INNOVATIONS IN BLOOD CANCER TREATMENT: NAVIGATING CAR T-CELL AND BISPECIFIC THERAPIES

DERIVED FROM THE LIVE ACTIVITY WHICH OCCURRED ON APRIL 10, 2025

This activity is supported by Autolus Therapeutics.

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WELCOME AND INTRODUCTIONS

Lesley Hoerst, BSN, RN
Senior Manager
Professional Education Programs
The Leukemia & Lymphoma Society
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Meeting space has been assigned to provide a Symposia supported by The Leukemia & Lymphoma Society during the Oncology Nursing Society's (ONS) 50th Annual Congress, April 10 – April 13, 2025, in Denver, CO. The Oncology Nursing Society's assignment of meeting space does not imply product endorsement.

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EDUCATIONAL OBJECTIVES

Upon completion, participants should be better able to:

- Describe the principles and mechanisms of CAR T- cell and bispecific therapies in treating blood cancers
- Identify clinical indications, including recent FDA approvals and therapies in clinical trials, and disparities in care
- Explain treatment protocols, including pre-treatment conditioning, infusion procedures, identifying and managing common adverse events, management of bispecific therapy in the community, and strategies to improve patient-centered care
- Assess the efficacy of CAR T-cell and bispecific therapies to make informed decisions about treatment options
- List resources and education to support patients, caregivers, and healthcare professionals

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CE DESIGNATION

Nursing Continuing Professional Development Contact Hours

Approval for nurses has been obtained by the National Office of The Leukemia & Lymphoma Society under Provider Number CEP 5832 to award 1.5 continuing education contact hours through the California Board of Registered Nursing.

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 (OCN, CBCN, CPHON AOCNP) 1.0*, Foundations of Transplant (BMTCN) 1.0*, Oncologic Emergencies (OCN, CPHON, AOCNP) 1.0*, Oncology Nursing Practice (OCN) 1.0*, Professional Practice /Performance (BMTCN, AOCNP) 0.5*, Psychosocial Dimensions of Care (AOCNP, CPHON, OCN, CBCN) 0.5*, Quality of Life (BMTCN) 0.5*, Roles of the APRN (AOCNP) 0.5*, Symptom Management, Palliative Care, Supportive Care (OCN, CPHON, AOCNP) 1.0*, Transplant Process and Infusion (BMTCN) 1.0*, Treatment (OCN, CBCN, AOCNP, CPHON) 1.5*.
Total points: 1.5
*Note that the course content applies to multiple subject areas across multiple credentials. The numerical value indicated above is the maximum amount 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.

Nurse Practitioner Continuing Education

This activity is approved for 1.5 contact hour(s) of continuing education (which includes 0.5 hour(s) of pharmacology) by the American Association of Nurse Practitioners®. Activity ID# 25057236. This activity was planned in accordance with AANP Accreditation Standards and Policies.

Social Worker Continuing Education

The Leukemia & Lymphoma Society (LLS) Provider Number 1105, is approved as an ACE provider to offer social work continuing education by the Association of Social Work Boards (ASWB) Approved Continuing Education (ACE) program. Regulatory boards are the final authority on courses accepted for continuing education credit. ACE provider approval period: 12/10/2023-12/10/2026. Social workers completing this course receive 1.5 clinical continuing education credits.

The Leukemia & Lymphoma Society (LLS) is recognized by the New York State Education Departments State Board for Social Work as an approved provider of continuing education for licensed social workers #0117. LLS maintains responsibility for the program. Social workers will receive 1.5 clinical CE contact hours for this activity.

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Our Mission:
Cure blood cancer and improve the quality of life of all patients and their families.

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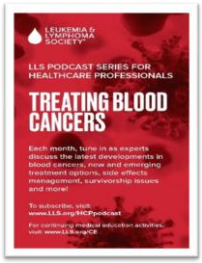
FREE LLS RESOURCES FOR HEALTHCARE PROVIDERS

- ❑ CME & CE courses: www.LLS.org/CE
- ❑ Fact Sheets for HCPs: www.LLS.org/HCPbooklets
- ❑ Videos for HCPs: www.LLS.org/HCPvideos
- ❑ Podcast series for HCPs: www.LLS.org/HCPpodcast



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FREE LLS RESOURCES FOR PATIENTS

- ❑ **Information Specialists** – Personalized assistance for managing treatment decisions, side effects, and dealing with financial and psychosocial challenges (IRC).

- ❑ **Nutrition Education Services Center (NESC)** – one-on-one **free** nutrition education and consultations to patients and caregivers of all cancer types with registered dietitians who have expertise in oncology nutrition.
  - ➢ www.LLSnutrition.org

- ❑ **Reach out Monday–Friday, 9 am to 9 pm ET**
  - Phone: (800) 955-4572
  - Live chat: www.LLS.org/IRC
  - Email: www.LLS.org/ContactUs
  - HCP Patient Referral Form: www.LLS.org/HCPreferral

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CLINICAL TRIAL SUPPORT CENTER (CTSC)

CTSC PROCESS FOR SUPPORTING PATIENTS

Information Resource Center (IRC): 800-955-4572

Complete an online referral form: www.LLS.org/CTSC

Email: CTSC@lls.org

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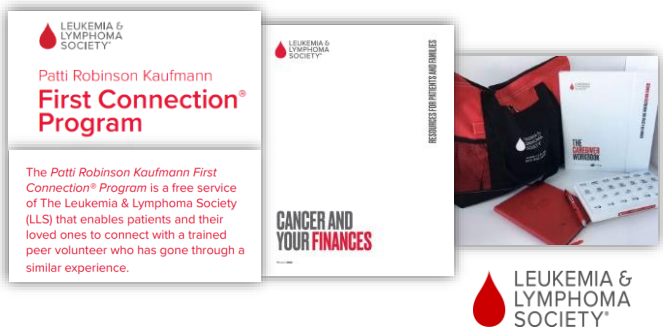
FREE LLS RESOURCES FOR PATIENTS AND CAREGIVERS

- **Webcasts, Videos, Podcasts, booklets**:
  - www.LLS.org/Webcasts
  - www.LLS.org/EducationVideos
  - www.LLS.org/Podcast
  - www.LLS.org/Booklets
- www.LLS.org/CARTtherapy
- **Support Resources**
  - Financial Assistance: www.LLS.org/Finances
    - Urgent Need
    - Patient Aid
    - Travel Assistance
  - Other Support: www.LLS.org/Support
    - LLS Regions
    - Online Weekly Chats Facilitated by Oncology SW
    - LLS Community Social Media Platform
    - First Connection Peer to Peer Program



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FREE LLS RESOURCES FOR YOUR PATIENTS

BOOKLETS AND FACT SHEETS

English – www.LLS.org/Booklets
Spanish – www.LLS.org/Materiales

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FACULTY

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FACULTY DISCLOSURES

Tara M. Graff, DO, MS, has financial relationships with the following:

Advisory Board: AbbVie, Adaptive Biotechnologies, AstraZeneca, BeiGene, BMS, Genmab, Incyte, Lilly
Consultant: AbbVie, ADC Therapeutics, AstraZeneca, Beigene, BMS, Genentech, Genmab, Gilead/Kite, Janssen, Pfizer,
Steering Committee: AbbVie, Genmab
Speaker: AbbVie, BeiGene, Genmab

Jonathan Gutman, MD, does not have any financial relationships with ineligible companies.

Michelle McDaniel, RN, CIONS President, does not have any financial relationships with ineligible companies.

Samantha Schad, MSN, RN, OCN, WTA-C, does not have any financial relationships with ineligible companies.

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CAR T 101

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Emily Whitehead
April, 2012

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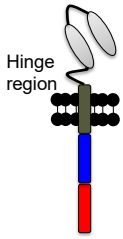
Chimeric Antigen Receptor T-cells

Ag recognition site

"T" body

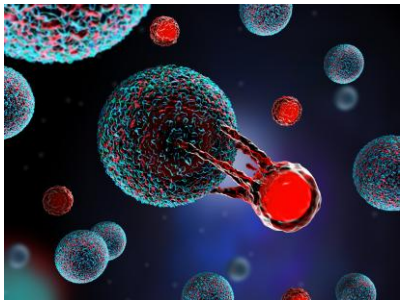


Immunoglobulin light/heavy chain from scFv

Transmembrane domain (CD8, CD4, CD28)

Co-stimulatory molecule (CD27, CD28, ICOS, 4-1BB, OX40)

Signaling molecule, that activates T-cell (CD3ζ chain or FcRY chain)



VECTOR

Viral (lenti-, Y-retrovirus)
Transposon (sleeping beauty)
mRNA
plasmid

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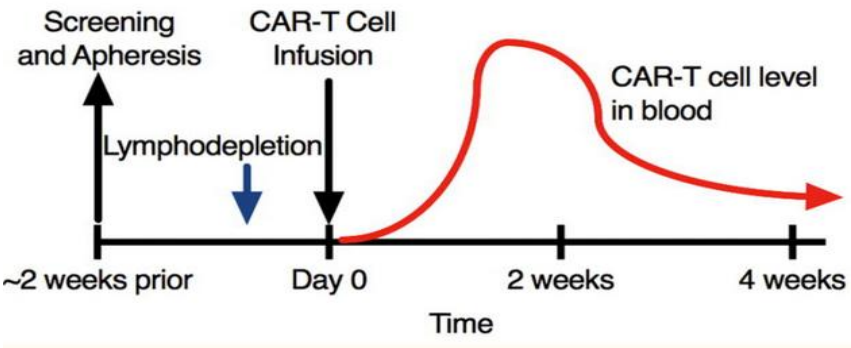
CAR T-cells: A Living Drug



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Hay KA, Turtle CJ. Chimeric Antigen Receptor (CAR) T Cells: Lessons Learned from Targeting of CD19 in B-Cell Malignancies. Drugs. 2017 Mar;77(3):237-245. doi: 10.1007/s40265-017-0690-8. PMID: 28110394; PMCID: PMC5603178.

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CAR T in Blood Cancers

Disease	Drug	ORR	CR	Reference
ALL (Peds)	Tisagenlecleucel (Kymriah®)	81%	60%	Maude, NEJM 2018
ALL (Adult)	Brexucabtagene autoleucel (Tecartus®)	71%	56%	Shah, Lancet 2021
DLBCL	Axicabtagene ciloleucel (Yescarta®)	82%	54%	Neelapu, NEJM 2017
DLBCL	Tisagenlecleucel (Kymriah®)	52%	40%	Schuster, NEJM 2017
DLBCL	Lisocabtagene maraleucel (Breyanzi®)	73%	54%	Abramson, Lancet 2020
Mantle Cell	Brexucabtagene autoleucel (Tecartus®)	94%	67%	Yang, NEJM 2020
Follicular	Axicabtagene ciloleucel (Yescarta®)	92%	74%	Jacobson, Lancet Onc 2022
Follicular	Tisagenlecleucel (Kymriah®)	86%	69%	Fowler, Nat Medicine 2022
MM	Idecabtagene vicleucel (Abecma®)	73%	33%	Munshi, NEJM 2021
MM	Ciltacabtagene autoleucel (Carvykti®)	97%	67%	Berdeja, Lancet 2021
ALL	Obecabtagene autoleucel (Aucatzyl®)	77%	55%	Roddie, NEJM 2024

Roughly 30-40% of ALL/NHL patients likely cured by CAR T — though lots of details…

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FDA Approved CAR T, April 2025

Name	Target	Disease	Approval Date/Indication	Company	Details
Lisocabtagene maraleucel (Breyanzi®)	CD19	DLBCL CLL Follicular Mantle cell	2021 R/R 2 or more lines 2022 2nd line for high risk, auto ineligible 2024 R/R 2024 R/R 2 or more lines 2024 R/R 2 or more lines	BMS	41BB 1:1 CD4:CD8 ratio
Tisagenlecleucel (Kymriah®)	CD19	Age ≤ 25 ALL DLBCL Follicular	2017 refractory, 2nd relapse 2018 R/R 2 or more lines 2022 R/R 2 or more lines	Novartis	41BB
Axicabtagene ciloleucel (Yescarta®)	CD19	DLBCL Follicular	2017 R/R 2 or more lines 2022 2nd line for high risk, auto ineligible 2021 R/R 2 or more lines	Kite/Gilead	CD28
Brexucabtagene autoleucel (Tecartus®)	CD19	Adult ALL Mantle cell	2021 R/R 2020 R/R	Kite/Gilead	CD28 WBC enrichment
Idecabtagene vicleucel (Abecma®)	BCMA	MM	2021 4 or more lines 2024 2 or more lines	BMS	41BB
Ciltacabtagene autoleucel (Carvykti®)	BCMA	MM	2022 4 or more lines 2024 1 or more lines	Janssen	41BB 2 BCMA targets
Obecabtagene autoleucel (Aucatzyl®)	CD19	Adult B-cell ALL	2024 R/R	Autolus	41BB Novel scFv Two infusions

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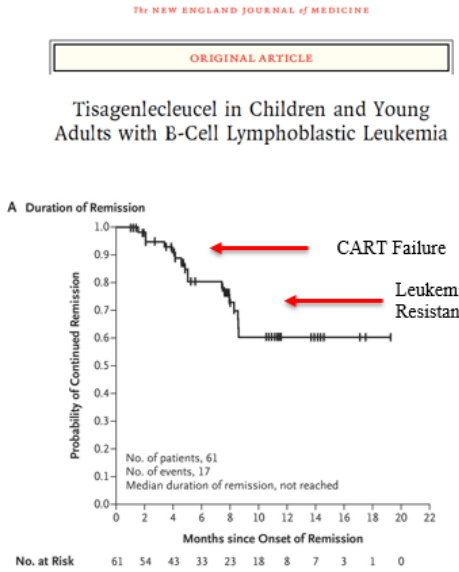
Reasons for Failure in Blood Cancers



Early loss of CAR Ts

Escape mutations leading to relapse

Maude, NEJM 2018

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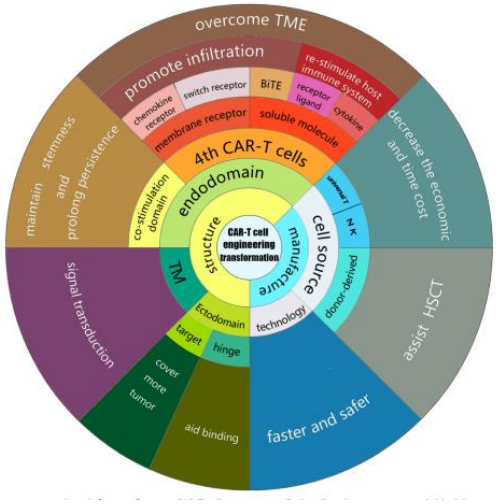
Future Directions (For All Cancers)



Overcoming antigenic heterogeneity: CD19 loss as a mechanism of escape→ Bispecific CD19/CD22 and CD19/CD20 CARs in trials

Improving CAR potency→ Next-generation exhaustion-resistant T-cells are currently in trials, remodel tumor microenvironment, combine with other drugs

Improve CAR T-cell persistence→ Armored CARs constitutively secrete cytokines that aid in T-cell expansion and persistence, optimizing T-cell ratios, combining co-stimulatory domains

Reduce toxicity→ Suicide switches

T-cell trafficking→ Can be enhanced through co-expression of chemokine receptors (CCR4), which drive cells to disease sites.

Decreasing manufacturing times, costs→ Manufacturing "Off the Shelf" — Allogeneic CARs In vivo?? Electroporation, other vectors

Huang, Journal of Heme Onc 2020

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Polling Question 1

How many CAR T trials were ongoing in Oncology in 2022?

a) 15
b) 60
c) 140
d) 230

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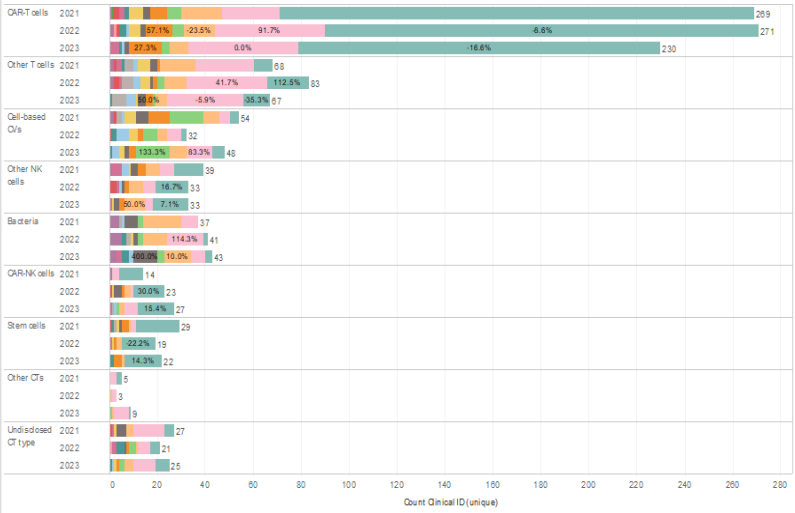
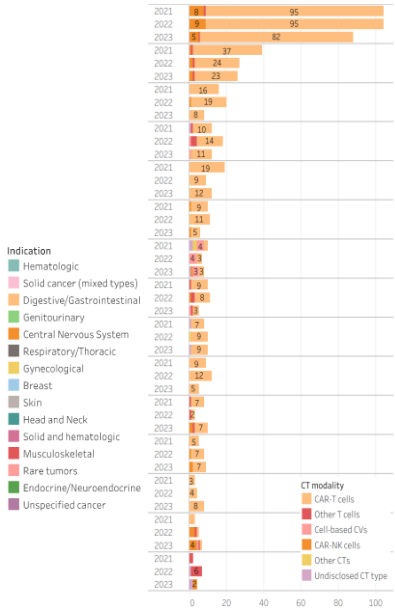
Cancer Immune Effector Cell Therapy Pipeline





Saez-Ibanez, Nat Reviews Drug Discovery 2024

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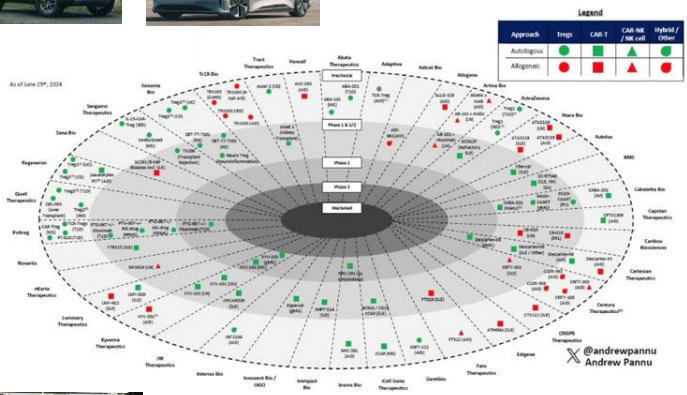
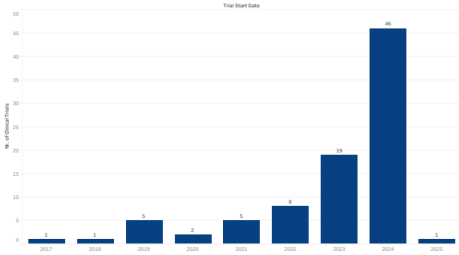
Cell Therapy for Autoimmune Disease Landscape

Supplementary Figure 15: Clinical trials testing gene-modified cell therapies in autoimmune disorders, by trial start date (Source: GlobalData, May 2024).







Saez-Ibanez, Nat Reviews Drug Discovery 2024

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Polling Question 2

How much does a CAR T cost (Drug Cost Alone – Not Care of Patient…)?

a) $10,000
b) $100,000
c) $400,000
d) $ 2,000,000

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Costs and Cost Effectiveness

Axicabtagene ciloleucel (Yescarta®)	$373,000 (2017) $424,000 (2024)
Brexucabtagene autoleucel (Tecartus®)	$373,000
Tisagenlecleucel (Kymriah®)	DLBCL $373,000 ALL $475,000
Lisocabtagene maraleucel (Breyanzi®)	$410,000
Idecabtagene vicleucel (Abecma®)	$419,500
Ciltacabtagene autoleucel (Carvykti®)	$465,000
Lifileucel (Amtagvi®)	$515,000
Afamitresgene autoleuce (Tecelra®)	$727,000
Obecabtagene autoleucel (Aucatzyl®)	$525,000

Cost effectiveness analyses are all over the map. Key modeling considerations include expected cure rates, remission durations, disease courses, alternative therapeutic options and associated costs, quality of life assessments, willingness to pay rates (generally $50,000 to $100,000 per quality-adjusted life-year).

- Thavorn K, et al.Economic Evaluations of Chimeric Antigen Receptor T-Cell Therapies for Hematologic and Solid Malignancies: A Systematic Review. Value Health. 2024 Aug;27(8):1149-1173.
- Kambhampati S, et al. Cost-effectiveness of second-line axicabtagene ciloleucel in relapsed refractory diffuse large B-cell lymphoma. Blood. 2022;140:2024-2036.
- Choe JH, et al. Cost-effectiveness of axicabtagene ciloleucel and tisagenlecleucel as second-line or later therapy in relapsed or refractory diffuse large B-cell lymphoma. JAMA Netw Open. 2022;5:e2245956.
- Perales MA, et al. The cost-effectiveness of axicabtagene ciloleucel as second-line therapy in patients with large B-cell lymphoma in the United States: an economic evaluation of the ZUMA-7 Trial. Transplant Cell Ther. 2022;28:750.e1-e6.
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- Choe JH, et al. Cost-effectiveness of second-line lisocabtagene maraleucel in relapsed or refractory diffuse large B-cell lymphoma. Blood Adv. 2024 Jan 23;8(2):484-496.
- Lin JK, et al. Cost Effectiveness of Chimeric Antigen Receptor T-Cell Therapy in Multiply Relapsed or Refractory Adult Large B-Cell Lymphoma. J Clin Oncol. 2019 Aug 20;37(24):2105-2119.
- Yamamoto C, et al. Cost-Effectiveness of Anti-BCMA Chimeric Antigen Receptor T Cell Therapy in Relapsed/Refractory Multiple Myeloma. Transplant Cell Ther. 2024 Jan;30(1):118.e1-118.e15.
- Furzer J, et al. Cost-effectiveness of Tisagenlecleucel vs Standard Care in High-risk Relapsed Pediatric Acute Lymphoblastic Leukemia in Canada. JAMA Oncol. 2020 Mar 1;6(3):393-401.
- Lin JK, et al. Cost effectiveness of chimeric antigen receptor T-cell therapy in relapsed or refractory pediatric B-cell acute lymphoblastic leukemia. *J Clin Oncol*. 2018.
- Whittington MD, et al. Long-term survival and value of chimeric antigen receptor T-cell therapy for pediatric patients with relapsed or refractory leukemia. *JAMA Pediatr*. 2018;172(12):1161-1168.

* At scale, manufacturing costs estimated at $18,000 to 20,000

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Polling Question 3

Case Study

Mr. Smith is a 63-year-old with relapsed diffuse large cell lymphoma. He lives with his wife and her chronically ill mother in Gillette, Wyoming and has Wyoming Medicaid. His disease relapsed 8 months after first treatment, and he has had a partial response to salvage chemotherapy.

Which of the following is not a major concern about the ability to move forward with CAR T therapy?

a) Insurance authorization
b) Local housing support
c) Disease progression
d) Follow up care
e) Need for a caregiver during therapy

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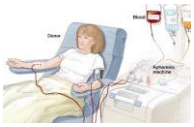
CAR T Therapy is Complicated

Disease assessment:
MD discusses &
prescribes IEC

CAR T Coordinator
Insurance Approval/Payer agreement
Disease staging
Comorbidity staging
Psych/Social (caregiver, resources)
Clinical trial coordination
(estimated 2-4 weeks)



Leukapheresis: 1 day

Bridging
therapy?

CAR T manufacturing
(17-25 days)

Lymphodepletion & CAR T-cell
infusion (clinic vs. hospital)

Monitoring for disease
response, adverse events
(local for 28 days,
no driving 8 weeks)

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In-Patient RN Role in CAR T-Cell Therapies

Samantha Schad, MSN, RN, OCN, WTA-C
Oncology Clinical Practice Leader
Hospital of the University of Pennsylvania
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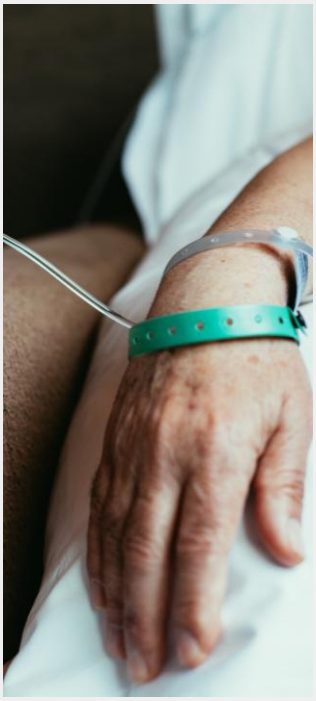

CAR T-Cell Infusion with Mr. M

- **Mr. M is a 67-year-old male with history of relapsed DLBCL and is anticipating his cell infusion today! His wife has been to all his appointments with him and plans to stay during the admission.**

- **Bedside RN Preparation for Re-infusion:**
  - Dedicated line available for infusion
  - Pre-hydration fluids administered if applicable
  - Pre-medications administered
  - Emergency medications are available
  - Educate patient and family on what to expect during cell infusion

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Infusion of Cell Product

- Cells thawed by ancillary department
- Double-checks of the product will be completed with provider, RN, and any ancillary staff
- Scan product if applicable
- Depending on the product and institution guidelines the actual method of administration can differ
- Administration of product to patient
  - Via bag or via syringe
- Timing (thaw to infusion completion)
- Vital sign monitoring

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Polling Question 4

Case Study

It is the day after the CAR T-Cell infusion. You walk into the room and Mr. M is shaking aggressively in bed. He is oriented and has the following vital signs:

- Temperature 103.4°F
- Heart Rate 154
- Respiratory Rate 32
- Blood Pressure: 90/55 (MAP 66)
- SpO_2: 85% room air

What side effect is Mr. M experiencing from his CAR T-Cell Infusion?

a. Neurotoxicity
b. Cytokine Release Syndrome
c. Hypogammaglobulinemia
d. Disseminated Intravascular Coagulation

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Post-Monitoring: CRS

- **What is Cytokine Release Syndrome (CRS)?**
  - A systemic inflammatory reaction that is caused by the release of interleukin-6 into the patient's bloodstream, causing symptoms of organ dysfunction
  - Cause symptoms such as **fever**, malaise, capillary leak syndrome, hypotension, and pulmonary edema
  - Symptoms of CRS can resemble **septic shock**
- **What should you be assessing and paying extra attention to?**
  - Vital signs
  - Neurological Assessment
  - Respiratory Assessment

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CRS Grading Scale

CRS Grade?

CRS Onset: Start date is a retrospective assessment of the date of onset of persistent fevers due to CRS and not explained by other events (i.e. sepsis). Fever defined as a temperature of ≥100.4°F/38°C.

CRS Offset: Stop date is date when patient is afebrile for 24 hours, off vasopressors for 24 hours and without CRS-related hypotension or hypoxia.

ASTCT Consensus Grading for CRS

CRS parameter	Grade 1	Grade 2	Grade 3	Grade 4
Fever	Temp ≥38C	Temp ≥38C	Temp ≥38C	Temp ≥38C
With either:				
Hypotension	None	Not requiring vasopressors	Requiring one vasopressor with or without vasopressin	Requiring multiple vasopressors (excluding vasopressin)
And/or:				
Hypoxia	None	Requiring low-flow nasal cannula equivalent to 6L or less	Requiring high-flow nasal cannula, facemask, non-rebreather mask, or Venturi mask	Requiring positive pressure (eg: CPAP, BiPAP, intubation and mechanical ventilation)

- Grading based on the worst symptom
- Grading will impact interventions and treatment taken
- Mr. M's most recent vitals
  - Temperature 103.4°F
  - Heart Rate 154
  - Respiratory Rate 32
  - Blood Pressure: 90/55 (MAP 66)
  - SpO_2: 85% room air
- Grade 2 CRS

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Lee, Daniel W. et al. ASTCT Consensus Grading for Cytokine Release Syndome and Neurologic Toxicity Associated with Immune Effector Cells. Biology of Blood and Marrow Transplantation, Volume 25, Issue 4, 625-638

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What Interventions Should You Anticipate?

- **Grade 1:** Continue supportive care
- **Grade 2:** Prevent patient from escalating to grade 3. Do they have increasing oxygen requirements and low blood pressure requiring multiple IVF boluses? Anticipate tocilizumab
- **Grade 3:** Administer tocilizumab and consider low-dose steroid. Did you have desired response within 2 to 12 hrs? Yes — continue supportive care; No — move to Grade 4 interventions
- **Grade 4:** Administer tocilizumab and high-dose steroid. Did you have desired response within 2 to 12 hrs? No — consider 3rd dose of tocilizumab and additional cytokine therapies

CRS Grade?

CRS Onset: Start date is a retrospective assessment of the date of onset of persistent fevers due to CRS and not explained by other events (i.e. sepsis). Fever defined as a temperature of ≥100.4°F/38°C.

CRS Offset: Stop date is date when patient is afebrile for 24 hours, off vasopressors for 24 hours and without CRS-related hypotension or hypoxia.

ASTCT Consensus Grading for CRS

CRS parameter	Grade 1	Grade 2	Grade 3	Grade 4
Fever	Temp ≥38C	Temp ≥38C	Temp ≥38C	Temp ≥38C
With either:				
Hypotension	None	Not requiring vasopressors	Requiring one vasopressor with or without vasopressin	Requiring multiple vasopressors (excluding vasopressin)
And/or:				
Hypoxia	None	Requiring low-flow nasal cannula equivalent to 6L or less	Requiring high-flow nasal cannula, facemask, non-rebreather mask, or Venturi mask	Requiring positive pressure (eg: CPAP, BiPAP, intubation and mechanical ventilation)

Grade 1: Continue supportive Care

Grade 2: Increasing oxygen requirement or falling blood pressure requiring multiple boluses

Consider tocilizumab administration

Grade 3: Tocilizumab and low-/high-dose steroids

Grade 4: Tocilizumab and high-dose sterioids

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Polling Question 5

Case Study

Three days later, Mr. M has recovered from his CRS symptoms. RN goes in to complete her morning assessment, and — while completing her neurological assessment including the Immune Effector Cell-Associated Encephalopathy (ICE) exam — RN notices that the patient thinks it is 1985 at the mall, is able to name 2 objects in the room, cannot count backwards by 10, and cannot write a sentence.

What side effect is Mr. M experiencing from his CAR T-Cell Infusion?

a) Neurotoxicity
b) Cytokine Release Syndrome
c) Liver Failure
d) Respiratory Distress
e) Macrophage Activation Syndrome

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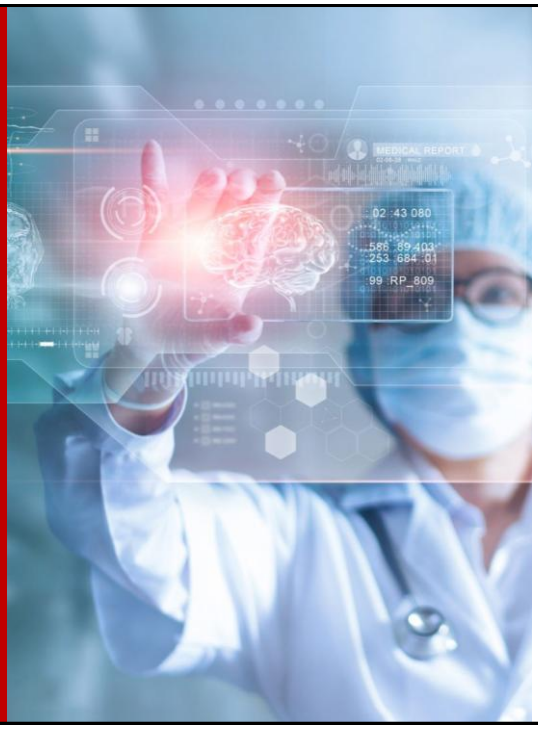

Neurotoxicity

- **Causes alterations in patient's neurological function/status**
- **Pathophysiology not yet completely understood**
  - Potentially from release of cytokines that pass through the brain's blood barrier leaking into brain matter and CSF
- **Signs & symptoms can resemble toxic encephalopathy**
  - Confusion
  - Difficulty word-finding
  - Speech or fine motor impairment
  - Seizures
  - Coma
  - Cerebral edema

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How do we Measure Neurotoxicity?

- Immune-Effector Cell Associated Neurotoxicity (ICANS) grading
- Patients will receive an ICANS grade based on the ICE score and neurological symptoms
  - Grade is dependent on the patient's worst symptom or score
  - ICE score is only one portion of the total ICANS grading

ASCT Consensus Grading of ICANS: Immune Effector Cell-Associated Neurotoxicity Syndrome*

Neurotoxicity Domain	Grade 1	Grade 2	Grade 3	Grade 4
ICE 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

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Nursing Assessment: Immune Effector Cell-Associated Encephalopathy (ICE) Scoring System

NORMAL SCORE: 10/10

Category	Event Descriptions
Orientation (4 points)	Year Month City Hospital
Naming (3 points)	Ability to name 3 objects (eg, point to clock, pen, button)
Following commands (1 point)	Ability to follow simple commands (eg, "Show me 2 fingers" or "Close you and stick out your tongue")
Writing (1 point)	Ability to write a standard sentence (eg, "Our national bird is the bald eag
Attention (1 point)	Ability to count backwards from 100 by 10

- Complete orientation questions
- Ask to name 3 objects
- Ask patient to follow simple commands
- Have patient write a sentence
  - Should be the same sentence daily
  - Upload image to chart if able, in case paper gets lost
- Ask patient to count backward from 100 by 10

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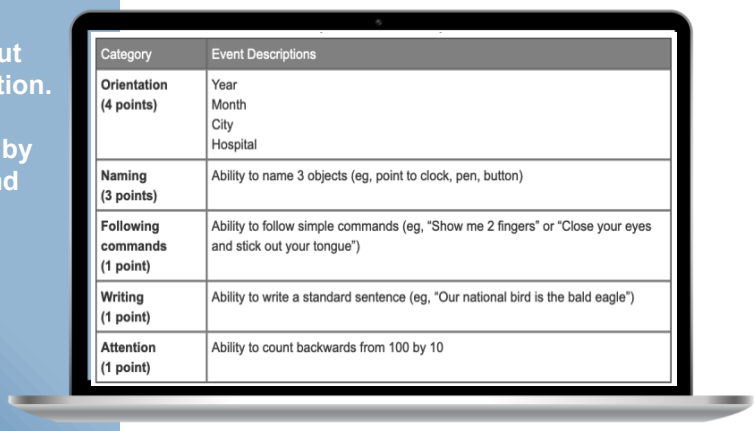
ICE Score for Mr. M

Mr. M thinks it is 1985 at the mall, but does know the month and city location. He is able to name 2 objects in the room and cannot count backwards by 10. He cannot write his sentence and cannot follow simple commands.

- 2 points for orientation
- 2 points for naming objects
- 0 points for commands
- 0 point for sentence
- 0 point for counting

- **ICE Score: 4/10**



Category	Event Descriptions
Orientation (4 points)	Year Month City Hospital
Naming (3 points)	Ability to name 3 objects (eg, point to clock, pen, button)
Following commands (1 point)	Ability to follow simple commands (eg, "Show me 2 fingers" or "Close your eyes and stick out your tongue")
Writing (1 point)	Ability to write a standard sentence (eg, "Our national bird is the bald eagle")
Attention (1 point)	Ability to count backwards from 100 by 10

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What Interventions Should the Nurse Anticipate?

Based off Mr. M's ICE score of 4/10, he is experiencing Grade 2 ICANS

➢ **Grade 2:**

- Start q4hr neuro checks, including q4hr ICE score
- Consider steroids and, if neuro changes do not improve, continue till resolution
- Institute seizure precautions and potential to add anti-seizure prophylaxis
- Potential to order MRI, LP, EEG, and neurology consult
- Lab goals: platelets over 30,000; fibrinogen > 150; INR,1.5

ASCT Consensus Grading of ICANS: Immune Effector Cell-Associated Neurotoxicity Syndrome*

Neurotoxicity Domain	Grade 1	Grade 2	Grade 3	Grade 4
ICE 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
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Motor findings‡	N/A	N/A	N/A	Deep focal motor weakness such as hemiparesis or paraparesis
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What Happens if Neurotoxicity Progresses?

- The next shift RN goes to assess Mr. M, and he is no longer arousable, scoring an ICE score 0/10 and no longer responding to sternal rub.
- Based on his ICE score, along with his neurological status, he is now Grade 4 Neurotoxicity
  - Grade 3 and Grade 4 toxicity involves administration of steroids and consideration to administer anakinra
  - Escalate to higher level of care

ASCT Consensus Grading of ICANS: Immune Effector Cell-Associated Neurotoxicity Syndrome*

Neurotoxicity Domain	Grade 1	Grade 2	Grade 3	Grade 4
ICE 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
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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

Grade 1: Q4hr neuro checks

Grade 2: Consider steroids, fall precautions, anti-seizure prophylaxis, and diagnostic tests

Grade 3: Steroids and consider anakinra administration

Grade 4: Steroids and consider anakinra or ruxolitinib

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Additional Nursing Considerations

Mr. M's family is extremely upset by the progression of his neurological status. They thought once his fever resolved, they were in the clear. They have gone through a wave of emotions of joy, finally getting to the point of administration of the cells, worry when he was experiencing CRS symptoms, which resolved causing hope, but only to have him experience severe neurotoxicity requiring ICU care.

- Education to family both prior and during treatment is key
  - Expected reactions
  - Unknown resolution

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A Week Later…

Mr. M is out of the ICU and has been fever free with an ICE score back to 10/10. The RN prepares the patient and caregiver for discharge!

Wallet Card: This contains information about the specific CAR T-cell therapy the patient received and information for the patient of when to alert their provider

- Fever (100.4°F or greater)
- Difficulty breathing
- Chills or shaking chills
- Confusion
- Dizziness or lightheadedness
- Severe nausea, vomiting, or diarrhea
- Fast or irregular heartbeat
- Severe fatigue or weakness

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Bispecific Bonanza
How/Why to Build a Program

Tara M. Graff, DO, MS
Medical Oncologist
Director of Clinical Research MCB/UIHSMG
Director of Cellular Therapy Exigent/ONCare
Des Moines, IA

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Polling Question 6

There is currently only one type of cellular therapy approved?

a) True
b) False

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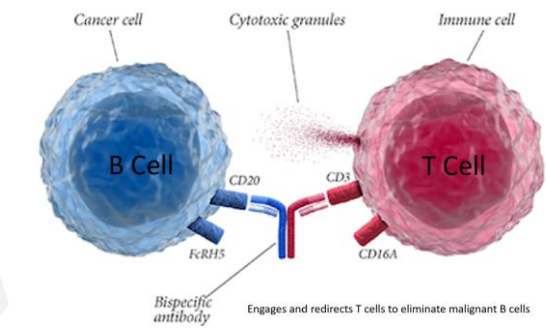
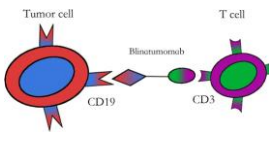
Types of Cellular Therapies

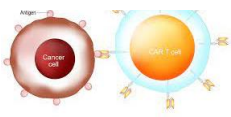
- BiTes
- Bispecific Antibodies
- CAR T-Cell Therapy



Roche



https://www.nih.gov/news-events/news-releases/immunotherapy-drug-improves-outcomes-some-children-relapsed-leukemia



Getty Image

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Who's My Match (CD3 Wants to Know)

- Epcoritamab, Glofitamab, Mosunetuzumab — target CD20
- Teclistamab and Eltranatamab — target BCMA
- Talquetamab — targets GRPC5D

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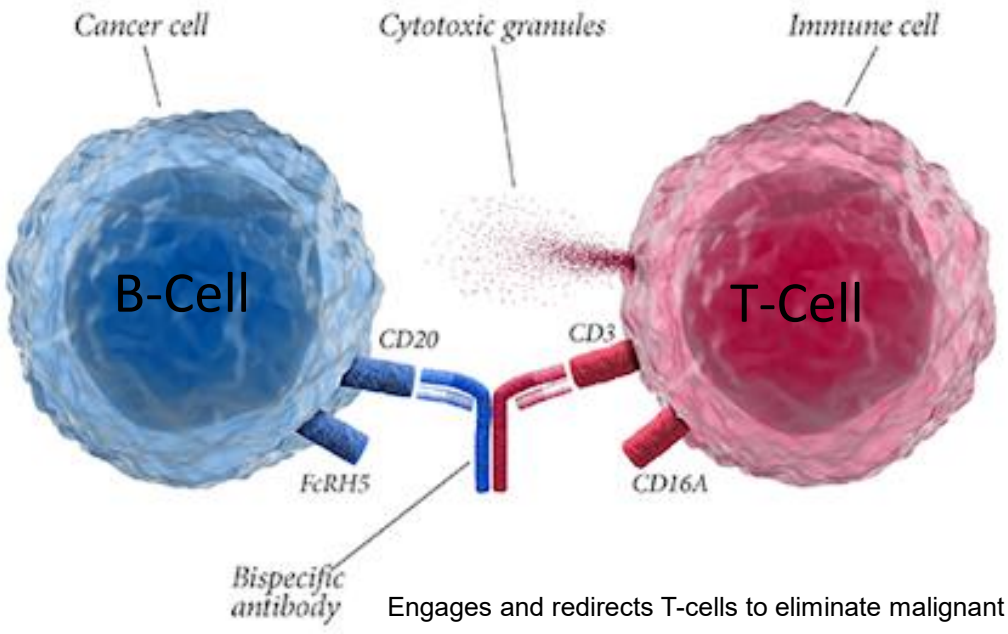

Engages and redirects T-cells to eliminate malignant B-cells

Roche

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Commercially-Approved BsAb

- Epcoritamab (Epkinly®) and Mosunetuzumab (Lunsumio™) (3L FL)
- Epcoritamab (Epkinly®) and Glofitamab (Columnvi™) (3L DLBCL)
- Teclistamab (Tecvayli®), Talquetamab (Talvey®), and Eltranatamab (Elrexfio®) (MM)
- Tarlatamab (Imdelltra™) (ES SCLC)
- Tebentafusp (Kimmtrak®) (Uveal Melanoma)

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Active Trials at MCB

- 1L Follicular Lymphoma with epcoritamab bysp (Epkinly®)/rituximab (Rituxan®)/ lenalidomide (Revlimid®) (outpatient)
- 2L DLBCL with epcoritamab bysp (Epkinly®) (outpatient trial)
- 3L FL with epcoritamab bysp (Epkinly®) (outpatient trial)
- Evolve NSCLC Trial
- LOTIS-7 loncastuximab (Zynlonta®) + Glofitamab (Columvi™)/Mosunetuzumab (Lunsumio™)
- Tec 7 (1L Teclistamab (Tecvayli®))
- Tec 9 (Teclistamab (Tecvayli®) outpatient study)
- Monumental 6 (Teclistamab (Tecvayli®)/Talquetamab (Talvey®) outpatient trial)

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Trials Coming

- CD19 Bispecific NHL (CLL and FL)
- Harmoni NSCLC trial
- Jazz Breast
- Olympia 6 (post CART trial with Odronextamab (Ordspono™)
- 1 more MM, Breast, and Lung, and 2 prostate

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Polling Question 7

As of today, only academic centers can do step-up dosing for bispecific antibodies?

a) True

b) False

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Bispecific Planning (Building Blocks)

Bispecific management team	Bispecific Needs (depends on which agent used)	Facility Management/Logistics
• Patient, Caregiver, Nurse Champions, APP, Physician, Pharmacist, Hospital System • Learning from like-minded centers • Mock patient • Inservice by experienced physician/treatment center	• Outpatient vs inpatient administration, timing for monitoring • **Concise Management Plan** • Plan for "Team" and patient/caregiver • All patients to have BP cuff, thermometer, Pulse Ox – and know how to use them (reach out to companies) • **Checklist for starting a patient**	• Communication with hospital system (ER, floors, on-call team, pharmacy) • Need for supportive meds (Toci, Anakinra, etc.) • Who has what — keeper of the "drugs" • 2 doses of Toci at all locations (per patient) • **How do you want to manage — **capabilities** • Patient no more than 30-60 min of nearest hospital or clinic with Toci stock

APP, advanced practice provider; BP, blood pressure; ER, emergency room; Toci, tocilizumab.

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Key Elements

- **Bispecific Team**
- Concise management plan (outpatient vs inpatient)
- Order sets initiated on inpatient side for CRS and ICANS
- Ongoing education; inservices
- Cooperation between clinic and hospital system/staff

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Bispecific Team

- Roles
- Knowledge/education
- Prepare for every scenario
- Take ownership

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Bispecific Team

- **Tara Graff, DO MS**
- Jane Osterson, COO
- Marcy Budish, Co-Director Chemotherapy Infusion
- Wendy Kralik, Co-Director Chemotherapy Infusion
- Corey Wilson, Director of Pharmacy
- **Maddie Koppin, Clinical Oncology Pharmacist**
- Amy Raedeker, APP Program Director
- **Brooke Walter, RN**
- **Michelle McDaniel, RN**
- **Kerry Mann, RN**
- **Kathy Adair, RN**
- **Katherine Hagge, RN**

##Research team

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Management Plans

Protocol For Bispecific Antibody Post-Treatment Monitoring for CRS/ICANS

- Ambulatory setting and post-hospital-discharge monitoring

Protocol for Bispecific Antibody Inpatient Management

- Appropriate order sets made for inpatient management CRS/ICANS
- Administration
- Reactions vs CRS
- Education on management
- When to call

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What do you do when you Start a Patient?

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- ❑ Bispecific Team Notified: Patient's Name, DOB, Drug and requested start date (prefer 7 days' notice)
- ❑ APP performing teach: has the individual been trained and do they have the necessary documents including ICE questionnaire for patient/caregiver
- ❑ Patients have a caregiver and if they do not, arrangements must be made. **Patients are excluded from outpatient observation and must be admitted if they are unable to provide a caregiver**
- ❑ If patient lives >60 min from the treatment center, it is preferred that the patient stay at hotel** during observation period. Inpatient admission for observation is last resort. **Hotel stays for patients who are on trial will be covered by the sponsor **please contact Dr. Graff for potential costs that could be covered by the sponsor.
  **Patients who are on commercial treatment can use the MCB Foundation for hotel stay coverage.
- ❑ Verify all patent and caregivers' numbers. Let caregiver know they will be called if patient does not answer
- ❑ Drug, Cycle # and day of set-up dosing must be updated in patient banner with each treatment
- ❑ Medical equipment must be purchased (or provided if cannot afford) and brought to first treatment appointment. **Equipment for patients who are on trial will be covered by the sponsor **please contact Dr. Graff for potential costs that could be covered by the sponsor.
- ❑ Patient and caregiver to demonstrate proper use and vitals to be taken on MCB equipment and patient's before leaving chemo suite
- ❑ If the patient is to be inpatient, then all medical equipment must be in the room before discharge and set of vitals to be done on the patient equipment and hospitals before discharge
- ❑ Those set of vitals (2 sets) must be the first email on Maddie's patient thread (ALWAYS use Maddie's thread)
- ❑ 10am and 4pm calls by doctor team: 10pm and 5am calls by bispecific team. Any additional calls also stay on thread

Created by Tara M Graff, DO, MS

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Communication

- Identify Bispecific in EMR
- SUD info *cycle, day
- Trial/Commercial
- Team assigned (A vs B)
- Monday (weekly) email
- Documents (CRS, ICANS, Drug)

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Dr. Graff will take all calls during the patient's monitoring period.

RNs on-call contact information:

Michelle McDaniel: 515-777-0871
Backup: 515-490-6142
Katheine Hagge: 515-306-8289
Back up (husband): 515-229-3018

Treatment Days and Days to monitor

06/24/24 C1 Day 1- RE-PRIME step up does 1 - 0.16mg- Mercy DT

On call: Team Michelle/Katherine from 5/29 through 6/1

Phone calls for dose 1 will be completed for 48 hours with the following schedule-

06/24 4pm- Graff Team
06/24 10pm- Brooke W
06/25 5am- Brooke W
06/25 10am and 4pm- Graff Team
06/25 10pm- Brooke W
06/26 5am- Brooke W
06/26 10am and 4pm- Graff Team

07/01/24 C1 Day 8 – RE-PRIME step-up dose 2 – 0.8mg
07/08/24 C1 Day 15 – step up dose 3 – 3 mg
07/15/24 C2 Day 22 – first full dose – 48 mg

Actemra rescue dose: 800mg – max dose

- I have a dose of Actemra on hand at the Mercy infusion suite if she should need a dose
- I have spoken with Mercy inpatient inventory team, and they also have a dose of Actemra on hand that they can use in emergency. The patient has a prescription of dexamethasone 4x4 mg tablets at home in case of CRS symptoms after discharge.

Monitoring Parameters:

Patient will monitor at home every 4 hours and report to the team if there is an issue. The RN who is calling the patient will get patients vitals for record and report to the team:

- Temperature (>100.4F)
- Blood pressure (Decrease in SBP >10mmHG an SBP <90mmHG)
- Heart rate (increased HR greater than 110bpm)
- Rash (present)
- Oxygenation (90% or less or a >5% change from last monitor)
- Sudden onset muscle pain/soreness
- General unwell feeling
- Headache
- Nausea
- Changes in mental status –use ICE scoring questionnaire to help with ICANS grading

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CRS/ICANs Risk Mitigation/Management (What Happens Before Toci)

- Education
- 1L NS IVF pre- and post-administration of bispecific
- Premedications (Dex steroid of choice)
- Dexamethasone 4 mg tablets × 4 (16 mg) as "pill in the pocket" for home
- Tylenol and NSAIDs
- Drug Bracelet
- Pocket Cards

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CRS Management

Definition: CRS is an acute systemic inflammatory syndrome characterized by fever and organ dysfunction
Symptoms: fever (required) with possible hypoxia, hypotension, tachypnea, nausea, headache, fatigue, myalgias, or malaise
Workup and evaluation:
- Pertinent history and physical examination including vital sign evaluation and evaluation of respiratory symptoms
- Review medications including BsAb received, last dose of antipyretic therapy, steroids, or anticytokine administration
- Assess for concurrent symptoms of neurotoxicity
- Assess for alternate diagnosis including infection (including neutropenic fever), venous thromboembolism, respiratory infection (including COVID-19 and influenza), volume overload or dehydration, and exacerbation of underlying cardiopulmonary condition. Treat as appropriate.
- For duration of symptoms over 1 week, consider excluding HLH/MAS[1,2]

Monitoring: consider monitoring patient for 1-2 h after infusion if outpatient administration of BsAb on day of step-up dosing
Next dose: follow prescribing label

Grade and definition	Management
Grade 1: Fever* of ≥100.4°F with/without constitutional symptoms requiring symptomatic treatment, no hypotension or hypoxia	Home: • A/P 650-1000 mg orally, can repeat, if recurrent fever, ≥6-8 h later if clinically stable • Recommend aggressive oral hydration • Continue to check temperature every 1-2 h and other vitals if able. Patients should recontact the clinic urgently or present to ED if BP goes <10 mm Hg below baseline AND <90 mm Hg systolic, new orthostatic symptoms, weakness, confusion, dizziness, or new hypoxia (<90%). Home vs outpatient/ED evaluation: • If refractory or recurrent fever (<6-8 h) consider dexamethasone 10 mg once. Home management may be appropriate if vital signs remain stable and no other concerning symptoms. Otherwise, patients should be evaluated in a health care facility. • Consider earlier administration of steroids and immediate in-person evaluation for patients with multiple disease risk factors or comorbidities (see text) • Consider daily dexamethasone with persistent symptoms Additional management: • Consider anticytokine therapy (eg, tocilizumab) in cases of protracted fever (eg, >48 h despite corticosteroids) • Early tocilizumab after trial of dexamethasone should be considered for patients with multiple medical risk factors (eg, comorbidities)
Grade 2: Fever of ≥100.4°F with either hypotension not requiring pressors and/or hypoxia managed with low-flow nasal canula or blow-by.	• All patients should be urgently evaluated in person. Recommend inpatient management for most cases of grade 2 CRS unless qualified outpatient day hospital/infusion center and no hypoxia. • If after hours without access to appropriate outpatient treatment area or if clinical scenario dictates, recommend ED evaluation • A/P 650-1000 mg as needed, up to 3-4 times daily • Dexamethasone 10 mg every 12 h • Administer IV fluids/supplemental oxygen as appropriate • Administer tocilizumabt if symptoms persist despite IV fluids and dexamethasone (~4-6 h after dosing) or if clinically unstable. Consider alternative agent (eg, anakinra or siltuximab) if persistent symptoms despite maximal dosing.
Grade 3: Fever of ≥100.4°F with either hypotension (BP <90/60 or <10 mmHg below, not responsive to fluids and/or hypoxia requiring high-flow nasal canula, face mask, or venturi mask)	• Emergent inpatient admission (floor or ICU) for hemodynamic monitoring, IV fluids, oxygen therapy, and vasopressors • A/P 1000 mg IV as needed up to 3-4 times daily when safe • Dexamethasone (eg, 10 mg IV Q 6 h), until resolution to grade ≤1, followed by dexamethasone taper • Evaluate for sepsis and consider empiric antibiotics • Administer tocilizumabt and consider alternative agent (eg, anakinra or siltuximab) if persistent grade 3 CRS despite maximal dosing • If refractory hypotension/hypoxia, admit to ICU
Grade 4: Fever of ≥100.4°F with any of the following: Life-threatening consequences, urgent intervention required; requiring multiple pressors and/or positive pressure respiratory support or mechanical intubation	• Inpatient admission to ICU for hemodynamic monitoring, IV fluids, oxygen therapy, and vasopressors • A/P 1000 mg IV as needed up to 3-4 times daily when safe • Dexamethasone (eg, 20 mg IV every 6 h), until resolution to grade ≤1, followed by dexamethasone taper • Administer tocilizumab and if repeated doses of tocilizumab have been used, consider alternative agent (eg, anakinra or siltuximab) if persistent grade 4 CRS despite maximal dosing of first agent

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ICE questionnaire		
Ask the patient the following questions (1 point per question):		
What year is it?	1 point	
What month is it?	1 point	
What city are you in?	1 point	
What street do you live on?	1 point	
Naming 3 objects (1 point per object) Hold up 3 separate available objects and see if the patient can easily identify what the objects are		
Object 1	1 point	
Object 2	1 point	
Object 3	1 point	
Following simple commands (1 point total):		
*Raise your left hand *Raise your right hand *Touch your fingertip to your nose	1 point	
Writing standard sentence		
"The sky is blue, and the grass is green"	1 point	
Attention to count backwards from 100 by 10	1 point	
Total point score:		

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ICANS Management

Definition: neurological AEs after BsAb therapy most frequently consist of headache and dizziness; occasionally, ICANS-like symptoms occur; these may or may not accompany CRS
Symptoms: delirium, dysgraphia, tremor, lethargy, difficulty concentrating, agitation, confusion, expressive aphasia, apraxia, depressed level of consciousness, encephalopathy, and seizures
Recommendations: patients and caregivers need to be educated on symptoms and patients cannot drive or operate heavy machinery if symptomatic
Workup and evaluation:
- Pertinent history and PE
- Review medications including last dose of antipyretic therapy, steroids, or anticytokine therapy
- Perform ICE score on all patients with neurologic symptoms
- Assess for alternate cause of symptoms; consider performing CT head, EEG, MRI, or LP, as appropriate
- Assess for concurrent symptoms of CRS (fever, hypoxia, and hypotension); treatment of CRS can occur concurrently if appropriate
- If any concern for neurological AEs exists, patient should be evaluated in outpatient center or ED. If any worsening symptoms (eg, somnolence, worsening confusion, weakness, etc), patients should be promptly referred to the ED

ICE scoring system	
Orientation to year, month, city, hospital	4 points
Naming 3 objects	3 points
Following simple commands	1 point
Writing standard sentence	1 point
Attention to count backward from 100 by 10	1 point

ICANS grading	Management
Grade 1: ICE 7-9 or depressed level of consciousness but awakens spontaneously	• Pending clinical scenario and social situation, can consider observation or close monitoring in outpatient setting. Can consider dexamethasone 10 mg × 1
Grade 2: ICE 3-6 or depressed level of consciousness but awakens to voice	• Admit patient to hospital for monitoring • Dexamethasone 10 mg IV every 12 h, followed by taper once grade ≥1
Grade 3: ICE 0-2 or depressed level of consciousness but awakens to tactile stimulus or any clinical seizure that resolves rapidly or focal/local edema on neuroimaging	• Monitor in ICU setting • Neurology consult • Dexamethasone 10 mg IV every 6 h, followed by taper once grade ≥1 • Use antiepileptics for seizure management as needed • Consider adding anakinra 100 mg every 12 h if symptoms persist beyond 24 h, continue until resolution
Grade 4: ICE is 0 or patient is unarousable or requires vigorous or repetitive tactile stimuli, or life-threatening prolonged seizure (>5 min) or repetitive seizures without return to baseline or deep focal motor weakness or diffuse cerebral edema on neuroimaging	• Monitor in ICU setting • Neurology consult • Dexamethasone 10 mg IV every 6 h, followed by taper once grade ≥1 • Use antiepileptics for seizure management as needed • Consider adding anakinra 100 mg every 12 h if symptoms persist beyond 24 h, continue until resolution

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Consensus Recommendations on the Management of Toxicity Associated with CD3xCD20 Bispecific Antibody Therapy

Jennifer L. Crombie[1*], Tara Graff[2*], Lorenzo Falchi[3*], Yasmin Karimi[4*], Rajat Bannerji[5], Loretta Nastoupil[6], Catherine Thieblemont[7], Renata Ursu[8], Nancy Bartlett[9], Victoria Nachar[4], Jonathan Weiss[4], Jane Osterson[2], Krish Patel[10], Joshua Brody[11], Jeremy S. Abramson[12], Matthew Lunning[13], Nirav N. Shah[14], Ayed Ayed[15], Manali Kamdar[16], Benjamin Parsons[17], Paolo Caimi[18], Ian Flinn[19], Alex Herrera[20], Jeffrey Sharman[21], Marshall McKenna[5], Philippe Armand[1], Brad Kahl[9], Sonali Smith[22], Andrew Zelenetz[3], Elizabeth Budde[20*], Martin Hutchings[23*], Tycel Philips[4*], Michael Dickinson[24*]

https://doi.org/10.1182/blood.2023022432

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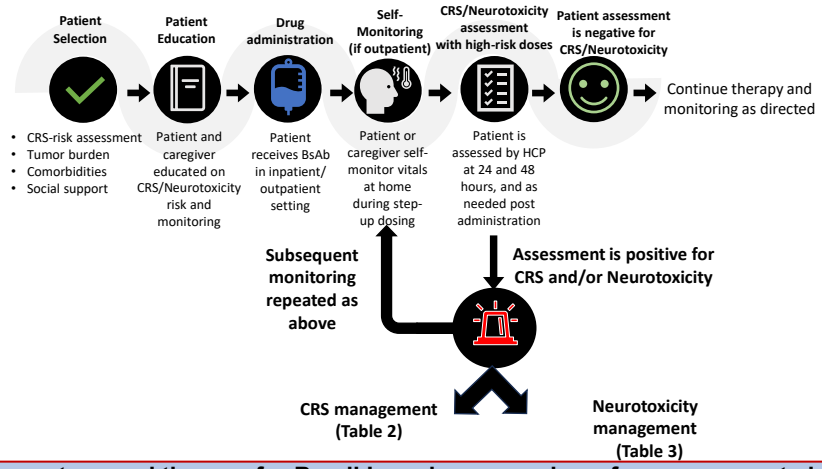
Bispecific Antibody (BsAb) Management in B-cell Lymphomas



- **BsAb represent a novel therapy for B-cell Lymphomas and a safe management plan for inpatient and/or outpatient use is essential.**
- *Crombie, **Graff** et al, Blood, DOI, PMID*

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Other Considerations

- Infection prophylaxis
- IVIG
- Toci for prophylaxis when appropriate, outpatient setting
- Educate on nuances

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Take-Home Points

- More drugs, more patients
- Nuances to all of these drugs—not all created the same
- Utilize like-mind sites
- Everyone needs to learn—cannot be a few people
- Time is now
- Ask questions, we all learn together

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Polling Question 8

How many Bispecific Antibodies are currently approved across all disease states?

a) Two
b) Three
c) Five
d) Eight

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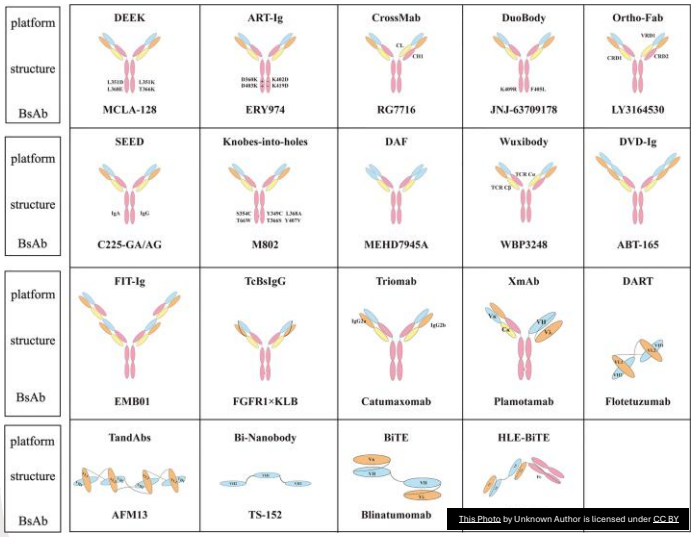
Thank You

Questions?



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Bispecific Nurse Management

For DLBCL, Follicular Lymphoma, and Multiple Myeloma

Michelle McDaniel, RN, CIONS President
Mission Cancer
Des Moines, IA

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Bispecific Medications Available

- **DLBCL**
  - Glofitamab (Columvi™)
  - Epcoritamab (Epkinly®)
- **Follicular Lymphoma**
  - Mosunetuzumab (Lunsumio™)
  - Epcoritamab (Epkinly®)
- **Multiple Myeloma**
  - Eltranatamab (Elrexfio®)
  - Teclistamab (Tecvayli®)
  - Talquetamab (Talvey®)
- **NSCLC**
  - Tarlatamab (Imdelltra™)

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How to Prepare for a Patient Receiving a Bispecific

- Patient must have a caregiver in the home to monitor for changes. If no caregiver available, they must be admitted.
- The patient must live less than 60 minutes from the treatment center or stay in a hotel or with family nearby.
- Nurse must review the medication list thoroughly. They cannot take any acetaminophen (Tylenol®) or NSAID containing products for 72 hours after administration. They will need acetaminophen (Tylenol®) and ibuprofen (Advil®) available if needed.
- Blood pressure medications also need to be addressed, if a patient is on 3-5 blood pressure medications, you may want to hold them or give strict parameters for when to take them.
- We must make sure we send in the “pill in the pocket” prior to them starting so they have it available.
- Make sure the correct phone numbers are in the chart for both the patient and the caregiver.
- Patient must have a thermometer, blood pressure cuff, and SpO_2 monitor at their initial appointment and show that they are competent in using them correctly.

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What is CRS?

Cytokine Release Syndrome (CRS) is an exaggerated systemic inflammatory response due to the binding of BsAb to its antigen on the surface of target cells, causing activation of immune (e.g., T-cells) and non-immune cells that results in the immense release of inflammatory cytokines.

Common Symptoms of CRS that we watch for

- Temperature (> 100.4°F)
- Blood pressure (Decrease in SBP > 10 mmHg and SBP < 90 mmHg)
- Heart rate (increased HR greater than 110 bpm)
- Rash (present)
- Oxygenation (90% or less or a > 5% change from last monitor)
- Sudden onset muscle pain/soreness
- General unwell feeling
- Headache
- Nausea
- Changes in mental status

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How to Monitor for CRS

- If inpatient, they are usually 1:1 nurse to patient ratio
- If outpatient, they must take their vital signs every 4 hours or as directed by the bispecific team
- On call staff will call the patient every 6 hours around the clock
- We will monitor with around the clock calls for 3 days following administration for C1. If they develop CRS during any of C1, we continue for C2D1
- We need to ask the questions to the patient or caregiver

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When to Bring Them In and How to Manage

- If 2 or more vitals are off from baseline, we will instruct them to come to the nearest treatment center
- Provide IVF
- Provide supplemental oxygen
- Give IV dexamethasone, famotidine (Pepcid®), diphenhydramine (Benadryl®)
- Monitor vitals every 15-30 minutes
- If no change in vitals or decrease stability — GIVE TOCI
- Monitor vitals for an additional 90 minutes; if still unstable or little to no change in vital signs = Admit!

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Case Study

Susan is a 71-year-old female with newly diagnosed Marginal Zone Lymphoma. CT shows splenomegaly and bone marrow biopsy shows that she has 20-25% involvement with Marginal Zone Lymphoma. You explain to her that, based on these findings, with her spleen bring primary white and marrow involvement, she needs treatment.

WHAT DO YOU CHOOSE FOR SUSAN?

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Starting Mosunetuzumab (Lunsumio™) Trial

You want to start Susan on mosunetuzumab (Lunsumio™) trial

What would be a concern for starting her on bispecific therapy?

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Polling Question 9

What Would Cause Concern for Starting Bispecific Therapy?

a) Living within 50 minutes of the nearest treatment center

b) Being able to demonstrate appropriate use of vitals equipment

c) Current smoker with no intent to stop

d) Living alone with no local family or friends

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Starting Mosunetuzumab (Lunsumio™)

- Susan received C1D1 of mosunetuzumab (Lunsumio™) 5 mg SQ injection. Your call team monitors her for the required 72 hours with no signs or symptoms of CRS/ICANS.
- You bring Susan back in for her ramp-up dosing of 45 mg SQ injection for C1D8.
- She was not feeling well today with low-grade temp, nausea, and fatigue, but this would only be a Grade 1 toxicity, even if it were CRS. Per protocol, she can proceed.
- On day two of your monitoring, you call Susan at 4PM, VS are as follows:
  BP — 134/84 P — 76 T — 98.8 SpO_2 — 98%
  She reports a very mild headache and back ache. VSS are stable, and you plan to call her back at the 10 PM check-in.
- You call Susan at 10 PM, VS are as follows:
  BP — 120/72 P — 98 T — 101.1 SpO_2 — 96%
  She reports chills and a headache and worsening back/body aches.

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Polling Question 10

What Do You Do?

a) Instruct Susan to go to her local ER for respiratory panel to R/O Flu/COVID?

b) Instruct Susan to take 1,000-1,300 mg of acetaminophen (Tylenol®) p.o. and call her back in 1 hour

c) Instruct Susan to do nothing and call her again at 5am check in

d) Instruct Susan to come into the closest treatment center to receive Toci

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What's Next?

Susan takes the 1,300mg of acetaminophen (Tylenol®) p.o. as instructed. You call her back at 11 PM for her 1 hour follow up. Her vitals at this time are:

- BP — 102/62
- P — 114
- T — 100.4
- SpO_2 — 96%

Susan complains of worsening fatigue and weakness, ongoing chills, rash at the injection site, and ongoing headache.

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Polling Question 11

What Do you Do Now?

a) Bring Susan in for closer monitoring and Toci

b) Have Susan take 16 mg of oral dexamethasone and have her come to the closest treatment center for closer monitoring and Toci

c) Explain to Susan that this is Grade 4 CRS and she needs to call 911 to be transported to her local ER

d) Instruct Susan to do nothing and call her back in 1 hour

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Bringing Susan In for Closer Monitoring

Susan arrives to the chemo suite at 12 AM; the on-call nurses and physician are there waiting for her.

She receives:

- 1L NS Bolus
- 20 mg of IV diphenhydramine (Benadryl®)
- 40 mg of IV famotidine (Pepcid®)

Vitals are monitored every 15 minutes. After an hour of monitoring. Susan's vitals are as follows:

- BP — 92/58
- P — 118
- T — 102.2
- SpO_2 — 98% on 2L NC

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TIME To Give Toci

At this point, patient has received everything we can give to help with CRS management without success. Vitals are worsening and she is not showing any improvement.
Your provider orders IV Toci to be given for her Grade 2 CRS.

You monitor Susan for another 90 minutes in the chemo suite after the Toci has been infused.

It is now 2 AM and her vitals are as follows:

- BP — 122/78
- P — 92
- T — 99.8
- SpO_2 — 96% on RA

Susan states her pain in her back and head are completely gone. She is stating that she is relieved of all of her prior symptoms, and she wants to go home and sleep. You discharge Susan home and instruct her to take her vitals again at 5 AM, and we will continue the monitoring calls from home.

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Follow Up

Susan is able to get through the rest of C1D8 without issues. She did have Grade 2 CRS that was able to be treated on an outpatient basis. Susan completes the rest of C1 while being monitored from home and does not develop any additional CRS symptoms. Susan completes all 17 cycles of her mosunetuzumab (Lunsumio™) trial.

Susan has a PET scan and bone marrow biopsy 1-2 months post completion of her bispecific therapy. There is no evidence of recurrent lymphoma seen on PET scan or BMBX.

Susan's scans continue to show NED 2 years post completion of her bispecific therapy!

YAY!!!!

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Questions?

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INNOVATIONS IN BLOOD CANCER TREATMENT: NAVIGATING CAR T-CELL AND BISPECIFIC THERAPIES

THANK YOU!

We have one goal: A world without blood cancers

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