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CAR-T 101: Overview of CAR-T Therapy and Management of Toxicities
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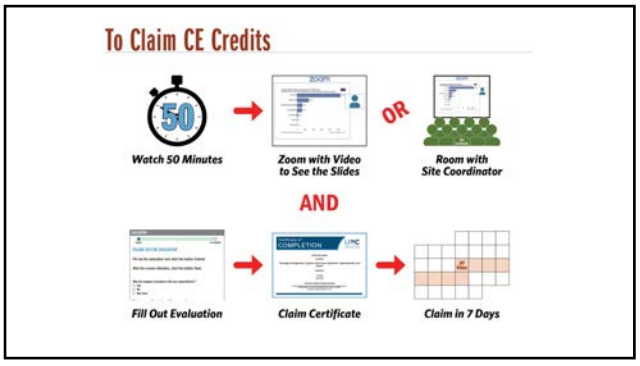
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Megan McElfresh, PA-C

Megan McElfresh, PA-C, graduated from Gardner Webb University in December 2009 with her bachelor's degree in Biology with a math and chemistry minor.

She then worked for a year as a CNA before attending PA school.

Megan graduated from Methodist University with her master's in medical science in 2013 and became a board-certified PA.

She has been working at UNC in the Bone Marrow Transplant and Cellular Therapy Program since August 2014.

Megan loves spending her free time hanging out with family or reading/listening to audiobooks and podcasts.

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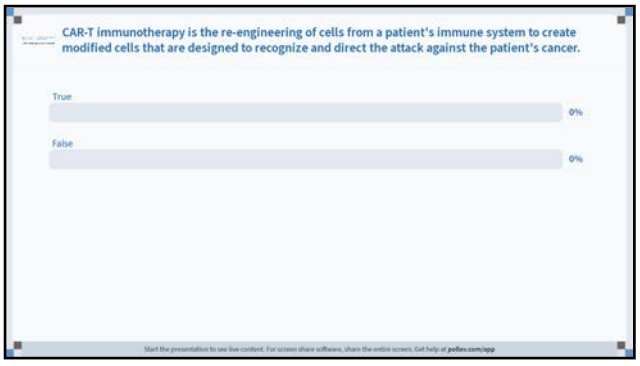

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CAR-T 101: Overview of CAR-T Therapy and Management of Toxicities

Megan McElfresh, PA-C
Megan.mcelfresh@unchealth.unc.edu

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Objectives

- Describe the collection process and the purpose of CAR-T cells.
- Describe the side effects of CAR-T Cells.
- Describe the treatment for Cytokine Release Syndrome post CAR-T.
- Describe the treatment of Neurotoxicity post CAR-T.

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WHAT IS CAR-T?

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Background

- Immunotherapy
  - Treatment that utilizes body's own immune system to fight cancer
- Lymphocytes
  - B lymphocytes (B Cells)
  - T lymphocytes (T Cells)
  - Natural killer cells (NK cells)

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CAR-T Therapy

- Chimeric Antigen Receptor T-Cell Therapy
- Therapy aimed at getting immune cells (*T cells)* to fight cancer by altering them in a lab so they can find and destroy cancer cells.
- Cancer often develops when tumor cells evade immune surveillance or suppress immune response, leading to cell proliferation.
  - Goal of CAR-T is to overcome the immune tolerance

National Cancer Institute (NCI). (NCI). CAR T cells: Engineering patients' immune cells to treat their cancers.

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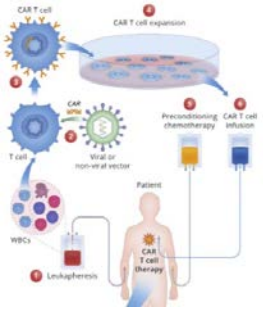
CAR-T Cell Process

- T Cells collected from a patient
- T Cells are re-engineered in a lab
- The re-engineered T cells (CAR-T cells) are multiplied
- Patient receives lymphodepleting chemotherapy
- CAR-T cells are infused into the patient



Ganatra et al – JACC 2019

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T-Cell Collection

- Blood draw or apheresis
- Leukapheresis collection
  - PIV or CVL
  - Apheresis machine
    - Pheresis out WBC (T-cells)
  - 3-5 hours
- Whole blood collection
  - Blood drawn
  - Density gradient centrifugation to remove RBC and granulocytes.

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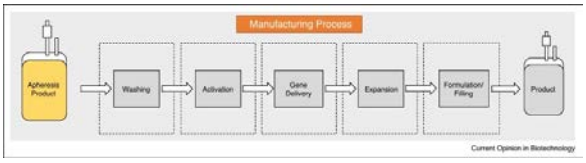
Cell Re-Engineering/Expansion

- Washing
- Activation
- Gene Delivery
- Expansion
- Formulation/Filling
- Delivery



Vormittag et al. A guide to manufacturing CAR T cell therapies.

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Lymphodepletion

Lymphodepleting conditioning regimens are essential to the success of CAR-T Cells

Effects of a conditioning regimen	
Lymphodepletion	Lowers total NK, B, and T cells
Fewer anti-CAR-T cell immune responses	Reduces anti-transgene immune reactions
Eradication of immune suppressor cells	Tregs and MDSCs
Modulation of tumor suppressive effects	Lowers IDO expression, increases levels of costimulatory molecules
Elimination of homeostatic cytokine sink	Increases IL-2, IL-7, IL-15, and MCP-1 expression levels
Increased expansion, function, and persistence of CAR-T cells	Better and durable tumor responses

Mohty et al. The EBMT/EHA CAR-T Cell Handbook, 2022.

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Lymphodepletion

- Typically fludarabine and cyclophosphamide x 3 days
- Given within a week of CAR-T cell infusion
  - Minimum of 2 rest days in between chemo and cell infusion to mitigate any negative effects of chemo on the cell infusion
- Side effects/Toxicities:
  - Pancytopenia and prolonged immune suppression
  - Increased risk of secondary malignancies
  - Fludarabine- fever and neurotoxicity
  - Cyclophosphamide- hemorrhagic cystitis and pericarditis

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Cell Infusion

- Cells infused through PIV or CVL (similar to blood transfusion)
- Can be performed in outpatient or inpatient setting
- Patient monitored for a designated time after cell infusion to monitor for side effects
- Pre-medications may be given to prevent side effects

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Timeline

- Obtain insurance authorization (days to weeks)
- Collect patient's T-cells (blood draw or apheresis)
  - if apheresis- require line placement and collection slot in apheresis lab
- Manufacture of cells and quality control ~2-6wks (can get "bridging therapy")
- Patient receives Lymphodepleting chemotherapy for usually 3 days
- CAR-T cell infusion ~2-4 days after completion of chemotherapy
- Not all patients make it to treatment

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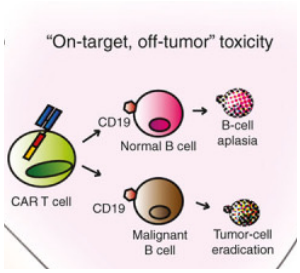
Challenges of CAR-T Cells: Finding a Suitable Target

- Must be on the surface of target cells
- Universal expression on malignant cells
- Limited off target expression/toxicity
- Example of antigens:
  - CD19
  - BCMA
  - CD30



Bonifant et al., Mol Ther Oncolytics, 2016

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Targeted Antigens

- ALL: CD19+
- Lymphomas: CD19+, CD30+ and CD30+/CCR4+ (UNC only)
- Multiple Myeloma: BCMA, CD138+ (UNC only)

- Solid Tumors:
  - HER-2 CAR-M (Macrophage) (Breast, H&N, Lung)
  - B7-H3 (Ovarian)
- *Pemphigus- CAAR-T (chimeric autoantibody receptor)*
- *Myasthenia Gravis- BCMA CAR-T*

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CAR-T PRODUCTS

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Development of CAR-T Products

- 1992- T Cell engineering begins
- 1993- 1st generation CAR-T cell developed but do not persist in the body thus not clinically effective
- 1994- Antigen specific T-Cells used in humans. Virus specific T-cells to prevent post-transplant infections and virally mediated cancers (CMV/EBV)
- 1998- Co-stimulation shown to provide necessary boost.
  - Introducing CD28 co-stimulatory molecule into T-cells allows them to persist in the body
- 2002- First effective CAR-T cells developed
  - Developed by MSK and targeted at prostate cancer antigen
- 2003- 2nd generation CAR-T cells developed against CD19
- 2017- First CARs cross the regulatory finish line
  - CD19 CAR-T therapy developed for ALL

CAR T Cells: Timeline of Progress, 1960

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CD-19+ CAR-T for ALL

- 1st FDA approved- Kymriah
  - Approved 2017 for relapsed/refractory B-ALL in pediatric and young adult (<25) patients
  - Based on ELIANA trial
- 2021 Tecartus approved for adult patients with relapsed/refractory B-ALL
- Data from 12 studies shows initial CR rates ranging from 62% to 86%, with the majority of these being deep minimal residual disease (MRD)-negative remissions

Cappell et al., *Nat Rev Clin Oncol 2023*

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CD-19+ CAR-T for Lymphoma

- 3 FDA approved products for relapsed/refractory large cell lymphoma
  - Yescarta approved 2017
  - Kymriah approved 2018
  - Breyanzi approved 2021
- Data from 10 studies indicates ORRs of 44–91% and CR rates of 28–68%

Cappell et al., *Nat Rev Clin Oncol 2023*

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BCMA CAR-T for Multiple Myeloma

Abecma approved March 2021
- Similar toxicity profile CD19 CAR-T treatments

2nd anti-BCMA CAR-T (Carvykti) now approved, UNC in the process of obtaining
- Different toxicity profile

Data from 6 studies shows ORRs of 73–100% and CR or stringent CR rates ranging from 33% to 83%

Cappell et al., *Nat Rev Clin Oncol 2023*

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Commercial CAR-T

Product	Target	Disease
Yescarta	CD19+	DLBCL/ Follicular
Tecartus	CD19+	Mantle Cell/Adult ALL
Breyanzi	CD19+	DLBCL
Kymriah	CD19+	DLBCL/ Follicular
Kymriah	CD19+	B-ALL (up to 25)
Abecma	BCMA	Mult Myeloma

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TOXICITIES AND MANAGEMENT

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Toxicities

- CRS
- Neurotoxicity
- Macrophage Activation Syndrome
- Tumor Lysis Syndrome
- B-Cell aplasia
- Cytopenia
- Infections

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CRS- Cytokine Release Syndrome

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CRS- Cytokine Release Syndrome

- Most common and expected toxicity of CAR-T therapy
- Due to systemic inflammatory response
  - CRP
  - Ferritin
  - LDH
  - IL-6
  - Fibrinogen
- Can occur between 1-21 days post CAR-T but typically between 2-7 days.
- Range of symptoms
  - Mild Flu-like
  - Serious
- Grading
  - 1-4

National Cancer Institute (NCI). (NCI). CAR T cells: Engineering patients' immune cells to treat their cancers.

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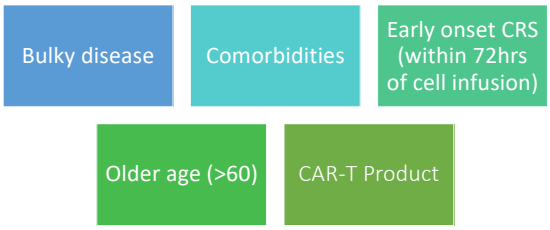
CRS Signs/Symptoms

Mild	Serious
• Nausea • Fatigue • Headache • Chills • **Fever**	• Hypotension • Tachycardia • Capillary leakage • Cardiac arrest • Cardiac arrhythmias • Cardiac Failure • Macrophage Activation Syndrome (MAS) • Hypoxia • Renal Insufficiency • Multiple organ failure

Yan Z et al. Front Immunol 2021

43

Risk Factors for Severe CRS



Yan Z et al. Front Immunol 2021

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CRS Grading Guidelines

- Grade 1- fever only
- Grade 2- fever + hypotension and/or hypoxia (</=6L NC)
- Grade 3- Grade 2, but on one pressor or high flow O2
- Grade 4- Grade 3, but on multiple pressors or positive pressure O2 (vent, BiPAP, CPAP)

UNC BMTCT Guideline Adult Management of CRS from CAR-T. 2022

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CRS Treatment- Tocilizumab

- Anti IL-6 receptor antibody
- Use does not seem to affect efficacy of CAR-T cell therapy
- Fever often resolves within a few hours and pressors/other supportive care measures can be weaned quickly
- Dosing
  - 8mg/kg given IV over 1 hr, can repeat every 8hr
  - Maximum 4 doses

UNC BMTCT Guideline Adult Management of CRS from CAR-T. 2022

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CRS Treatment- Corticosteroids

- Suppress inflammatory response
- Since suppress T- Cell function and can induce T-cell apoptosis, concern that could interfere with efficacy of CAR-T therapy
- Recent data questions this, may not be as suppressive to cells as originally thought, especially in lymphoma patients

UNC BMTCT Guideline Adult Management of CRS from CAR-T. 2022

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CRS Treatment

- Grade 1- Symptomatic management (Tylenol, anti-emetics, pain medication)
  - Consider Toci if grade 1 (fever) persists >24 hrs
  - Give Toci if grade 1 (fever) persists >72 hrs
- Grade 2- Tocilizumab +/- steroids if high risk
- Grade 3- Tocilizumab + Steroids
- Grade 4- Tocilizumab + Steroids

UNC BMTCT Guideline Adult Management of CRS from CAR-T. 2022

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CRS- Other considerations

- Fever occurs with CRS, however, patients may have other causes of fever.
- Plan for infectious workup and administer antibiotics at the same time as treating for CRS.

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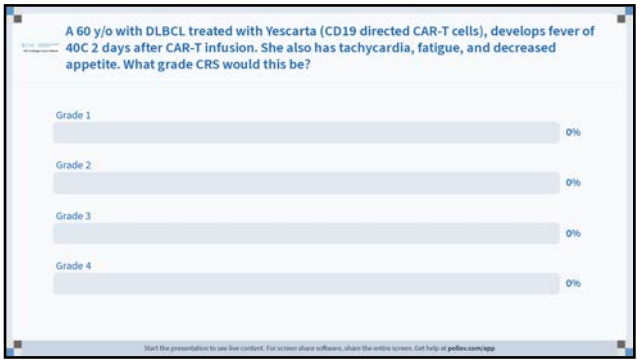

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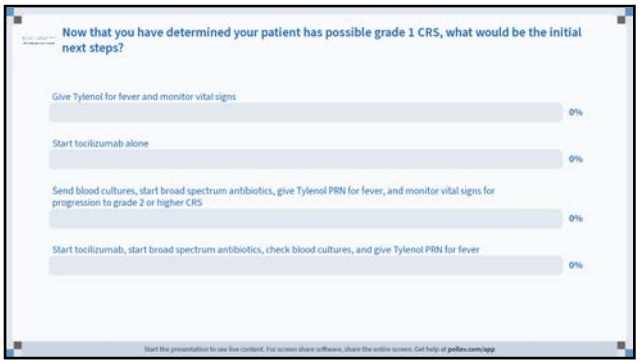

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ICANS- Immune-effector Cell Associated Neurotoxicity Syndrome

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Neurotoxicity/ICANS

Mechanism of action unknown
- Systemic inflammation and cytokine production causes cascade of BBB disruption, increased vascular permeability, and endothelial cell activation
- Increased cytokines in CSF

Usually occurs within first 2 weeks post CAR-T infusion but can occur up to 8 weeks post.
- No driving for 8 weeks post CAR-T infusion

Can occur in conjunction with CRS but typically will occur later, once CRS has subsided

Bianca et al. Pubmed 2018

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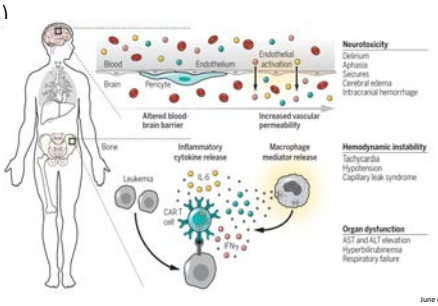
Immune Effector Cell Associated Neurotoxicity Syndrome (ICANS)



June et al., Science 2018

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Neurotoxicity/ICANS- Signs and Symptoms

- Typically present with toxic encephalopathy
  - Diminished attention, language disturbance/aphasia, impaired handwriting
- Severe symptoms
  - Seizures, motor weakness, increased intracranial pressure, papilledema, cerebral edema, unresponsiveness
- Symptoms are usually reversible if treated with steroids

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ICE Score: Immune-effector Cell Encephalopathy Score

Table 1. ICE Score

Assessment	Score (10 = No impairment)
Orientation	
• Year	1
• Month	1
• City	1
• Hospital	1
Name 3 Objects (example: point to clock, pen, and button)	3
Ability to follow simple commands (eg, "Show me 2 fingers" or "Close your eyes and stick out your tongue"	1
Ability to write a standard sentence	1
Ability to count backwards from 100 by 10	1
Total	10

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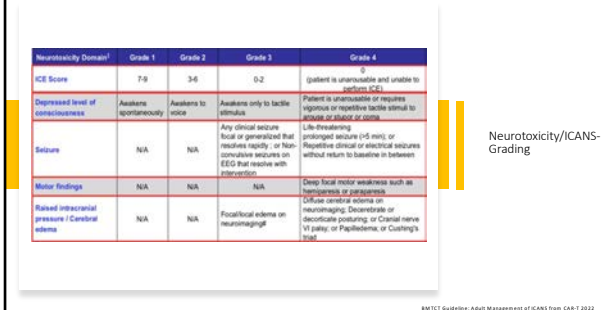

Neurotoxicity/ICANS-Grading

BMTCT Guideline: Adult Management of ICANS from CAR-T 2022

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Neurotoxicity/ICANS- Mangagment

- Grade 1- Supportive measures
  - Start Keppra prophylaxis (if not already on)
  - Consult Neurology
- Grade 2-4- Same as grade 1 + steroids
  - Dexamethasone 10mg IV q6-12hrs until improvement to grade 1, then taper
  - Treat Seizures with standard anti-epileptic therapy
- Further workup to consider
  - Brain MRI
  - LP
  - EEG

* Tocilizumab does not cross the BBB, therefore not effective. However, if occurring with CRS administer tocilizumab per CRS guideline

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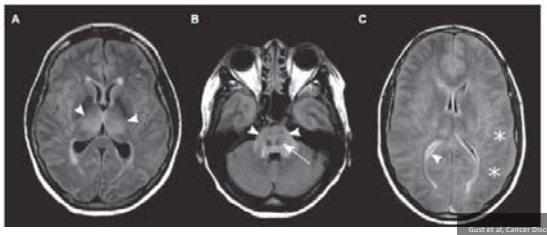

Gust et al, Cancer Discovery 2017

ICANS Imaging

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YESCARTA CRS/Neurotoxicity RISK

- Yescarta has high risk of CRS and neurotoxicity
- For DLBCL patient receiving Yescarta give prophylaxis to prevent CRS/ICANS
  - Dexamethasone 10mg PO x3 day
  - Starts on day of cell infusion

BMTCT Guideline: Adult Management of ICANS from CAR-T. 2022.

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Prophylaxis-Keppra

- For patient's with higher risk of ICANS we start prophylaxis with Keppra
  - Yescarta and Tecartus
- Prevent seizures
- Dose: Keppra 500 mg BID for seizure prophylaxis x 21 days, then taper to 500mg daily x 1 wk, then 250mg daily x 1 wk beginning Day 0

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Anakinra

- Potential treatment option for refractory CRS or ICANS
  - Mainly ICANS
- 2nd or 3rd line agent for treatment of CRS/ICANS
- IL-1 receptor blockade
- 100mg SQ daily
- clinical trials investigating early and/or prophylactic use are ongoing

Paolo et al., Blood Adv 2020

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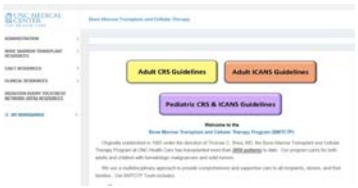
Guidelines on UNC Intranet under BMT/CT Page



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Case Question 3

52 y/o male with DLBCL receives yescarta. On day 6 he developed a hand tremor and mental status changes. You perform an ICE score and he is unable to count backwards, tell you what city or hospital he is in, or write a sentence. He has an ICE score of 6. What Grade ICANS does he have?

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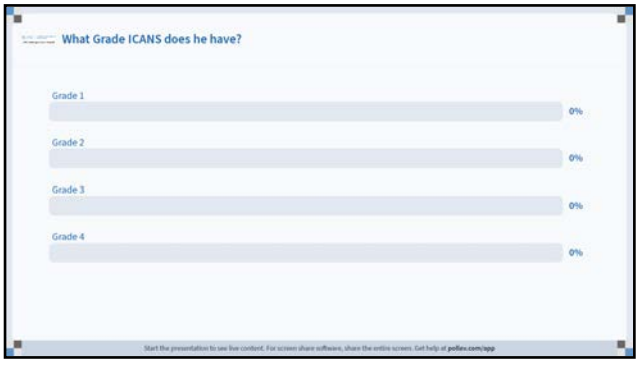

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OTHER TOXICITIES

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Macrophage activation syndrome (MAS)

- More routinely seen in rheumatologic disorders such as juvenile rheumatoid arthritis
- Uncontrolled activation and proliferation of macrophages, and T lymphocytes, with a marked increase in circulating cytokines
- So, basically CRS out of control with marked inflammation resulting
- Can lead to hepatosplenomegaly, DIC, pancytopenia
- Consider if peak ferritin >10K during CRS and develops LFT abnormalities, AKI, or pulmonary edema
- Management:
  - tocilizumab and steroids initially as you would CRS

Martin-Rojas RM. Rev Clin Esp. 2022

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Tumor Lysis syndrome

- Most likely to occur while undergoing lymphodepletion chemotherapy
- Can also be delayed in CAR-T therapy (ie. Around the time of cell proliferation)
- Release of lysed tumor cells contents, can lead to renal failure and massive electrolyte abnormalities
- More concern in CD19+ CARs, and pts with large tumor burden

Management:

- Monitor chemistries more frequently (either q12h or q8h)
- High risk patients receive prophylaxis with allopurinol +/- IV fluid hydration

Ikeda AK . Tumor lysis syndrome. eMedicine.Medscape.com. WebMD LLC; 2012

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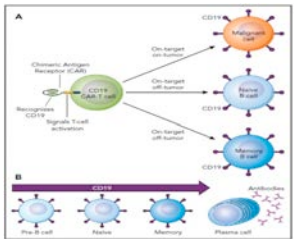
B Cell Aplasia/Hypogammaglobulinemia

"On target off tumor" toxicity of CD19 CAR-T cells

In adults, generally don't treat with IVIG unless patient has recurrent infections, or significantly low IgG level

Can monitor IgG levels



Hill and Seo, Blood 2020

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Cytopenias

- Cytopenias persist > 1 month in ~1/3 of patients who get CD19-directed CAR-T cells
- Resolve by 3 months in most patients but some patients have more persistent low counts, specifically neutropenia or thrombocytopenia
- Can treat with growth factors and transfusions, if needed
- If persistent, may need to rule out treatment related MDS

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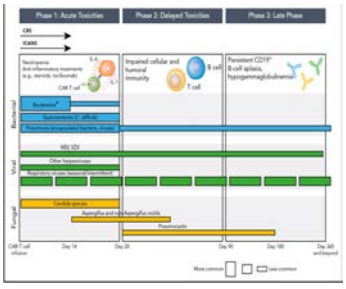
Infection Risk

- Infection risk Factors
  - Extensive past treatments
  - Lymphodepletion
  - Treatment for CRS and ICANS
  - B cell aplasia
- Patients at high risk for opportunistic infections even at 1 year+ out from treatment including viral infections and PJP



Hill and Seo, Blood 2020

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Infection Prevention

- Start Valtrex on day of cell infusion
- Start Levaquin/fluconazole if ANC <0.5
- Bactrim or other PJP prophylaxis starts at day +30 and continues through 1 year or until CD4 >200. Start checking CD4 at 3 months post CAR-T

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UNC CAR-T Studies

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UNC Research CAR-T

Trial	Target	Disease
LCCC-1606	CD30+/CCR4+	Mostly Hodgkin; some CTCL
LCCC-1813	CD19+/Safety switch	DLBCL
LCCC-1541	CD19+/Safety switch	B-ALL
LCCC-1603	CD138+	MM
CARISMA	HER-2 CAR-M	Solid tumors
LCCC-1818	B7-H3	Ovarian

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CD30+ CAR-T Cells for Lymphoma

LCCC 1532

41 patients received treatment
Median 7 lines of prior therapy
CRS in 10pts, all Grade 1
No Neurotoxicity

ORR: 72%
CR 19%
1yr PFS: 36%, 1yr OS: 94%

Ramos et al. Anti-CD30 CAR-T Therapy. Pubmed, 2020

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LCCC 1606:

- Like 1532, but combined with CCr4+
- Uses the same CD30+ CAR, but compares it to a CD30+ CAR WITH A CCR4+ CAR
- The thought is that the CCR4 will help the CD30+ find it's targets and have better penetration
- Ongoing study

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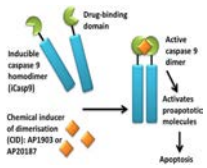
LCCC 1541 (CD19+ CAR for ALL w/suicide switch)

- CD19-directed CAR-T cells with inducible caspase 9 safety switch in patients with relapsed/refractory ALL
- Embedded safety switch activated by AP1903 (Rimiducid)
- When activated -> CAR-T cells die
- In mouse studies, CAR-T cell death was dose-dependent so may be able to kill desired amount of cells and keep some cells alive
- New Amendment for the trial allows for dose titration based on degree of toxicity



Garret and Brown. Frontiers, 2014

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Exotic CARs

- CARISMA (HER2, CAR macrophage):
  - Solid tumors
- Metastatic Ovarian Ca- LCCC1818
  - No Lymphodepletion
  - Given as 3 weekly infusions, into a peritoneal catheter
- Pemphigus:
  - Pharmaceutical sponsored trial
  - Chimeric autoimmune antigen receptor
  - Managed primarily by Dermatology
- Myasthenia Gravis:
  - BCMA CAR-T
  - Managed by Neurology
- Others
  - Osteosarcoma
  - Glioblastoma

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References

- National Cancer Institute (NCI). (NCI). CAR T cells: Engineering patients' immune cells to treat their cancers. Accessed at https://www.cancer.gov/about-cancer/treatment/research/car-t-cells on December 19, 2019.
- Joshua A. Hill, Susan K. Seo; How I prevent infections in patients receiving CD19-targeted chimeric antigen receptor T cells for B-cell malignancies. *Blood* 2020; 136 (8): 925–935. doi: https://doi.org/10.1182/blood.2019004000
- Ganatra S, Carver JR, Hayek SS, Ky B, Leja MJ, Lenihan DJ, Lenneman C, Mousavi N, Park JH, Perales MA, Ryan TD, Scherrer-Crosbie M, Steingart RM, Yang EH, Zaha V, Barac A, Liu JE. Chimeric Antigen Receptor T-Cell Therapy for Cancer and Heart: JACC Council Perspectives. J Am Coll Cardiol. 2019 Dec 24;74(25):3153-3163. doi: 10.1016/j.jacc.2019.10.049. PMID: 31856973; PMCID: PMC8211027.
- Bonifant CL, Jackson HJ, Brentjens RJ, Curran KJ. Toxicity and management in CAR T-cell therapy. Mol Ther Oncolytics. 2016 Apr 20;3:16011. doi: 10.1038/mto.2016.11. PMID: 27626062; PMCID: PMC5008265.
- Bianca D. Santomasso, Jae H. Park, Darin Salloum, Isabelle Riviere, Jessica Flynn, Elena Mead, Elizabeth Halton, Xiuyan Wang, Brigitte Senechal, Terence Purdon, Justin R. Cross, Hui Liu, Behroze Vachha, Xi Chen, Lisa M. DeAngelis, Daniel Li, Yvette Bernal, Mithat Gonen, Hans-Guido Wendel, Michel Sadelain, Renier J. Brentjens; Clinical and Biological Correlates of Neurotoxicity Associated with CAR T-cell Therapy in Patients with B-cell Acute Lymphoblastic Leukemia. *Cancer Discov* 1 August 2018; 8 (8): 958–971. https://doi.org/10.1158/2159-8290.CD-17-1319
- June CH, O'Connor RS, Kawalekar OU, Ghassemi S, Milone MC. CAR T cell immunotherapy for human cancer. Science. 2018 Mar 23;359(6382):1361-1365. doi: 10.1126/science.aar6711. PMID: 29567707.
- Vormittag P, Gunn R, Ghorashian S, Veraitch FS. A guide to manufacturing CAR T cell therapies. Curr Opin Biotechnol. 2018 Oct;53:164-181. doi: 10.1016/j.copbio.2018.01.025. Epub 2018 Feb 18. PMID: 29462761.
- Gargett, T., & Brown, M. P. (2014, October 7). The inducible caspase-9 suicide gene system as a "safety switch" to limit on-target, off-tumor toxicities of chimeric antigen receptor T cells. Frontiers. https://www.frontiersin.org/articles/10.3389/fphar.2014.00235
- Ramos CA, Grover NS, Beaven AW, Lulla PD, Wu MF, Ivanova A, Wang T, Shea TC, Rooney CM, Dittus C, Park SI, Gee AP, Eldridge PW, McKay KL, Mehta B, Cheng CJ, Buchanan FB, Grilley BJ, Morrison K, Brenner MK, Serody JS, Dotti G, Heslop HE, Savoldo B. Anti-CD30 CAR-T Cell Therapy in Relapsed and Refractory Hodgkin Lymphoma. J Clin Oncol. 2020 Nov 10;38(32):3794-3804. doi: 10.1200/JCO.20.01342. Epub 2020 Jul 23. PMID: 32701411; PMCID: PMC7655020.

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References

- Gust J, Hay KA, Hanafi LA, Li D, Myerson D, Gonzalez-Cuyar LF, Yeung C, Liles WC, Wurfel M, Lopez JA, Chen J, Chung D, Harju-Baker S, Özpolat T, Fink KR, Riddell SR, Maloney DG, Turtle CJ. Endothelial Activation and Blood-Brain Barrier Disruption in Neurotoxicity after Adoptive Immunotherapy with CD19 CAR-T Cells. Cancer Discov. 2017 Dec;7(12):1404-1419. doi: 10.1158/2159-8290.CD-17-0698. Epub 2017 Oct 12. PMID: 29025771; PMCID: PMC5718945.
- Mohty M, Minnema MC. Lymphodepleting Conditioning Regimens. 2022 Feb 7. In: Kröger N, Gribben J, Chabannon C, et al., editors. The EBMT/EHA CAR-T Cell Handbook [Internet]. Cham (CH): Springer; 2022. Chapter 25. Available from: https://www.ncbi.nlm.nih.gov/books/NBK584177/ doi: 10.1007/978-3-030-94353-0_25
- Cappell, K.M., Kochenderfer, J.N. Long-term outcomes following CAR T cell therapy: what we know so far. *Nat Rev Clin Oncol* **20**, 359–371 (2023). https://doi.org/10.1038/s41571-023-00754-1
- *CAR T cells: Timeline of progress.* (1960). Memorial Sloan Kettering Cancer Center. https://www.mskcc.org/timeline/car-t-timeline-progress
- Paolo Strati, Sairah Ahmed, Partow Kebriaei, Loretta J. Nastoupil, Catherine M. Claussen, Grace Watson, Sandra B. Horowitz, Anne Rain T. Brown, Bryan Do, Maria A. Rodriguez, Ranjit Nair, Elizabeth J. Shpall, Michael R. Green, Sattva S. Neelapu, Jason R. Westin; Clinical efficacy of anakinra to mitigate CAR T-cell therapy–associated toxicity in large B-cell lymphoma. *Blood Adv* 2020; 4 (13): 3123–3127. doi: https://doi.org/10.1182/bloodadvances.2020002328
- Yan Z, Zhang H, Cao J, Zhang C, Liu H, Huang H, Cheng H, Qiao J, Wang Y, Wang Y, Gao L, Shi M, Sang W, Zhu F, Li D, Sun H, Wu Q, Qi Y, Li H, Wang X, Li Z, Liu H, Zheng J, Qian W, Zhang X, Xu K. Characteristics and Risk Factors of Cytokine Release Syndrome in Chimeric Antigen Receptor T Cell Treatment. Front Immunol. 2021 Feb 23;12:611366. doi: 10.3389/fimmu.2021.611366. PMID: 33708205; PMCID: PMC7940756..
- BMTCT Guideline: Adult Management of CRS from CAR-T. 2022
- BMTCT Guideline: Adult Management of ICANS from CAR-T. 2022.
- Martín-Rojas RM, Gómez-Centurión I, Bailén R, Bastos M, Díaz-Crespo F, Carbonell D, Correa-Rocha R, Pion M, Muñoz C, Sancho M, Gómez Fernández I, Oarbeascoa G, Pérez-Corral A, Martínez-Laperche C, Anguita J, Buño I, Menárguez J, Díez-Martín JL, Kwon M. Hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS) following treatment with tisagenlecleucel. Clin Case Rep. 2022 Jan 7;10(1):e05209. doi: 10.1002/ccr3.5209. PMID: 35028140; PMCID: PMC8741874.
- Ikeda AK . Tumour lysis syndrome. *eMedicine.Medscape.com*. WebMD LLC; 2012.

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Questions/Comments?
Nobody has responded yet.
Hang tight! Responses are coming in.

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Thank You . . .
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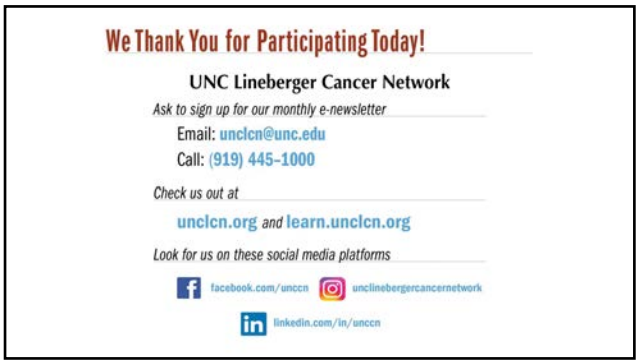
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