

UNC Lineberger Cancer Network

Presented
October 18, 20

Let's Take a BITE Out of CNS and Neurotoxicity October 18

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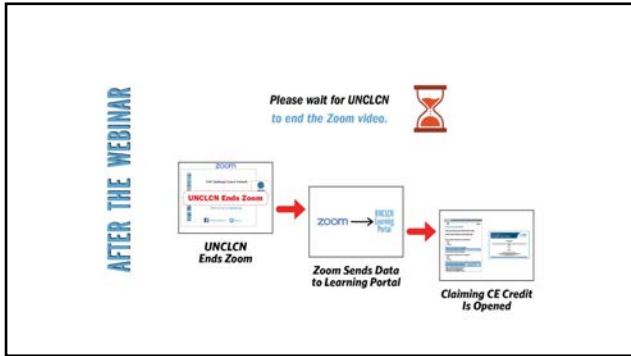
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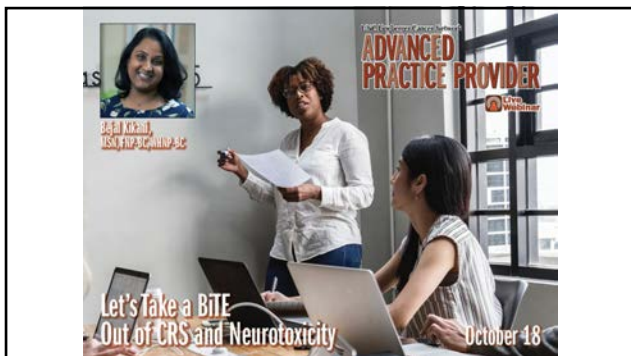
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Presented
October 18, 20

OUR PRESENTER



Bejal Kikani,
MSN, FNP-BC, WHNP-BC

Bejal Kikani, MSN, FNP-BC, WHNP-BC, went to ECU for her undergraduate studies and UNC for graduate school.

She has worked at UNC for over 15 years and has been with malignant inpatient hematology for 4 years.

Bejal has developed a true passion for the care of patients with blood cancers and enjoys being able to tie in her interest in infectious diseases.

She is active in helping to roll out inpatient clinical trials and enjoys being a resource for CRS/ICANS management tips.

She is also involved in DEI projects and enjoys teaching.

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OUR PRESENTER

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OUR PRESENTER

5. Bejal Kikani, MSN, FNP-BC, WHNP-BC, went to ECU for her undergraduate studies and UNC for graduate school.

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OUR PRESENTER

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OUR PRESENTER

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OUR PRESENTER

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4. She has worked at UNC for over 15 years and has been with malignant inpatient hematology for 4 years.
3. She is active in helping to roll out inpatient clinical trials and enjoys being a resource for CRS/ICANS management tips.
2. She is also involved in DEI projects and enjoys teaching.

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OUR PRESENTER

1. Has three feisty and rambunctious kids: 6-year-old (Avi) and 3-year-old twins (Veda and Meera)
2. She is also involved in DEI projects and enjoys teaching.
3. She is active in helping to roll out inpatient clinical trials and enjoys being a resource for CRS/ICANS management tips.
4. She has worked at UNC for over 15 years and has been with malignant inpatient hematology for 4 years.
5. Bejal Kikani, MSN, FNP-BC, WHNP-BC, went to ECU for her undergraduate studies and UNC for graduate school.

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Cytokine Release Syndrome (CRS) does not involve the possibility of multiple organ dysfunction that is most often caused by immunotherapy.

All Done 100%

All Notes 0%

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Cytokine Release Syndrome (CRS) does not involve the possibility of multiple organ dysfunction that is most often caused by immunotherapy.

True 0%

False 0%


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**Let's take a BiTE out of
CRS and Neurotoxicity**

Bejal Kikani, MSN, FNP-BC, WHNP-BC
Inpatient Malignant Hematology
October 18, 2023





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Disclosures

Co-Investigator. No direct compensation

Janssen
Gilead
Regeneron
Amgen




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What is your current level of comfort for managing CRS/ICANS as potential toxicities to immunotherapy?

Comfortable	0%
Somewhat comfortable, I need to see it in practice	0%
Not at all comfortable, I would like to learn more about it	0%



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Learning objectives

- Examine the pathophysiology of cytokine release syndrome (CRS) and neurotoxicity caused by T-cell engaging therapies
- Discuss the signs of CRS and neurotoxicity as toxicities of T-cell engaging therapies
- Identify the grade of CRS and neurotoxicity
- Discuss treatment recommendations for CRS and neurotoxicity based on the associated grading





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Relevance to practice

Immunotherapy as cancer-directed therapy has evolved, particularly in the field of T cell-engaging therapies

Toxicities: Cytokine Release Syndrome (CRS) and Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS).

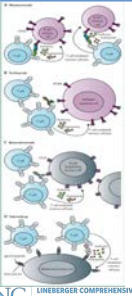


Role of the APP

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On the market

Drug	Disease	Pharmacological Category
Blinatumomab	ALL	Anti-CD19/CD3
Tecclistamab	MM	Anti-BCMA/AntiCD3
Talquetamab	MM	Anti-GPRC5D/AntiCD3
Mosunetuzumab	FL	Anti-CD20/CD3
CAR-T	ALL, MM, Lymphoma	Anti-BCMA/Anti-CD19
Tebentafusp	Uveal melanoma	Anti-CD3

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**CRS
PATHOPHYSIOLOGY**

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Cytokine Release Syndrome

Cytokine Release Syndrome (CRS) is an acute systemic inflammatory syndrome characterized by **fever** and multiple organ dysfunction that is most often caused by immunotherapy.

Shimada et al. 2018, J Immunotherapy Oncol
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Mechanism of action

T-cell engager attaches to antigen on tumor cell, attracting a T-cell

T-cell attaches to tumor cell by T-cell receptor complex

T-cells (host) attack the tumor cell

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The Perfect Storm

T-cell engager attaches to antigen on tumor cell, attracting a T-cell

T-cell attaches to tumor cell by T-cell receptor complex

T-cells (host) attack the tumor cell

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Step-up Dosing

The "first-dose effect"

Priming with incremental dose increase to reduce risk of CRS/ICANS

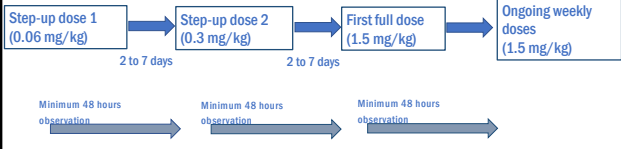
Formulations:

- Continuous IV infusion
- SQ injections
- 2-4 hour IV infusions



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Example of step-up dosing: Teclistamab Initiation





Step-up dose 1 (0.06 mg/kg) → Step-up dose 2 (0.3 mg/kg) → First full dose (1.5 mg/kg) → Ongoing weekly doses (1.5 mg/kg)

2 to 7 days 2 to 7 days

Minimum 48 hours observation Minimum 48 hours observation Minimum 48 hours observation

Per the package insert, ramp-up can be shortened from Days 1, 4, and 7 to Days 1, 3 and 5 if no CRS at time of next dose.



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What vital sign abnormality must be present in order to meet the definition of CRS?

Hypotension 0%

Hypoxia 0%

Fever 0%

All of the above 0%

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**CRS
GRADING
&
MANAGEMENT**

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CRS Grading Guidelines

- [ASTCT 2018](#)
- [NCCN 2022](#)
- [ASCO 2021](#)

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Protocol

<p>CRS Grading</p> <p>Grade 1 (CTCAE v4.03): self-limited, flu-like symptoms, fever $\geq 38.0^{\circ}\text{C}$, tachycardia ≥ 100 bpm, hypotension ≥ 1 mmHg.</p> <p>Grade 2 (CTCAE v4.03): self-limited, flu-like symptoms, fever $\geq 38.5^{\circ}\text{C}$, tachycardia ≥ 120 bpm, hypotension ≥ 2 mmHg.</p> <p>Grade 3 (CTCAE v4.03): self-limited, flu-like symptoms, fever $\geq 39.0^{\circ}\text{C}$, tachycardia ≥ 140 bpm, hypotension ≥ 3 mmHg.</p> <p>Grade 4 (CTCAE v4.03): self-limited, flu-like symptoms, fever $\geq 39.5^{\circ}\text{C}$, tachycardia ≥ 160 bpm, hypotension ≥ 4 mmHg.</p> <p>Grade 5 (CTCAE v4.03): self-limited, flu-like symptoms, fever $\geq 40.0^{\circ}\text{C}$, tachycardia ≥ 180 bpm, hypotension ≥ 5 mmHg.</p>	<p>CRS Management</p> <p>Grade 1 (CTCAE v4.03): Supportive care (eg, analgesics, IV fluids).</p> <p>Grade 2 (CTCAE v4.03): Supportive care (eg, analgesics, IV fluids, oxygen), corticosteroids (eg, prednisone 1 mg/kg/d).</p> <p>Grade 3 (CTCAE v4.03): Supportive care (eg, analgesics, IV fluids, oxygen), corticosteroids (eg, prednisone 2 mg/kg/d).</p> <p>Grade 4 (CTCAE v4.03): Supportive care (eg, analgesics, IV fluids, oxygen), corticosteroids (eg, prednisone 4 mg/kg/d).</p> <p>Grade 5 (CTCAE v4.03): Supportive care (eg, analgesics, IV fluids, oxygen), corticosteroids (eg, prednisone 8 mg/kg/d).</p>	<p>CRS Prevention</p> <p>Grade 1 (CTCAE v4.03): No prophylaxis.</p> <p>Grade 2 (CTCAE v4.03): Prophylactic corticosteroids (eg, prednisone 1 mg/kg/d).</p> <p>Grade 3 (CTCAE v4.03): Prophylactic corticosteroids (eg, prednisone 2 mg/kg/d).</p> <p>Grade 4 (CTCAE v4.03): Prophylactic corticosteroids (eg, prednisone 4 mg/kg/d).</p> <p>Grade 5 (CTCAE v4.03): Prophylactic corticosteroids (eg, prednisone 8 mg/kg/d).</p>
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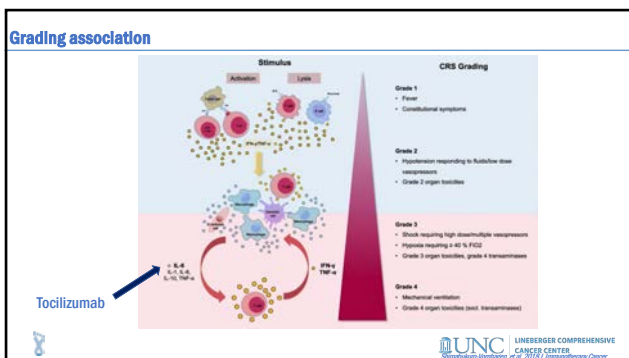
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CRS Grading	CRS Management
Grade 1: Fever $\geq 38^{\circ}\text{C}$, not attributable to any other cause Hypotension: none Hypoxia: none	- Supportive care (i.e., antipyretics, IV hydration) - Vital signs every 30 minutes for 2 hours after symptoms onset, pulse oximetry, twice daily CMPs - For Initial Fever: Follow Fever SOP. Use clinical judgment for subsequent fevers
Grade 2: Fever $\geq 38^{\circ}\text{C}$, not attributable to any other cause plus Hypotension: not requiring vasopressors And/or Hypoxia: requiring low-flow nasal cannula (FiO_2 oxygen delivered at $\leq 6\text{ L/min}$) or blow-by *Hypotension: SBP $< 90\text{ mm Hg}$ or if symptomatic	- Notify Attending Physician - IV fluid bolus and/or oxygen as needed - Cardiac tele, vital signs every 30 minutes for 2 hours after symptoms onset, pulse oximetry, twice daily CMPs - Tocilizumab 8 mg/kg IV over 1 hour (max dose 800 mg/dose). Repeat every 8 hours if no improvement. Limit to a maximum of three doses in a 24-hour period, with a maximum of four doses total - Hypotension after 2L boluses (consider LR) and after 1-2 doses of tocilizumab, consider dexamethasone 10 mg IV every 12 hours for 1-2 doses - Manage per Grade 3 if no improvement within 24 hours of starting tocilizumab

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CRS Grading	CRS Management
Grade 3: Fever $\geq 38^{\circ}\text{C}$, not attributable to any other cause plus Hypotension: requiring a vasopressor with or without vasopressin And/or Hypoxia: requiring high-flow nasal cannula, facemask, nonrebreather mask, or Venturi mask *Hypotension: SBP $< 90\text{ mm Hg}$ or if symptomatic	- Notify Attending Physician - Grade 2 Supportive care and include vasopressors as needed - Consider ECHO to assess cardiac function and conduct hemodynamic monitoring - Tocilizumab as per Grade 2 if max dose is not reached within 24-hour period - IV dexamethasone 10 mg IV every 6 hours (or equivalent) and rapidly taper once symptoms improve - If refractory despite max dose tocilizumab and dexamethasone, manage as per Grade 4 - If on Monumen-TAL, contact MD prior to dexamethasone
Grade 4: Life threatening Fever $\geq 38^{\circ}\text{C}$, not attributable to any other cause plus Hypotension: requiring multiple vasopressors (excluding vasopressin) -And/or Hypoxia: requiring positive pressure (i.e., CPAP, BiPAP, intubation, and mechanical ventilation) SBP $< 90\text{ mm Hg}$ or if symptomatic	- Notify Attending Physician - Continue supportive care as per Grade 3 plus mechanical ventilation as needed - Administer tocilizumab as per Grade 2 if maximum is not reached within 24-hour period - Initiate high-dose methylprednisolone at a dose of 500 mg IV every 12 hours for 2 days, followed by 250 mg IV every 12 hours for 2 days, 125 mg IV every 12 hours for 2 days, and 60 mg IV every 12 hours until CRS improvement to Grade 1 - If not improving, consider methylprednisolone 1G IV 2 times a day - If on Monumen-TAL, contact MD prior to dexamethasone

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Tocilizumab

FDA approved in 2017 for use in CRS

anti-IL-6 receptor antagonist (inhibits IL-6 by blocking IL-6 receptors)

Prevents proinflammatory effects

Does not cross the BBB

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Case study

68yoM with R/R IgG Kappa MM presented for Teclistamab initiation. On D3 (48h after first step-up dose), developed acute L sided mid-sternal and back pain. Improved with IV toradol and protonix. Few hours later, found to be febrile.

Objective:
48h after 1st dose/D3=
Afebrile, normotensive on RA.
Few hours later, febrile to 39.2, remained normotensive and on RA. ICE score 10/10. Exam benign.

Differential Dx:
CRS
Infectious
MI
Aortic dissection
GERD

Orders:
BCx, EKG, CBC, CMP,
Troponin, CRP

*Per the package insert, ramp-up can be shortened from Days 1, 4, and 7 to Days 1, 3 and 5 if no CRS at time of next dose.

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Case study

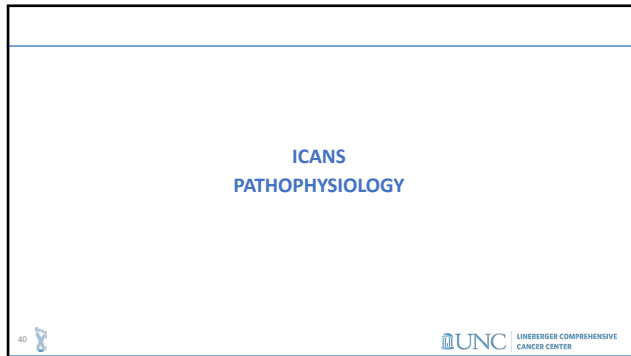
CRS Management

CRS Grade 1

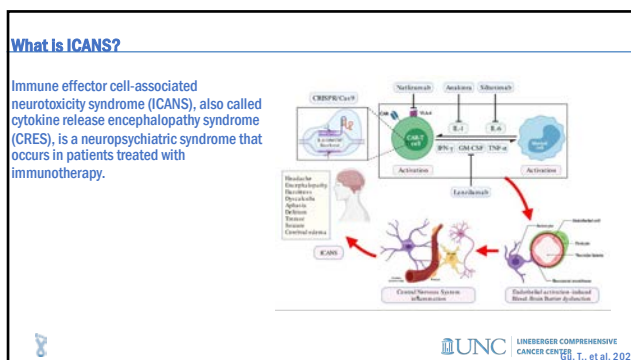
Tx:
BCx
APAP

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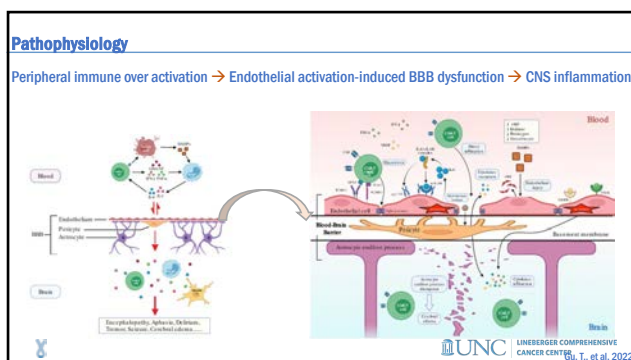
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ICANS GRADING & MANAGEMENT

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ICANS Grading Guidelines

- ASTCT 2018
- NCCN 2022
- ASCO 2021

Management of Immunotherapy-Related Toxicities
Management of Immune-Related Adverse Events in Patients Treated With Chimeric Antigen Receptor T-Cell Therapy: ASCO Guideline

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ICE ICE Baby...let's talk about the ICE Score

----- Neurotoxicity Grading and Management -----

Use ICE (Immune Effector Cell-Associated Encephalopathy) score and ICANS (Immune Effector Cell-Associated Neurotoxicity Syndrome) grading in combination when determining management of neurotoxicity



Immune Effector Cell-Associated Encephalopathy (ICE) Score	
Orientation	Your Month, City, Hospital & Floors
Naming	Ability to name 3 objects (eg, point to clock, pen, button)
Follow Commands	Ability to follow simple commands (eg, "Show me 2 fingers," "Close your eyes and stick out your tongue")
Writing	Ability to write a standard sentence (eg, "Our national bird is the bald eagle")
Attention	Ability to count backwards from 100 to 0 by 10
Total: 16 points	

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Tammy's ICE Score



ICE score		
Orientation (4pts)	Year, Month, City, Hospital	4
Naming (3pts)	Ability to name 3 objects	
Follow Commands (1pt)	Ability to follow simple commands	
Writing (1pt)	Ability to write a standard sentence	
Attention (1pt)	Ability to count backwards from 100 by 10	
Total:		

46  

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Tammy's ICE Score



ICE score		
Orientation (4pts)	Year, Month, City, Hospital	4
Naming (3pts)	Ability to name 3 objects	3
Follow Commands (1pt)	Ability to follow simple commands	
Writing (1pt)	Ability to write a standard sentence	
Attention (1pt)	Ability to count backwards from 100 by 10	
Total:		

47  

47

Tammy's ICE Score



ICE score		
Orientation (4pts)	Year, Month, City, Hospital	4
Naming (3pts)	Ability to name 3 objects	3
Follow Commands (1pt)	Ability to follow simple commands	1
Writing (1pt)	Ability to write a standard sentence	
Attention (1pt)	Ability to count backwards from 100 by 10	
Total:		

48  

48

Tammy's ICE Score



ICE score		
Orientation (4pts)	Year, Month, City, Hospital	4
Naming (3pts)	Ability to name 3 objects	3
Follow Commands (1pt)	Ability to follow simple commands	1
Writing (1pt)	Ability to write a standard sentence	1
Attention (1pt)	Ability to count backwards from 100 by 10	
Total:		

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Tammy's ICE Score

ICE score		
Orientation (4pts)	Year, Month, City, Hospital	4
Naming (3pts)	Ability to name 3 objects	3
Follow Commands (1pt)	Ability to follow simple commands	1
Writing (1pt)	Ability to write a standard sentence	1
Attention (1pt)	Ability to count backwards from 100 by 10	0
Total: 9 out of 10		



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ICANS Grading

ICANS Grading System: ICANS grade is determined by the most severe event (ICE score, level of consciousness, seizure, motor findings, raised ICP/cerebral edema) not attributable to any other cause, for example, a patient with an ICE score of 3 who has a generalized seizure is classified as grade 3 ICANS.

Neurotoxicity Domain	Grade 1	Grade 2	Grade 3	Grade 4
ICE Score	7/9	3-6	0-2	0 (unconscious and unable to perform CCI)
Depressed LOC	Awakens spontaneously	Awakens to voice	Awakens only to tactile stimulus	Unarousable or requires continuous stimulus or noxious stimuli to arouse. Dispor or coma
Seizure	N/A	N/A	Any clinical seizure (focal or generalized) that requires rescue or (b) convulsions (rigidity or ECG that is not resolute with intervention)	Life-threatening prolonged seizure (1-5 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 Diffuse cerebral edema on neuroimaging
Increased ICP/cerebral Pathy	N/A	N/A	Focal/hoor edema on neuroimaging	discreetly or bilaterally increased intracranial pressure, or clinical signs of papilloedema or Cushing's triad

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28yoF with R/R ALL with severe acute onset headache within 10 minutes of initiation of blinatumomab infusion. VSS, afebrile. What is an assessment tool you would use to evaluate her neurological status?

CRS 0%

ICE Score 0%

ICANS 0%

None of the above 0%


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ICANS Management

Grading	Management (neurotoxicity only)
Grade 1:	<ul style="list-style-type: none"> Notify covering provider Daily neuro exam
Grade 2:	<ul style="list-style-type: none"> Notify Attending Physician Notify covering provider 1 dose of dexamethasone 10 mg IV and reassess. Can repeat every 6-12 hours, if no improvement. Daily neuro exam
Grade 3:	<ul style="list-style-type: none"> Notify Attending Physician ICU level of care recommended START Dexamethasone 10 mg IV Q6H or methylprednisolone, 1 mg/kg IV Q2H Anti-epileptic if concern for seizures (q 1000cc)
Grade 4:	<ul style="list-style-type: none"> Notify Attending Physician ICU level of care recommended START methylprednisolone 16 1000 mg/day (may consider twice a day) for 3 days, followed by rapid taper at 250 mg every 12 h for 2 days, 125 mg every 12 hours for 2 days, and 60 mg every 12 hours for 2 days Treat convulsive status epilepticus

Reference: NCCN Guidelines Version 1.2022 https://www.nccn.org/professionals/physician_gf/pdf/neurotoxicity.pdf

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Wait...why not tocilizumab?

Tocilizumab does not cross the BBB

Tocilizumab has the *opposite* effect on ICANS. Peripheral IL-6 no longer binding, excess IL-6 crosses into BBB.

Administer for concurrent ICANS and CRS

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Case study

70yoF with R/R kappa MM presented for teclistamab initiation. Step-up dose 1 tolerated well. The day after step-up dose 2, RRT for confusion, inability to track, walk or follow commands and generalized weakness. VSS, Temp > 38.0, SBP 140-150s, mildly tachycardia.

CRS Severity	CRS Management
Grade 1 Fever > 38°C, not attributable to other cause Headache, myalgia, malaise Diarrhea, nausea, vomiting Pruritus	1. Discontinue anti-tumor therapy for 24 hours 2. Supportive care: oral acetaminophen for fever, oral NSAIDs for pain, oral antiemetics for nausea, oral ondansetron for vomiting, oral antihistamines for pruritus 3. Hydration
Grade 2 Fever > 38°C, not attributable to other cause Headache, myalgia, malaise Diarrhea, nausea, vomiting Pruritus Tachycardia, RR > 20 Hypotension, SBP < 90 mmHg	1. Discontinue anti-tumor therapy for 24 hours 2. Supportive care: oral acetaminophen for fever, oral NSAIDs for pain, oral antiemetics for nausea, oral ondansetron for vomiting, oral antihistamines for pruritus 3. Hydration 4. Discontinue anti-tumor therapy for 24 hours 5. Discontinue anti-tumor therapy for 24 hours 6. Discontinue anti-tumor therapy for 24 hours 7. Discontinue anti-tumor therapy for 24 hours 8. Discontinue anti-tumor therapy for 24 hours 9. Discontinue anti-tumor therapy for 24 hours 10. Discontinue anti-tumor therapy for 24 hours 11. Discontinue anti-tumor therapy for 24 hours 12. Discontinue anti-tumor therapy for 24 hours 13. Discontinue anti-tumor therapy for 24 hours 14. Discontinue anti-tumor therapy for 24 hours 15. Discontinue anti-tumor therapy for 24 hours 16. 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Grade 3 Fever > 38°C, not attributable to other cause Headache, myalgia, malaise Diarrhea, nausea, vomiting Pruritus Tachycardia, RR > 20 Hypotension, SBP < 90 mmHg Confusion, inability to track, walk or follow commands Generalized weakness	1. Discontinue anti-tumor therapy for 24 hours 2. Supportive care: oral acetaminophen for fever, oral NSAIDs for pain, oral antiemetics for nausea, oral ondansetron for vomiting, oral antihistamines for pruritus 3. Hydration 4. Discontinue anti-tumor therapy for 24 hours 5. Discontinue anti-tumor therapy for 24 hours 6. Discontinue anti-tumor therapy for 24 hours 7. Discontinue anti-tumor therapy for 24 hours 8. Discontinue anti-tumor therapy for 24 hours 9. Discontinue anti-tumor therapy for 24 hours 10. Discontinue anti-tumor therapy for 24 hours 11. Discontinue anti-tumor therapy for 24 hours 12. Discontinue anti-tumor therapy for 24 hours 13. Discontinue anti-tumor therapy for 24 hours 14. Discontinue anti-tumor therapy for 24 hours 15. 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CRS Grade 1

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Let's break it down

RRT for confusion, inability to track, walk or follow commands and generalized weakness. ICE 0/10

ICE score		
Orientation (4pts)	Year, Month, City, Hospital	0
Naming (3pts)	Ability to name 3 objects	0
Follow Commands (1pt)	Ability to follow simple commands	0
Writing (1pt)	Ability to write a standard sentence	0
Attention (1pt)	Ability to count backwards from 100 by 10	0
Total:		0

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ICANS Grade and Management

ICE score = 0

ICANS Grading System: ICANS grade is determined by the most severe event (ICE score, level of consciousness, seizures, hyperkalemia, renal dysfunction) observed in any other cause. For example, a patient with an ICE score of 4 who has a seizure is graded as grade 3 ICANS.

ICANS Grade	Grade 1	Grade 2	Grade 3	Grade 4
Depressed LOC	Asymptomatic	Asymptomatic to mild	Asymptomatic to moderate	Disorientation and/or requires continuous supervision or constant bedside care
Seizure	Any clinical seizure (partial or generalized)	Any clinical seizure (partial or generalized)	Any clinical seizure (partial or generalized)	Any clinical seizure (partial or generalized)
Motor findings	None	None	None	None
Increased INR/Partial Thromboplastin Time	None	None	None	None

ICANS= Grade 3

Tx
Dexamethasone 10mg IV for ICANS
Tocilizumab at 8 mg/kg for CRS (concurrent)

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Case study

73yoF with refractory MM admitted for teclistamab initiation. The day following first step-up dose, APP called to bedside for mild rigors/chills. Endorses a mild headache. Temp 37.2, SBP 130-140's, HR 90's, SPO2 upper 90's on RA, RR18. ICE score 10/10. Demerol given, APAP deferred to avoid fever masking.

One hour later, patient febrile to 38.2 with rigors and hypotensive 89/41.

CRS Grading	CRS Management
Grade 1 Fever > 38°C, not attributable to any other cause. Myalgias/arthralgias. Fatigue/asthenia.	Supportive care eg, antipyretics, or hydration. If vital signs remain stable for 2 hours after symptoms resolve, consider discontinuing anti-CRS. Use clinical judgment for subsequent steps.
Grade 2 Fever > 38°C, not attributable to any other cause. Moderate rigors/chills, myalgias/arthralgias. Headache. Diarrhea/nausea/vomiting. Blood test abnormalities (eg, leukopenia) (documented at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100).	Notify Attending Physician. If not better in 24 hours or worse as needed. Consider IV fluids. Consider IV acetaminophen 10 mg/kg q 6 hours (max 3000 mg daily). Consider IV morphine 2 mg q 4 hours (max 30 mg daily). Consider IV ondansetron 8 mg q 8 hours (max 32 mg daily). Consider IV loperamide 2 mg q 12 hours (max 8 mg daily). Consider IV fluids. Consider IV fluids. Consider IV fluids.
Grade 3 Fever > 38°C, not attributable to any other cause. Severe rigors/chills, myalgias/arthralgias. Severe headache. Severe diarrhea/nausea/vomiting. Blood test abnormalities (eg, leukopenia) (documented at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100).	Grade 2 management and reduce temperature as needed. Consider IV fluids to assess cardiac function and conduct ECG. Consider IV acetaminophen 10 mg/kg q 6 hours (max 3000 mg daily). Consider IV morphine 2 mg q 4 hours (max 30 mg daily). Consider IV ondansetron 8 mg q 8 hours (max 32 mg daily). Consider IV loperamide 2 mg q 12 hours (max 8 mg daily). Consider IV fluids. Consider IV fluids. Consider IV fluids.
Grade 4 Fever > 38°C, not attributable to any other cause. Severe rigors/chills, myalgias/arthralgias. Severe headache. Severe diarrhea/nausea/vomiting. Blood test abnormalities (eg, leukopenia) (documented at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100).	Grade 3 management and reduce temperature as needed. Consider IV fluids to assess cardiac function and conduct ECG. Consider IV acetaminophen 10 mg/kg q 6 hours (max 3000 mg daily). Consider IV morphine 2 mg q 4 hours (max 30 mg daily). Consider IV ondansetron 8 mg q 8 hours (max 32 mg daily). Consider IV loperamide 2 mg q 12 hours (max 8 mg daily). Consider IV fluids. Consider IV fluids. Consider IV fluids.

CRS Grade 2

Tx: IVF bolus with good response, acetaminophen, demerol, and Tocilizumab. BCx collected

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Patient then received home regimen of methadone, trazodone, gabapentin, and lorazepam. RRT activated for AMS, awakens to voice.

ICE score	Year, Month, City, Hospital	1
Orientation (4pts)	Year, Month, City, Hospital	1
Naming (3pts)	Ability to name 3 objects	1
Follow Commands (1pt)	Ability to follow simple commands	1
Writing (1pt)	Ability to write a standard sentence	0
Attention (1pt)	Ability to count backwards by 10 from 100	0
Total:		3

ICANS Grading System: ICANS grade is determined by the most severe event (ICE score, level of consciousness, seizure, motor findings, visual QEEG) recorded and not attributable to any other cause; for example, a patient with an ICE score of 3 who has a prolonged seizure is classified as grade 3 ICANS.

Neurotoxicity Domain	Grade 1	Grade 2	Grade 3	Grade 4
ICU Score	7-9	3-6	0-2	0 (intubated and unable to perform ICE)
Depressed LOC	Answers spontaneously	Answers to verbal or visual	Answers only to tactile stimulus	Continuous vigorous or purposeful stimulus to arouse. Slips or falls.
Seizure	N/A	N/A	Any clinical seizure (focal or generalized) that requires therapy or hospitalization	Life-threatening prolonged seizure (> 5 min) or multiple seizures without return to baseline or between seizures.
Motor findings	N/A	N/A	N/A	Deep focal motor responses such as an arm abduction.
Increased RPP/Convulse Policy	N/A	N/A	N/A	Diffuse cerebral motor on hour-long EEG or hour-long EEG with focal motor activity.

ICANS Grade 2

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ICANS Grading and Management

Neurotoxicity Management	Management (neurotoxicity only)
Grade 1:	Notify covering provider Daily neuro exam
Grade 2:	Notify Attending Physician Notify covering provider 1 dose of dexamethasone 10 mg IV and reassess. Can repeat every 6-12 hours, if no improvement. Daily neuro exam
Grade 3:	Notify Attending Physician ICU level of care recommended START dexamethasone 10 mg IV Q8h or methylprednisolone, 1 mg/kg IV Q2h Anti-reflexic if concerns for seizures (eg, benzodiazepine)
Grade 4:	Notify Attending Physician ICU level of care recommended START methylprednisolone IV 5000 mg/day (may consider twice a day) for 3 days, followed by rapid taper at 250 mg every 12 h for 2 days, 125 mg every 12 hours for 2 days, and 60 mg every 12 hours for 2 days. Treat convulsive status epilepticus

DDx: CRS, ICANS with seizure, Sepsis, Over sedation

Tx: ICU, Narcan gtt, IV Dexamethasone

Follow up: 1 of 2 (peripheral) BCx + for strep mutans

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64yoM with MM receives first dose of talquetamab. 28 hours after dose, patient develops AMS with Grade 3 ICANS without CRS. Which intervention would not be warranted for this patient?

- Dexamethasone 0%
- Tocilizumab 0%
- Keppra 0%
- None of the above 0%

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There's an app for that

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Created by CAR-T team at MD Anderson


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There's a dot phrase for that

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Future directions

- Prophylaxis for CRS/ICANS? Reduce efficacy of treatment?
- Role of siltuximab, ruxolitinib, anakinra, dasatinib, and cyclophosphamide
- Improve the safety of T cell-engaging immunotherapy



64

What is your current level of comfort for managing CRS/ICANS as potential toxicities to immunotherapy?

Comfortable	0%
Somewhat comfortable, I need to see it in practice	0%
Not at all comfortable, I would like to learn more about it	0%

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Hung-Jui (Ray) Tan, MD, MSHPM

RESEARCH TO PRACTICE
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4:00 PM
Catawba Indian Nation & Lung Cancer Institute:
Partners in Healing
Daniel R. Carrissa, MD, MS
Darcy Dooze, RN, RN
Kia Dungan, PA-C
Melisa Wheeler, RN, MPH

RESEARCH TO PRACTICE
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