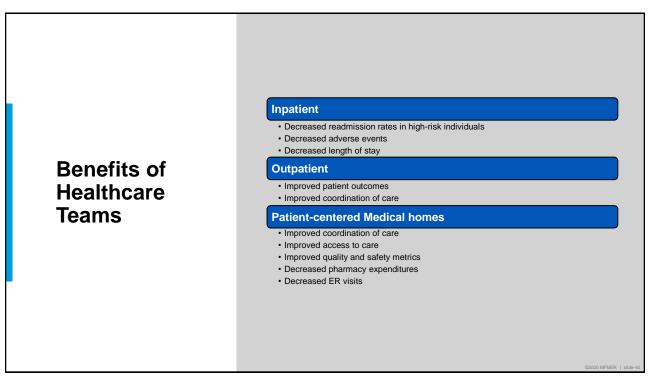
Definition:

 Professionals from various roles who enter a collaborative relationship with the patient to deliver coordinated high value, and patient centered health care

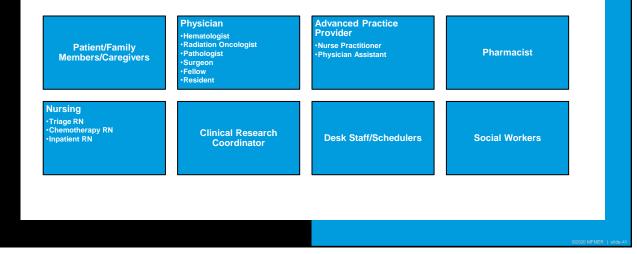
Qualities of a Healthcare team

- Mutual accountability
- · Work closely together to solve problems
- Shared goals
- · Clear roles and responsibilities
- Mutual trust
- Ability to adapt quickly
- Continuous learning
- Individualized coaching

39



Individuals in Care Team





FREE LLS RESOURCES FOR PATIENTS Information Specialists - Personalized assistance for managing treatment decisions, side effects, and dealing with financial and psychosocial challenges (IRC). □ Clinical Trial Nurse Navigators – RNs and NPs provide a personalized service for patients seeking treatment in a clinical trial, sift through the information and provide information to bring back to their HC team (CTSC). www.LLS.org/CTSC ۶ Registered Dieticians – (LLS) provides <u>PearlPoint Nutrition Services</u> to patients/caregivers of all cancer types, free nutrition education and one-on-one consultations by phone or email. LEUKEMIA 6 LYMPHOMA SOCIETY" ⊳ www.LLS.org/Nutrition Personaliz Reach out Monday–Friday, 9 am to 9 pm ET Phone: (800) 955-4572 0 Live chat: www.LLS.org/IRC 0 Email: infocenter@LLS.org 0 HCP Patient Referral Form: www.LLS.org/HCPreferral 0 LEUKEMIA & LYMPHOMA OCIETY

43

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