CAR T-CELL AND BISPECIFIC THERAPIES: CLINICAL APPLICATIONS AND NURSING MANAGEMENT

DERIVED FROM THE LIVE ACTIVITY WHICH OCCURRED ON APRIL 26, 2024.

Supported by an educational grant from Bristol Myers Squibb.

Held in conjunction with the Oncology Nursing Society's 49th Annual Congress

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WELCOME AND INTRODUCTIONS

Lauren Berger, MPH
Senior Director
Professional Education & Engagement
The Leukemia & Lymphoma Society
Rye Brook, NY

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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) 49th Annual Congress, April 24 – April 28, 2024 in Washington, DC. The Oncology Nursing Society's assignment of meeting space does not imply product endorsement.

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Educational Objectives

At the conclusion of this symposium, participants will be able to:

- Describe the role of CAR T- cell therapy and bispecifics in treating blood cancer
- Apply knowledge of communication strategies, streamlined patient assessment, disparities in care, and strategies for multidisciplinary teams to improve patient-centered care
- Explain data surrounding CAR T-cell and bispecific therapies including their proper application, efficacy, and adverse events, and resources to support patients and their caregivers
- Optimize patient assessment to ensure effective, individualized patient care including implementation of bridging therapy when indicated
- Utilize appropriate tools to properly assess risk for progression and response to cellular therapies

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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 of the Pediatric Hematology and Oncology Patient (CPHON), Cellular Collection, Preparative Regimens, and Infusion (BMTCN), Early Post-Transplant Management and Education (BMTCN), Foundations of Transplant (BMTCN), Late Post-Transplant Management and Education (BMTCN), Oncologic Emergencies (OCN, CPHON, AOCNP), Professional Practice/Performance (BMTCN, AOCNP), Psychosocial Dimensions of Care (AOCNP, CPHON, ONC, CBCN), Quality of Life (BMTCN), Symptom Management, Palliative Care, Supportive Care (OCN, CPHON, AOCNP), Transplant Process and Infusion (BMTCN), Treatment (OCN, CBCN, AOCNP, CPHON).

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 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.

Nurse Practitioner Continuing Education

This education activity will be submitted to the American Association of Nurse Practitioners® for approval of up to XX contact hours of accredited education

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 leukemia, lymphoma, Hodgkin's disease and myeloma, and improve the quality of life of patients and their families.

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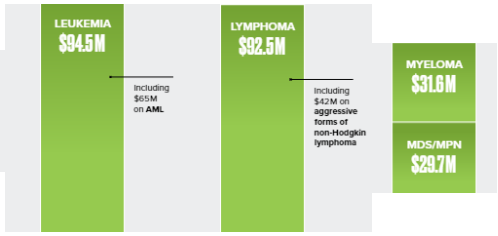
Breakthrough Research: Improving Treatments and Enhancing Quality of Life

LLS HAS INVESTED MORE THAN
$1.7 BILLION
IN RESEARCH FOR ALL TYPES OF BLOOD CANCER SINCE OUR FOUNDING

LLS HELPED ADVANCE MORE THAN
70%
OF THE BLOOD CANCER TREATMENTS APPROVED BY THE FDA OVER THE LAST 2 DECADES

RESEARCH INVESTMENT
$248.3 MILLION
in multi-year research commitments for all forms of blood cancer



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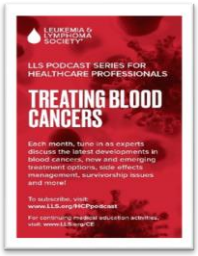
Free LLS Resources for Healthcare Providers

- 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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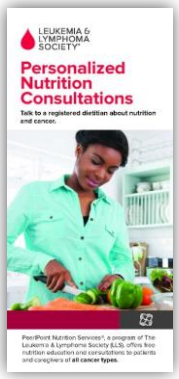
Free LLS Resources for Patients

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

- **Clinical Trial Nurse Navigators** – RNs 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

- **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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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 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

Jessica Kassay-McAllister DNP, RN, AGACNP-BC, has no financial relationships with ineligible companies.

Krithika Shanmugasundaram, MD, has no financial relationships with ineligible companies.

Dan T. Vogl, MD, MSCE, has financial relationships with the following companies:

Advisory Board/Consultant: AbbVie, CSL Behring, Genentech, Takeda
Research/Grant: Active Biotech, Takeda

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CAR-T and Bispecific Antibody Therapies

Jessica Kassay-McAllister, DNP, AGACNP
Krithika Shanmugasundaram, MD
Dan Vogl, MD

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Myth Busting Question

Patients requiring chronic narcotic pain management are not candidates for CAR-T or bispecific antibodies.

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Myth Busting Question

CAR T cells are clearly more effective for myeloma than bispecific antibodies.

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Myth Busting Question

You should avoid using steroids ever with CAR-T cells or bispecific antibodies because it decreases the efficacy of treatment.

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Myth Busting Question

Bispecific antibodies for myeloma are too dangerous and complicated to give in a community practice.

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Myth Busting Question

Patients with delirium who are within 30 days of CAR-T therapy should not receive steroids as it will make the delirium worse.

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Learning Objectives

- Describe the role of CAR T- cell therapy and bispecifics in treating blood cancer
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- Utilize appropriate tools to properly assess risk for progression and response to cellular therapies

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Agenda

- Mechanism of CAR T-cell therapy
- Indications and Efficacy
- Toxicities of CAR
- Barriers to Access

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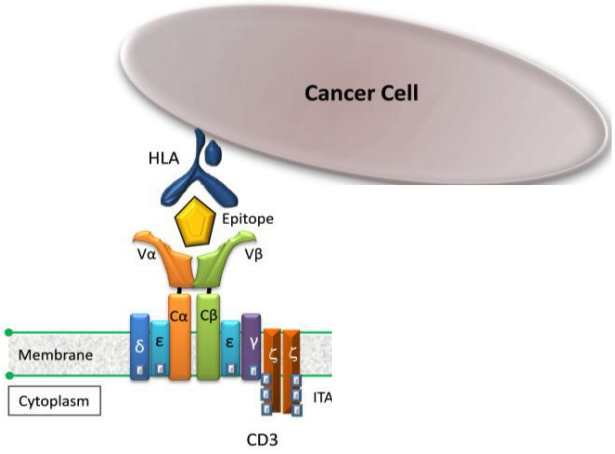
Harnessing the Immune System



T-Cell Receptor (TCR)

1. Fujiwara, Hiroshi. "Adoptive immunotherapy for hematological malignancies using T cells gene-modified to express tumor antigen-specific receptors." *Pharmaceuticals* 7.12 (2014): 1049-1068.

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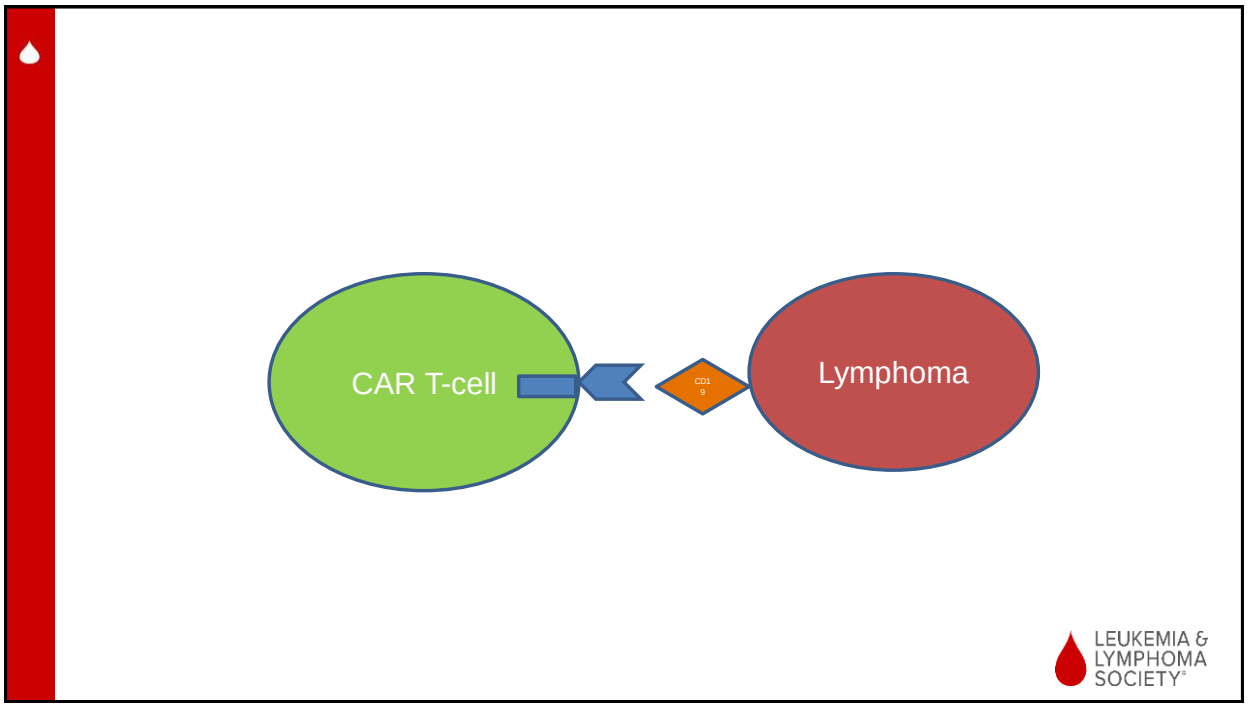
CAR T-cell
CD19
Lymphoma
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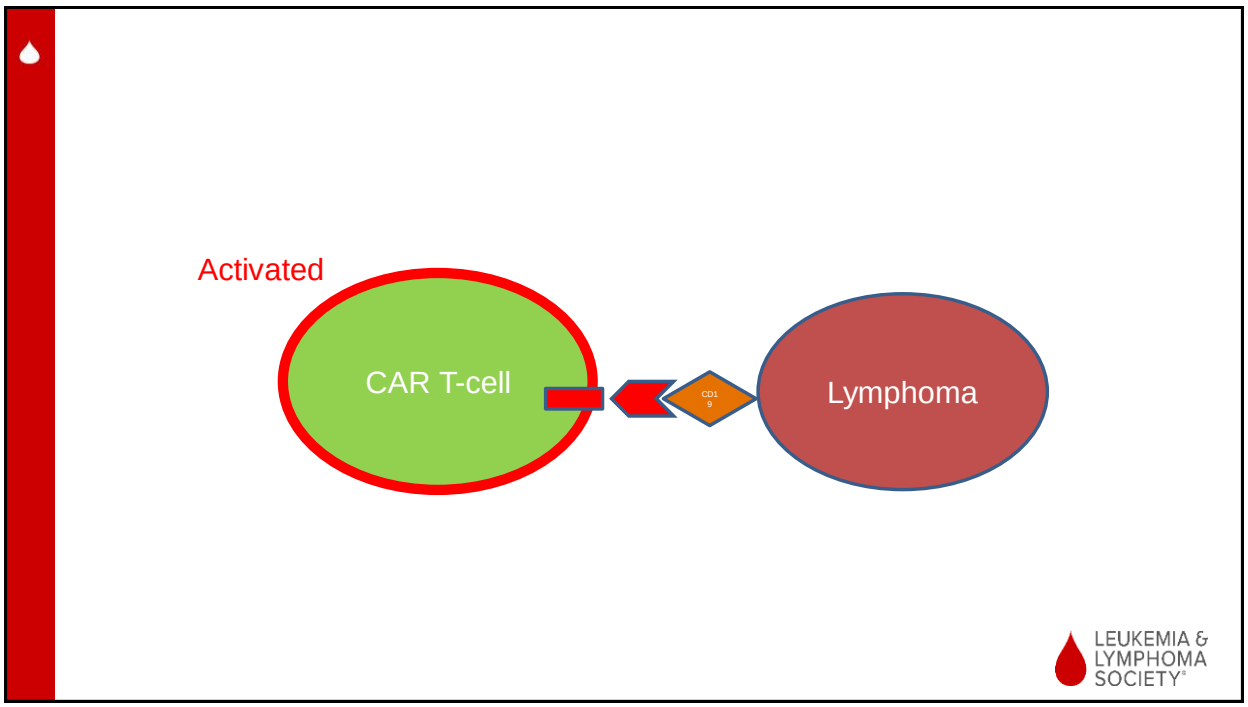
Activated
CAR T-cell
CD19
Lymphoma
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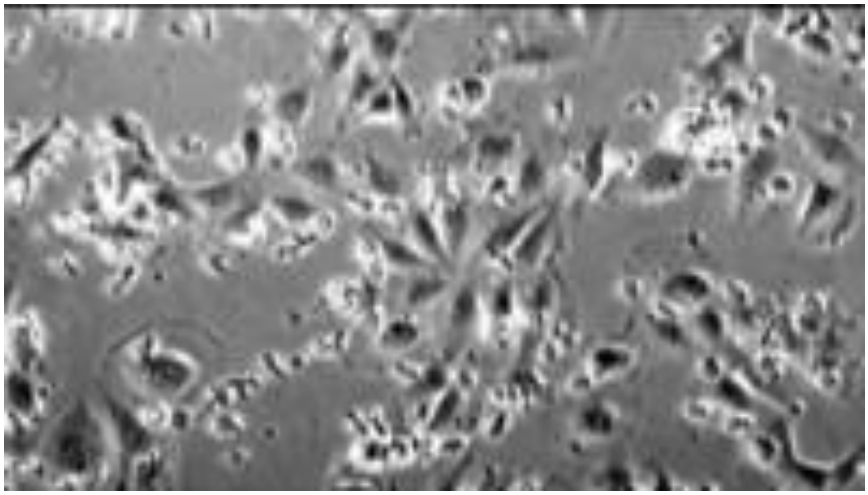

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Indications

- **B-ALL**
- **Multiple Myeloma**
- **NHL**
  - DLBCL
  - Follicular lymphoma
  - Mantle Cell Lymphoma (MCL)
  - CLL

ALL IN RELAPSED/REFRACTORY SETTING

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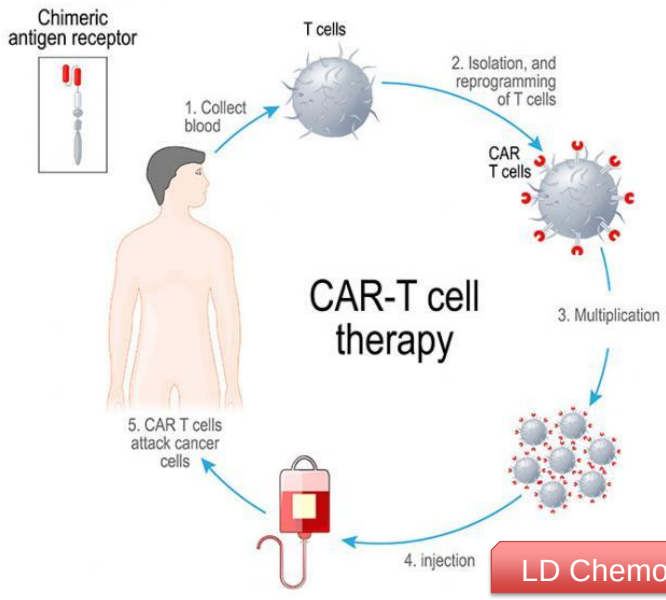

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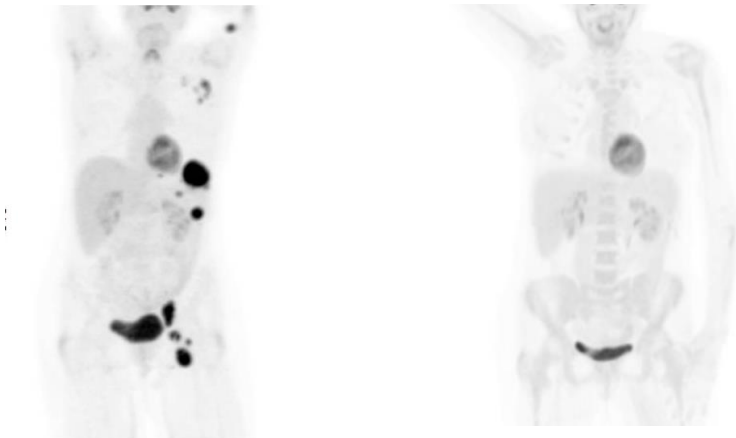
Response

53 yoF with R/R DLBCL **2 months post**



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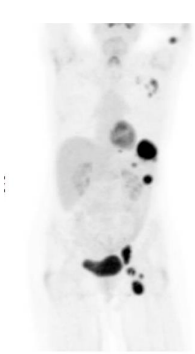
Case Study

54 yoM with diagnosis of DLBCL, NOS



R-EPOCH x6C

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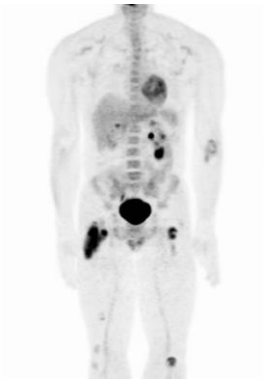
Case Study

2.5 years later - Relapsed



Auto Txplt?

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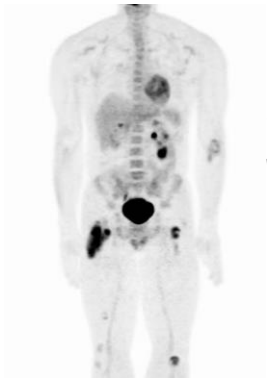
Case Study

2.5 years later - Relapsed



R-ICE x1 → Progressive disease

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R/R Large B-cell Lymphoma

FDA-approved in 3rd line setting

1) Tisagenlecleucel (Kymriah®)

2) Axicabtagene Ciloleucel (Yescarta®)

3) Lisocabtagene Autoleucel (Breyanzi®)

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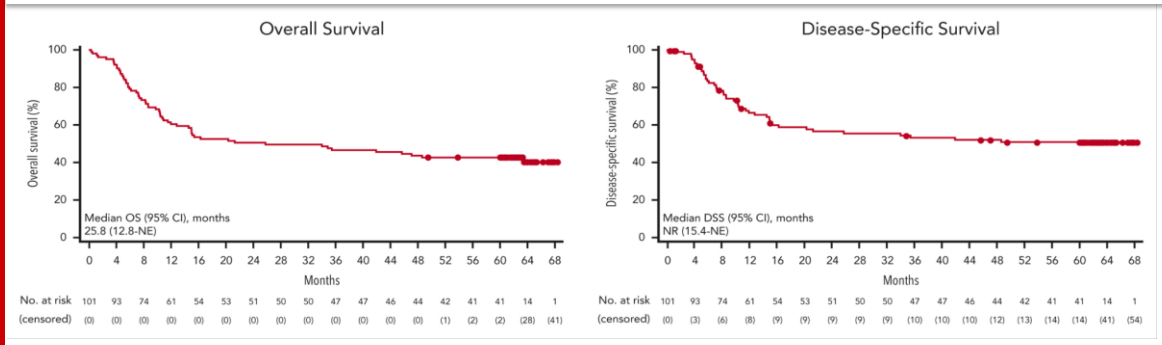
Long-Term Survival With Axi-Cel in Patients with Refractory Large B-Cell Lymphoma



Functionally, this is a cure!

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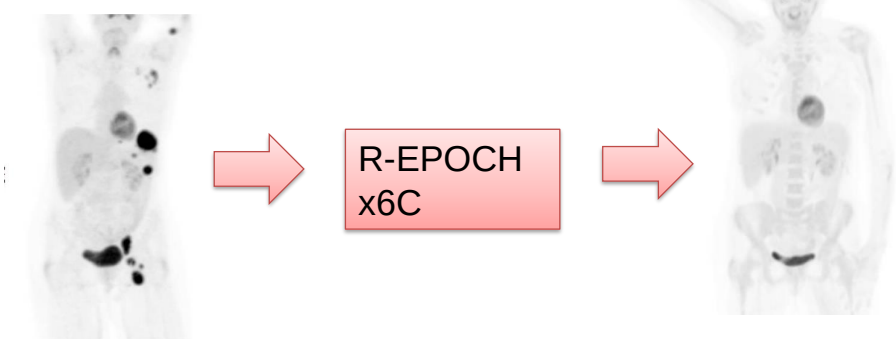
Case Study

72 yoM with diagnosis of DLBCL, NOS



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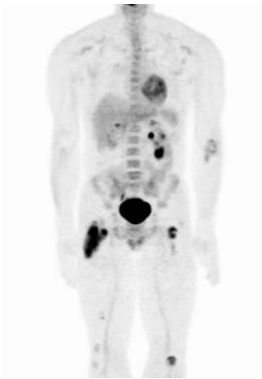
Case Study

2 years later, now 74 yo age



Auto-Transplant?

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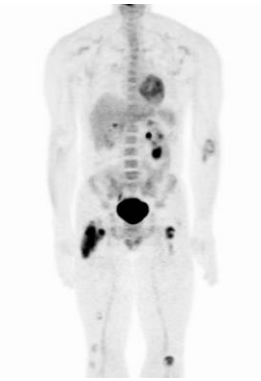
Case Study

2 years later, now 74 yo age



Liso-Cel

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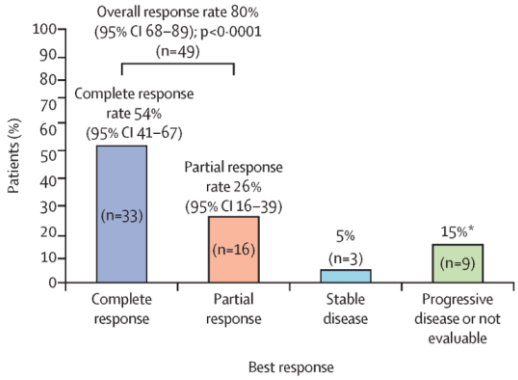
R/R DLBCL, TNE patients

PILOT Study: Transplant-ineligible patients

- **Age >70**
- **Co-morbidities**



Seghal et al, Lancet Oncology, 2022

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R/R DLBCL, TNE patients

PILOT Study: Transplant-ineligible patients

- **Age >70**
- **Co-morbidities**

- **Adverse Events:**
  - No Grade 4 or 5 CRS
  - No Grade 4 or 5 ICANS
  - 4 pts with grade 3 neutropenia (7%)
  - No treatment-related deaths

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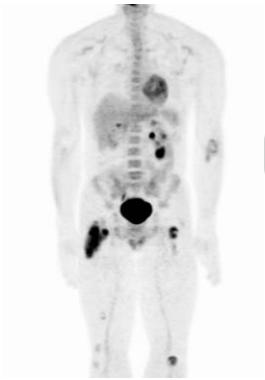
Case Study

Evaluate for Response?



Liso-Cel

PET within 3 months

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Toxicities

- Tumor Lysis Syndrome (TLS)
- Cytokine Release Syndrome (CRS)
- Immune Effector Cell Associated Neuro-toxicity Syndrome (ICANS)
- Late complications: pancytopenia and hypogammaglobinemia

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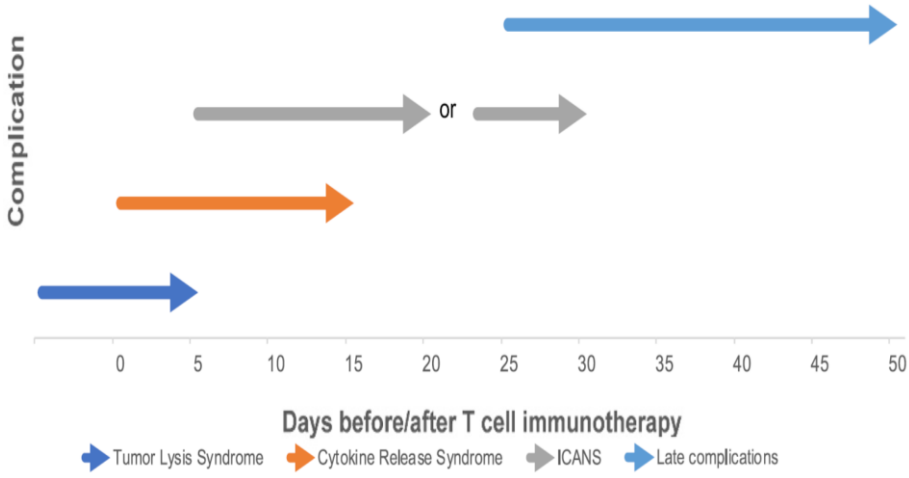
Timeline of Complications



Varadarajan, I. and Lee, D.W., 2019. Management of T-Cell Engaging Immunotherapy Complications. *The Cancer Journal*, *25*(3), pp.223-230.

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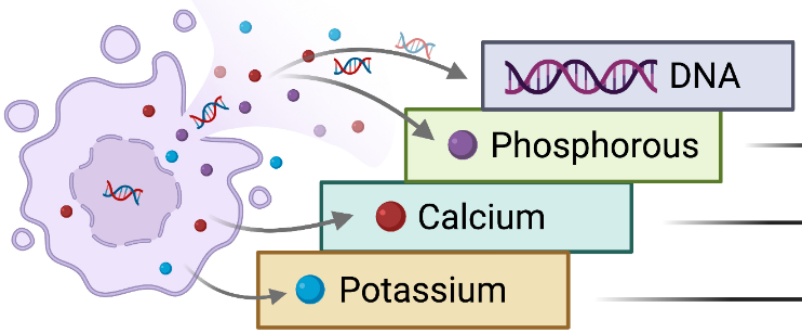
Tumor Lysis Syndrome

When cancer cells die, or "lyse" they release their contents into the blood:



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Tumor Lysis Syndrome

- Arrhythmia
- Renal Injury
- Muscle Weakness, spasm
- Seizure

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Cytokine Release Syndrome (CRS)

- Systemic inflammatory response caused by the release of inflammatory cytokines.
- Spectrum of clinical features from fevers to multiorgan failure.

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Polling Question

When CRS is suspected, there is no need to perform an infectious workup. True or False?

A. True
B. False

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Polling Question

CRS is characterized by extreme inflammatory response triggered by increased IL-2, IL-6, tumor necrosis factor-alpha and other inflammatory cytokines. ____ is a required initial finding to diagnose CRS of any grade.

A. Rash
B. Neutropenia
C. Fever
D. Hypotension

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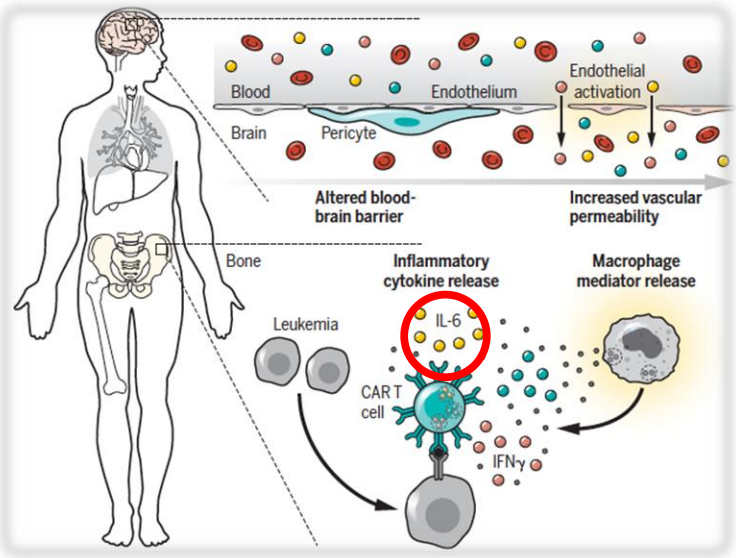
CRS



June C, Science 2018

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Constitutional
- Fever ± rigors
- Malaise/fatigue
- Myalgias
- Arthralgias
- Headache

CRS symptoms

Riegler, L.L., Jones, G.P. and Lee, D.W., 2019. *Therapeutics and clinical risk management*, *15*, p.323.

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CRS

- CRS : 70-98% of patients
- Median time to onset is ~ 5 days (range, 1-12 days)

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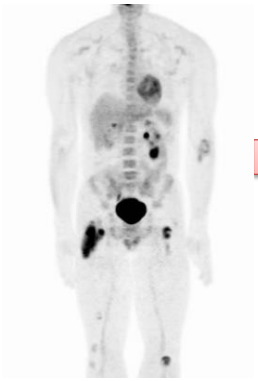
Case Study



Liso-Cel

12 hours after infusion of CAR T-cells, noted T 101.5F

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Evaluation of Patient

- **Vitals:** 101.5F, HR 122, BP120/80, and O2 sat 87% on RA
- **Exam:**
  - Tachycardic with regular rhythm
  - Port noted under skin to R chest with erythma. Not ttp, no obvious fluctuance.
  - Abdomen nontender/nondistended
  - Appropriate neurologically but tired appearing

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Workup/Treatment

- **Infectious Workup**
  - BCx, imaging, urine cx, line assessment
- **Treatment**
  - Antibiotics if neutropenic/HD instability
  - Tocilizumab (anti-IL6)
  - Steroids
  - Consider ICU consult

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Workup/Treatment

- **Infectious Workup**
  - BCx, imaging, urine cx, line assessment
- **Treatment**
  - Antibiotics if neutropenic/HD instability
  - **Tocilizumab (anti-IL6)**
  - **Steroids**
  - Consider ICU consult

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Severity of CRS

Grade 1-4

- Grade 1: fever
- Grade 2: fever + hypoxia (NC)
- Grade 3: fever + **hypoxia (HFNC) or vasopressors**
- Grade 4: intubated or on multiple pressors **(ICU)**

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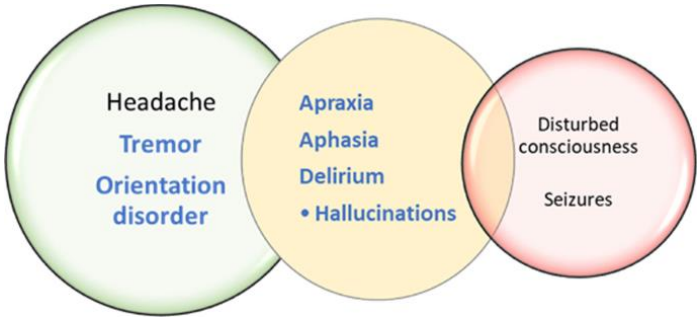
Immune Effector Cell Associated Neurotoxicity (ICANS)



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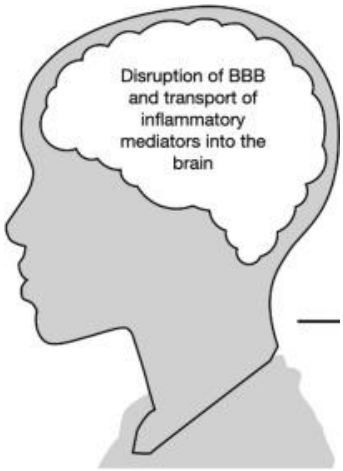
ICANS – Encephalopathic State

Can range from mild tremors to seizures and loss of consciousness

Early signs are diminished attention, mild aphasia, and/or handwriting changes



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Risk Factors

- Tumor burden
- CNS involvement
- Age
- KPS

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ICANS

- Occurs in 30-35% of patients
  - associated with high-grade CRS and high-disease burden
- Delayed ICANS is classified by seizure activity or episodes of confusion that occur, in roughly 10% of this population, between 14-28 days following the infusion (Schuster, 2019)

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Case Study

Our patient is now day +14: acutely confused, agitated, became aggressive with partner and staff

Next Steps? Differential?

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Next Steps

Consider

- ICANS
- Infection
- Medication/sedation
- Delirium

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ICE Score

Out of 10 points

- Orientation (person, place, date mo/year)
- Name 3 objects
- Follow 2 commands
- Write a sentence
- Counting backwards by 10s

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ICE Score

ICE	Question	Points
Orientation	Year, Month, city, hospital	4
Naming	Ability to name 3 objects	3
Following commands	Follow 2 simple commands	2
Attention	Count backwards from 100 by 10	1
Writing	Write a simple sentence	1

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ICANS Grading

Neurotoxicity Domain	Grade 1	Grade 2	Grade 3	Grade 4
ICE score	7-9	3-6	0-2	0 – Unable to perform ICE

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ICANS Grading

Neurotoxicity Domain	Grade 1	Grade 2	Grade 3	Grade 4
ICE score	7-9	3-6	0-2	0 – Unable to perform ICE
Depressed level of consciousness	Spontaneous awakening	Awakens to voice	Awakens only to tactile stimulus	Not arousable to tactile stimulus, Coma

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ICANS Grading

Neurotoxicity Domain	Grade 1	Grade 2	Grade 3	Grade 4
ICE score	7-9	3-6	0-2	0 – Unable to perform ICE
Depressed level of consciousness	Spontaneous awakening	Awakens to voice	Awakens only to tactile stimulus	Not arousable to tactile stimulus, Coma
Seizure	N/A	N/A	Any clinical or non convulsive seizures that resolve with Intvn	Prolonged seizure >5 mins. EEG activity –not resolving with Intvn

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ICANS Grading

Neurotoxicity Domain	Grade 1	Grade 2	Grade 3	Grade 4
ICE score	7-9	3-6	0-2	0 – Unable to perform ICE
Depressed level of consciousness	Spontaneous awakening	Awakens to voice	Awakens only to tactile stimulus	Not arousable to tactile stimulus, Coma
Seizure	N/A	N/A	Any clinical or non convulsive seizures that resolve with Intvn	Prolonged seizure >5 mins. EEG activity –not resolving with Intvn
Motor Findings	N/A	N/A	N/A	Hemiparesis, paraperisis
Elevated ICP/Cerebral edema	N/A	N/A	Focal or Local edema on Neuro-image	Diffuse cerebral edema on imaging

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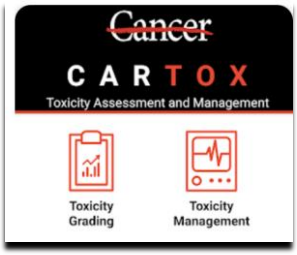
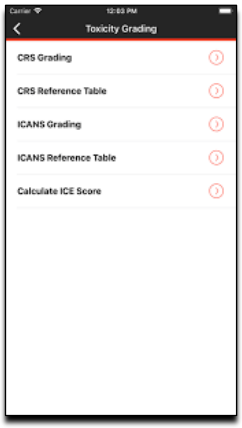
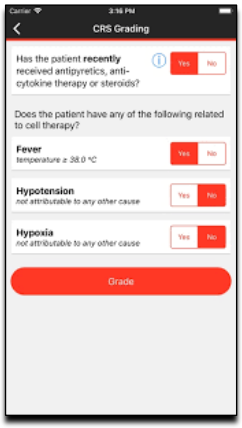
Cartox App







Developed by Sherry Adkins, RN, MSN, ANP-C
The University of Texas MD Anderson Cancer Center

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Next steps -ICANS

- CT Head, MRI Brain as soon as possible
- Start on steroids
- Ophtho consult -> papilledema
- Neuro Onc consult

Consider

- Infection -> cultures, imaging, abx if neutropenic
- Medication/sedation-> review, decrease polypharmacy
- Delirium -> PT/OT, reorientation

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Common Barriers to CAR T

- Insurance
  - ~$300,000 to $450,000 per product
- Caregiver
- Lodging
- Disease status

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Myeloma Case – Part 1

- 60 year-old woman with no sig PMHx, presenting with fatigue, back pain, vertebral compression fractures, anemia, hypercalcemia, monoclonal gammopathy, and bone marrow plasmacytosis

- **2017 Treatment line 1**:
  - VRd with VGPR
  - MEL ASCT with CR
  - Len maintenance x2 years
- **2019 Treatment line 2:**
  - Dara/carfilzomib/dex with PR and progression
- **2020 Treatment line 3:**
  - elotuzumab/pomalidomide/dex with PR and progression
- **2021 Treatment line 4:**
  - Cyclophosphamide/bortezomib/dex with PD
- **2021 Assessed for ide-cel**
  - T cell apheresis
  - Bridging therapy with selinexor/car/pom/dex
  - LD chemo with fludarabine/cyclophosphamide

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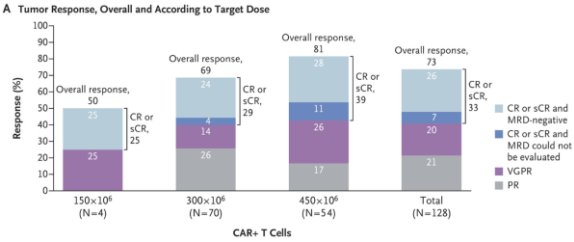
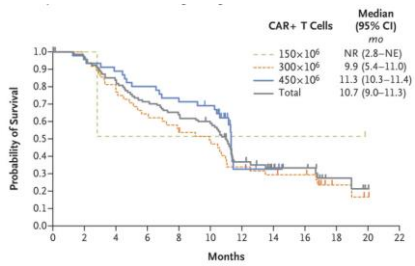
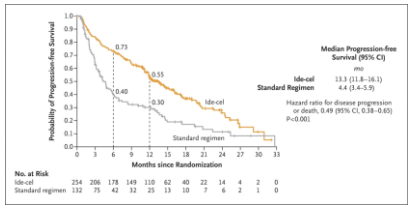
Ide-cel (KarMMA studies)







Munshi et al., N Engl J Med 2021; 384:705-716
Rodriguez-Otero P et al. N Engl J Med 2023;388:1002-1014

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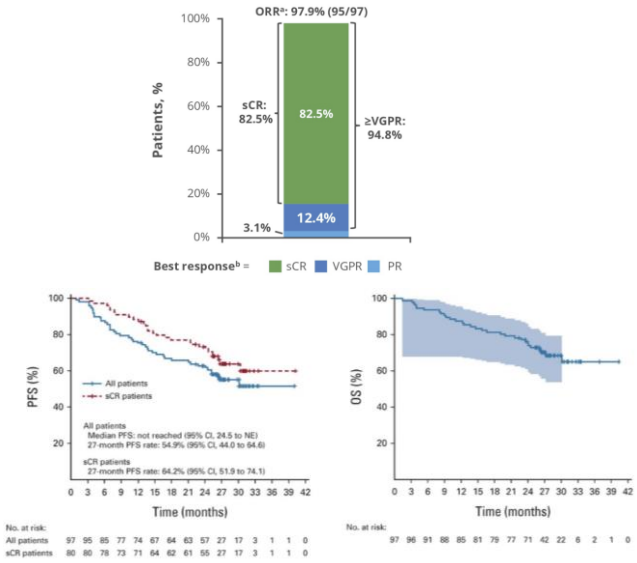
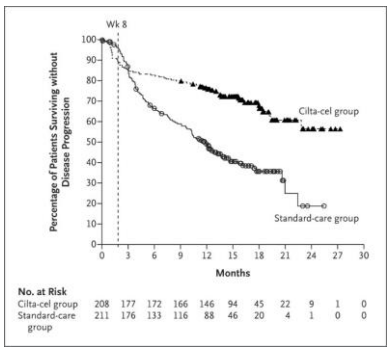
Cilta-cel (CARTITUDE studies)





San-Miguel J et al. N Engl J Med2023;389:335-347

Martin et al., DOI: 10.1200/JCO.22.00842 *Journal of Clinical Oncology* 41, no. 6 (February 20, 2023) 1265-1274.

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Ide-cel and Cilta-cel for Myeloma

- Same inpatient toxicities as other CAR T cells
  - CRS
  - ICANS
  - Cytopenias
  - Fevers
- Same management of toxicities
  - Toci for CRS
  - Steroids for ICANS
- Differences
  - Timing of CRS
    - ide-cel: typically day 0-1
    - cilta-cel: typically day 5-10
- Late toxicities
  - Cytopenias (especially with ide-cel)
  - Neurologic toxicities (especially with cilta-cel)
    - Peripheral neuropathy
    - Nerve palsies
    - Guillain-Barre Syndrome
    - Parkinsonian Syndrome

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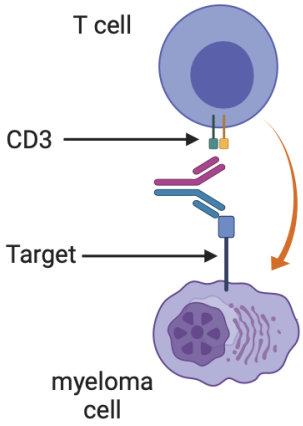
Bispecific Antibody

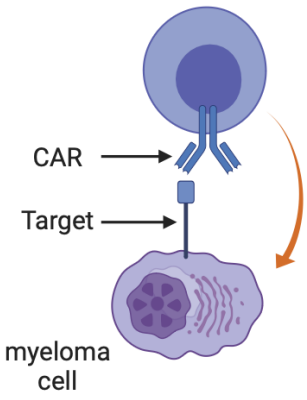
BCMA
Teclistamab*
Elranatamab*
Limvoseltamab
Alnuctamab
ABBV-383

GPRC5D
Talquetamab*
Forimtamig

FCRH5
Cevostamab



CAR T Cell



BCMA
Ide-cel*
Cilta-cel*
PHE-885
BMS-986354
GC012F
ALLO-715
CART-ddBCMA

GPRC5D
BMS-986393
MCARH109

*Therapies with marketing authorization

Image created with BioRender.

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Myeloma Case – Part 2

- **60 year-old woman with IgG lambda myeloma**
  - Line 1: VRd -> MEL ASCT -> Len maint
  - Line 2: Dara/carfilzomib/dex
  - Line 3: elotuzumab/pomalidomide/dex
  - Line 4: Cyclophosphamide/bortezomib/dex
- **2021 ide-cel**
  - Bridging with selinexor/car/pom/dex
  - Cytopenias lasting 3 months, requiring intermittent transfusions and G-CSF, then resolved
  - Myeloma response: VGPR for 15 months, then progression
- **12/2022: teclistamab**
  - Admitted for step-up dosing
  - Grade 2 CRS treated with tocilizumab
  - Grade 1 ICANS treated with steroids
  - Myeloma response sCR x1 year

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Using Bispecific Antibodies in Clinical Care: Managing Toxicity

- **Cytokine release syndrome / ICANS**
  - Step-up dosing requires expertise in identifying and managing CRS and ICANS
  - Tocilizumab is an important component of the management of CRS
    - Not mentioned in the package inserts or REMS programs
    - Used in 36% of patients in the phase 2 trial of teclistamab
- **Neutropenia**
  - 64% grade 3/4 with teclistamab
  - Consider CMV reactivation
  - Concomitant supportive G-CSF is effective
- **Infection risk**
  - Profound immune paresis: Use IVIG supplementation to maintain IgG > 400 mg/dL
  - Risk of shingles: Use acyclovir or valacyclovir
  - Pneumocystis pneumonia: Use TMP-SMX

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Infection Risk

CAR T cells may not confer more infection risk than other MM therapies

Infection risk on Phase 3 CAR T studies for MM

	CAR T		Standard Care	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
CARTITUDE-4	62%	27%	71%	25%
KARMMA-3	58%	29%	54%	20%

San Miguel et al., N Engl J Med 2023;389:335-34
Rodriguez-Otero et al., N Engl J Med 2023;388:1002-1014

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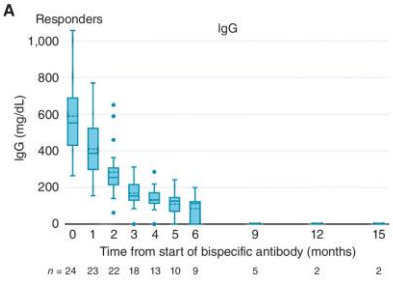
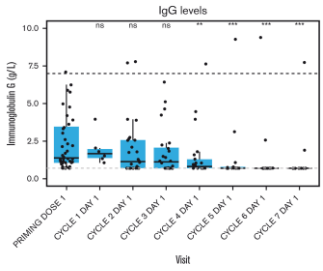
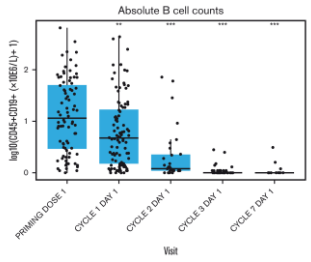
Infection Risk

- CAR T cells may not confer more infection risk than other MM therapies
- Continuously dosed anti-BCMA bispecific antibodies have significant infection risk







Lancman et al., Blood Cancer Discov (2023) 4 (6): 440–451.
Frerichs et al., Blood Advances, 8(1):194
Nooka et. Al., Cancer https://doi.org/10.1002/cncr.35107 2023

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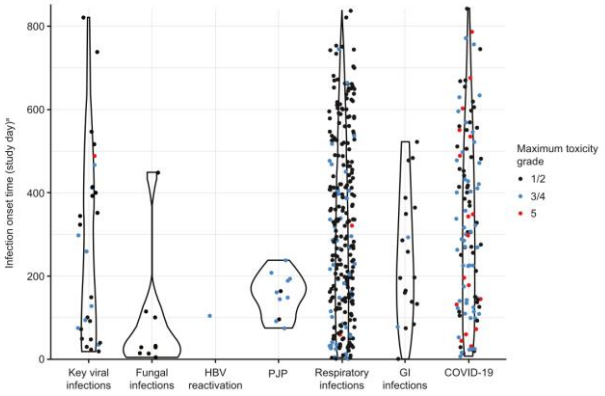
Infection Risk

- CAR T cells may not confer more infection risk than other MM therapies
- Continuously dosed anti-BCMA bispecific antibodies have significant infection risk



Lancman et al., Blood Cancer Discov (2023) 4 (6): 440–451.
Frerichs et al., Blood Advances, 8(1):194
Nooka et. Al., Cancer https://doi.org/10.1002/cncr.35107 2023

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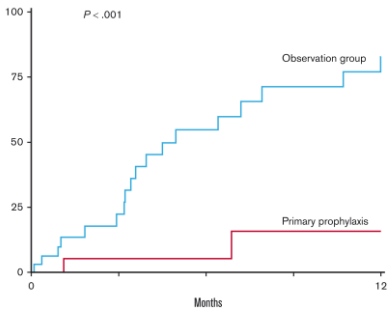
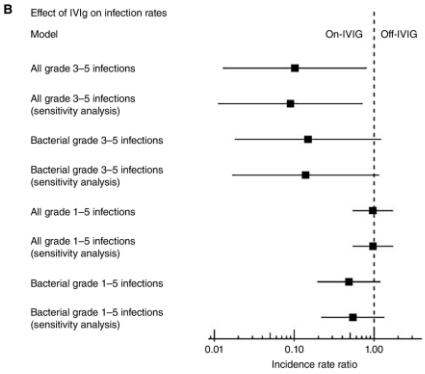
Infection Risk

- CAR T cells may not confer more infection risk than other MM therapies
- Continuously dosed anti-BCMA bispecific antibodies have significant infection risk

IVIG likely significantly reduces the risk of severe infection on anti-BCMA bsAb





Lancman et al., Blood Cancer Discov (2023) 4 (6): 440–451.
Frerichs et al., Blood Advances, 8(1):194
Nooka et. Al., Cancer https://doi.org/10.1002/cncr.35107 2023

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Polling Question 5

Which premedications need to be given for myeloma bispecifics during routine outpatient administration**:**

A. steroids
B. diphenhydramine
C. acetaminophen
D. all of the above
E. none of the above

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Using Bispecific Antibodies: Administration and Dosing

- **Location**
  - Initial dosing should be given at a center with expertise in management of CRS
    - Typically inpatient dosing, but outpatient can be considered with appropriate resources
  - Ongoing dosing can be continued in the community (outpatient, no premeds, no observation)
- **For teclistamab: consider q2 week dosing**
  - Per package insert: weekly dosing
  - Clinical trial permitted Q2 week dosing after 6 months in complete response
  - Penn plan: change to Q2 week dosing at best response
- **Consider outpatient rechallenge after dose interruption**
  - Per package insert: repeat inpatient step-up dosing (0.06→0.3→1.5) after delay of >28 days
  - Penn plan: outpatient single dose of 0.3 mg/kg → 1.5 mg/kg weekly

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Myeloma Case – Part 3

- **60 year-old woman with IgG lambda myeloma**
  - Line 1: VRd -> MEL ASCT -> Len maint
  - Line 2: Dara/carfilzomib/dex
  - Line 3: elotuzumab/pomalidomide/dex
  - Line 4: Cyclophosphamide/bortezomib/dex
  - Line 5: ide-cel
- **12/2023: teclistamab**
  - Myeloma response sCR x1 year
  - Progressive disease with extramedullary plasmacytomas, biopsy shows no BCMA expression
- **12/2023: talquetamab**
  - Admitted for step-up dosing
  - Grade 1 CRS, no ICANS
  - Myeloma response: sCR ongoing @5 months
  - Severe dysgeusia, mild palmar desquamation

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Management of Talquetamab Toxicities

- **Oral and taste toxicities**
  - Dysgeusia
  - Dry mouth
  - Dysphagia
  - Weight loss
- **Management**
  - saliva substitute sprays and rinses
  - dose holds & adjustments
  - dietary modifications
  - good oral care
- **Skin and nail toxicity**
  - Dry skin
  - Hand or foot peeling
  - Nail thinning and peeling
  - Pruritis
  - Diffuse macules and papules
  - Injection site reactions
- **Management**
  - Moisturizing lotions
  - Ammonium lactate for peeling
  - Nail hardeners and topical vitamin E
  - loratadine
  - topical steroids

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Questions?

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CAR T-CELL AND BISPECIFIC THERAPIES: CLINICAL APPLICATIONS AND NURSING MANAGEMENT

Thank you for joining us.

Held in conjunction with the Oncology Nursing Society's 49th Annual Congress

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Slides for Reference

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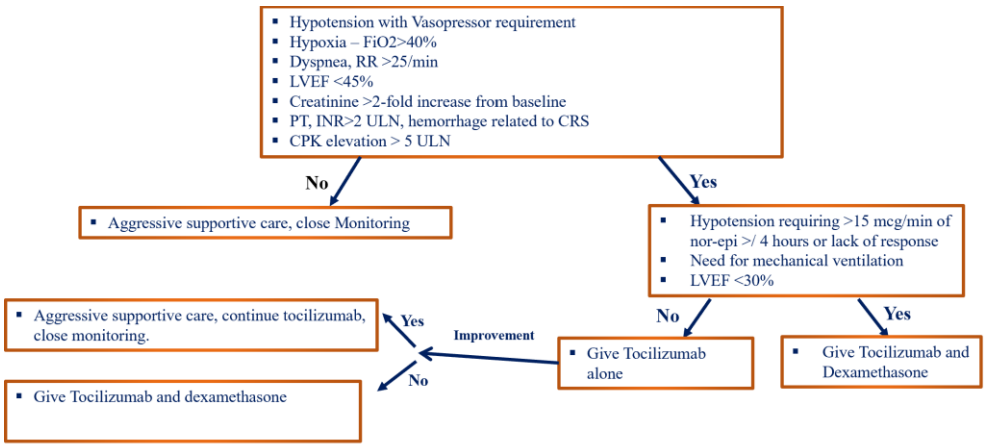
CRS Management Algorithm



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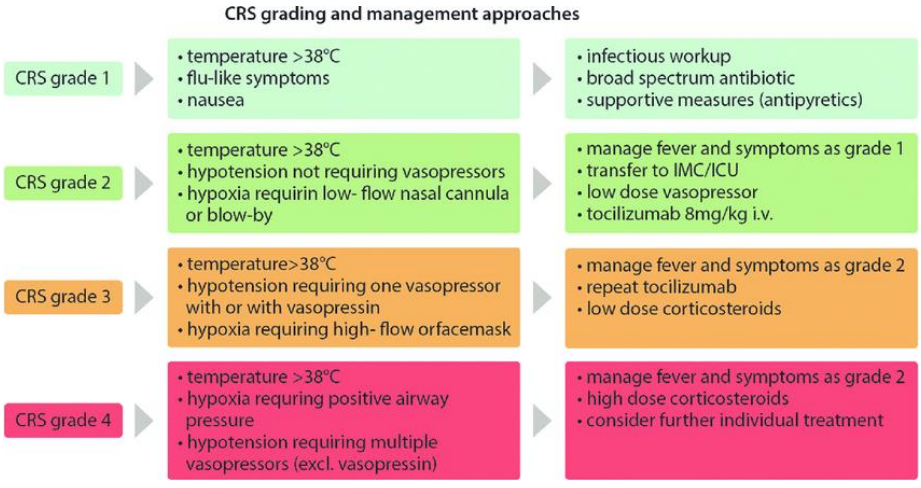
CRS Grading



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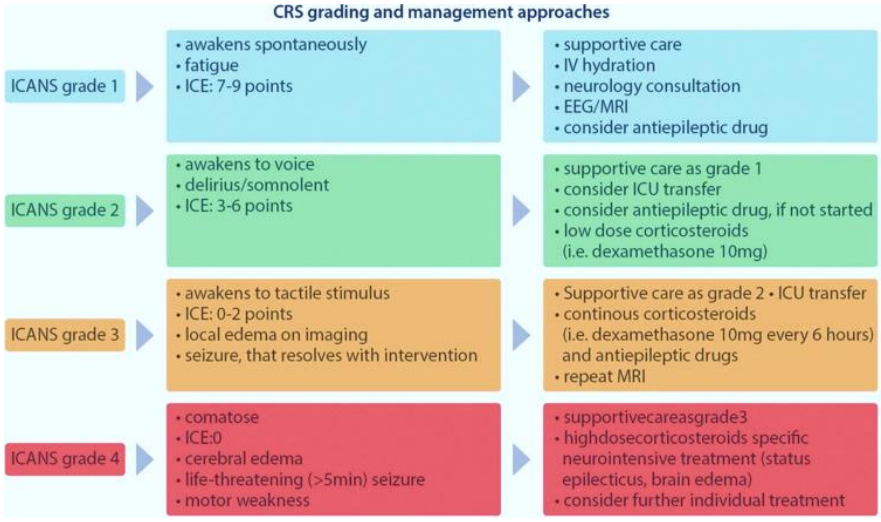
ICANS CONT…



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ASTCT ICANS Grade	Management
Grade 1	-Consider seizure prophylaxis with levetiracetam if not already started. -Review of medications, avoid medications that can cause CNS depression. -Swallowing assessment and aspiration precautions. -Neurocognitive assessment Q6hrs using ICE scoring system. -Neurology consult. -Consider EEG. -Consider lumbar puncture with opening pressure and samples for chemistry, cytology, virology, & culture. -Brain imaging (MRI preferred if no contraindication). Spinal MRI based on neurological findings. -For febrile patients, infectious workup per institutional guidelines. -Consider tocilizumab if concurrent CRS.
Grade 2	-Supportive care and workup per Grade 1. -Consider dexamethasone 10mg IV every 6hrs or methylprednisolone equivalent. -Tocilizumab if concurrent CRS. -Consider transfer to intensive care unit.
Grade 3	-Supportive care and workup per Grade 1. -Transfer to intensive care unit. -Dexamethasone 10–20mg IV every 6 hours or methylprednisolone equivalent. -High-dose methylprednisolone (1000mg/day) for focal/local edema. -Seizure control with benzodiazepines (for short-term control) and levetiracetam ± lacosamide. -If evidence of increased ICP (stage 1–2 by fundoscopy or opening pressure >20 mmHg), urgent neurology consultation to guide management. -Repeat neuroimaging if persistent grade ≥3 ICANS.
Grade 4	-Supportive care and workup per Grade 1. -Transfer to intensive care unit, may need mechanical ventilation for airway protection. -High-dose methylprednisolone 1000mg/day for 3 days followed by taper. -Seizure control per Grade 3. -Management of raised ICP per neurology/neurosurgery intensive care recommendations. May use hyperosmolar therapy (mannitol/hypertonic saline), hyperventilation strategy.

Note: Data from references.[6,8,17,18]
Abbreviations: ASBMT, American Society for Transplantation and Cellular Therapy; ICANS, immune effector cell-associated neurotoxicity syndrome; CRS, cytokine release syndrome; EEG, electroencephalogram; ICE, Immune effector Cell-associated Encephalopathy; ICP, intracranial pressure; IV, intravenous.

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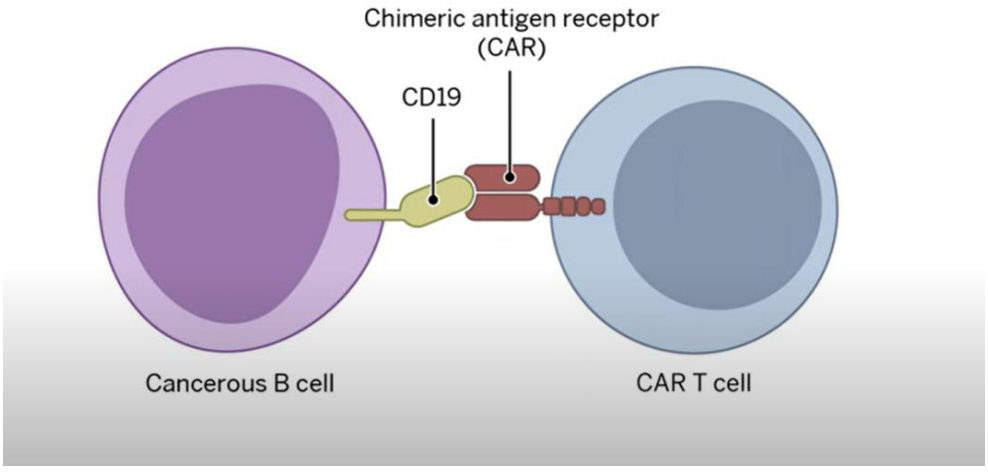

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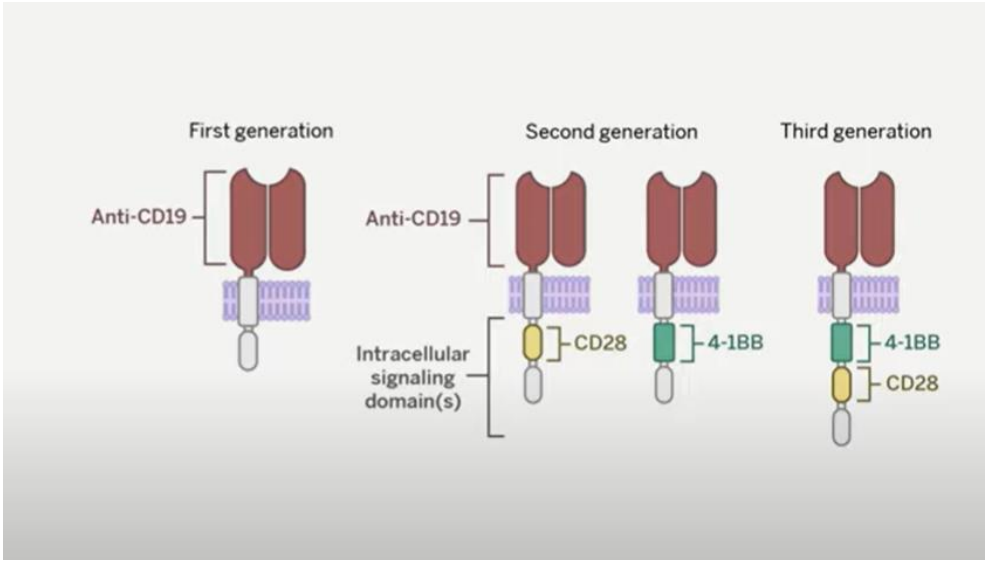

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ASTCT Consensus Grading

CRS Parameter	Grade 1	Grade 2	Grade 3	Grade 4
Fever*	Temperature ≥38°C	Temperature ≥38°C	Temperature ≥38°C	Temperature ≥38°C
		With		
Hypotension	None	Not requiring vasopressors	Requiring a vasopressor with or without vasopressin	Requiring multiple vasopressors (excluding vasopressin)
		And/or†		
Hypoxia	None	Requiring low-flow nasal cannula‡ or blow-by	Requiring high-flow nasal cannula‡, facemask, nonrebreather mask, or Venturi mask	Requiring positive pressure (eg, CPAP, BiPAP, intubation and mechanical ventilation)

- *Fever – defined as Temp > 38C.
- † CRS Grade is determined by the more severe event
- ‡ Low flow nasal cannula – O2< 6L/min

Lee, D.W., et al, 2018. ASBMT consensus grading for cytokine release syndrome and neurological toxicity associated with immune effector cells. *Biology of Blood and Marrow Transplantation*.

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