

SUSTAIN

Systematic Uptake and Standardization of Treatment
Advances Through an Integrated Network for
BISPECIFIC ANTIBODY THERAPY

Provided by  UK HealthCare

 The
France
Foundation

Planning Committee



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- Ayman Qasrawi, MD, has served as a consultant for Sanofi Pharmaceuticals. The financial relationship ended in June 1, 2026.

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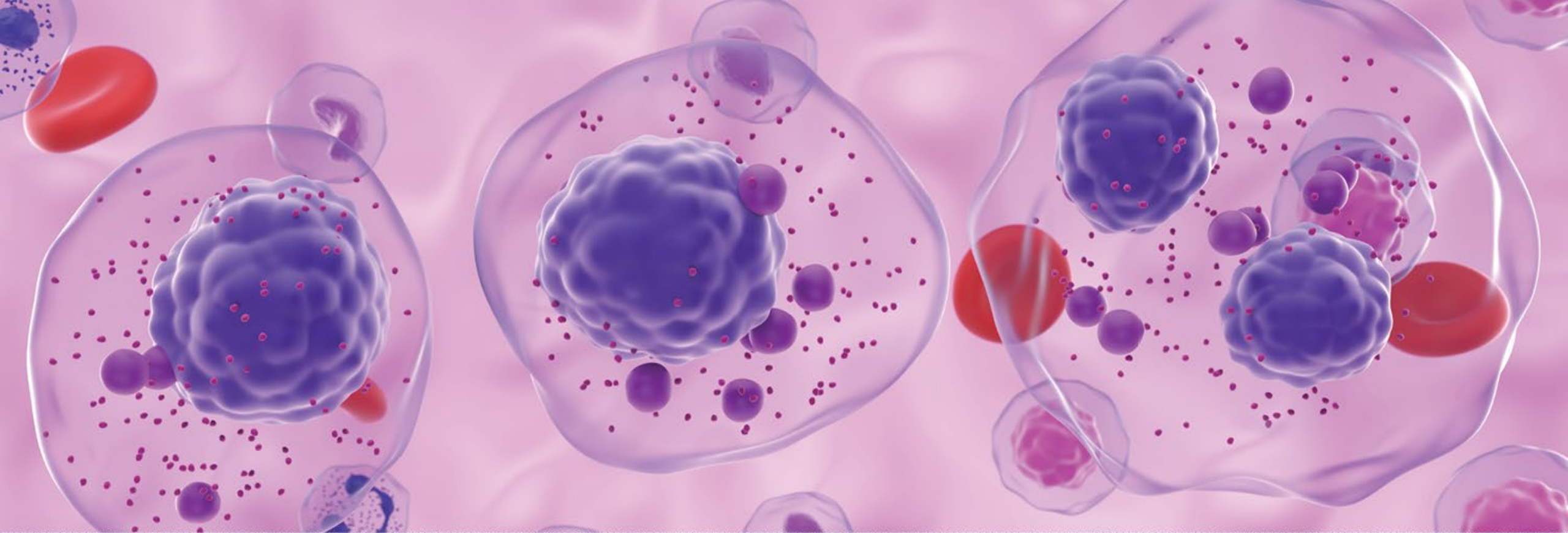
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For full course
information, visit:





**Session 4: ICANS—Neurotoxicity
Recognition, Grading, and Intervention
Strategies**



Curriculum Learning Objective

- Educate multidisciplinary teams on BsAb pharmacology; recognition and grading of adverse events; and appropriate interventions including, when to escalate care
- Establish emergency response protocols, multidisciplinary rapid response teams, and clear communication pathways with UKHC for complex cases
- Train providers in appropriate patient selection criteria, risk stratification, and patient/caregiver education regarding expectations, monitoring requirements, and symptom reporting



Session Objectives

- Recognize and grade ICANS following bispecific antibody therapy
- Incorporate monitoring strategies to detect and manage ICANS early
- Apply appropriate ICANS management



What Do You Know?



Which monitoring approach best aligns with ASTCT recommendations for early detection of ICANS in patients receiving bispecific antibodies?

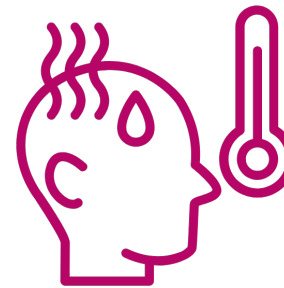
- A. Baseline and daily ICE-based neurologic assessments during risk period
- B. Routine brain MRI at baseline and at set intervals
- C. Continuous EEG monitoring for all patients
- D. Symptom-triggered neurologic assessments only

Adverse Events Associated With BsAbs

BsAbs are associated with potentially serious and fatal adverse events including:



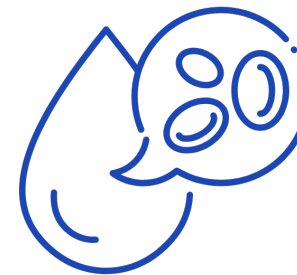
ECHO #3 reviewed important considerations for monitoring and managing patients with CRS



Cytokine release syndrome (CRS)



Immune effector cell-associated neurotoxicity syndrome (ICANS)



Cytopenias



Infection

Pre-Medications Reduce the Risk of ICANS Prior to Infusion

	Teclistamab and Talquetamab	Elranatamab	Linvoseltamab
Pre-Medications	<ul style="list-style-type: none"> Acetaminophen 650-1000 mg PO Diphenhydramine 50 mg PO/IV (PO defaulted) Dexamethasone 16 mg PO/IV (PO defaulted) 	<ul style="list-style-type: none"> Acetaminophen 650 mg PO Diphenhydramine 25 mg PO/IV (PO defaulted) Dexamethasone 20 mg PO/IV (PO defaulted) 	<ul style="list-style-type: none"> Acetaminophen 650 mg PO Diphenhydramine 25 mg PO/IV (PO defaulted) Dexamethasone 40 mg PO/IV
	<ul style="list-style-type: none"> Given 1 hour prior to BsAb dose Required for all step-up doses and the first treatment dose PRN thereafter if CRS with prior dose or delay in treatment schedule 		

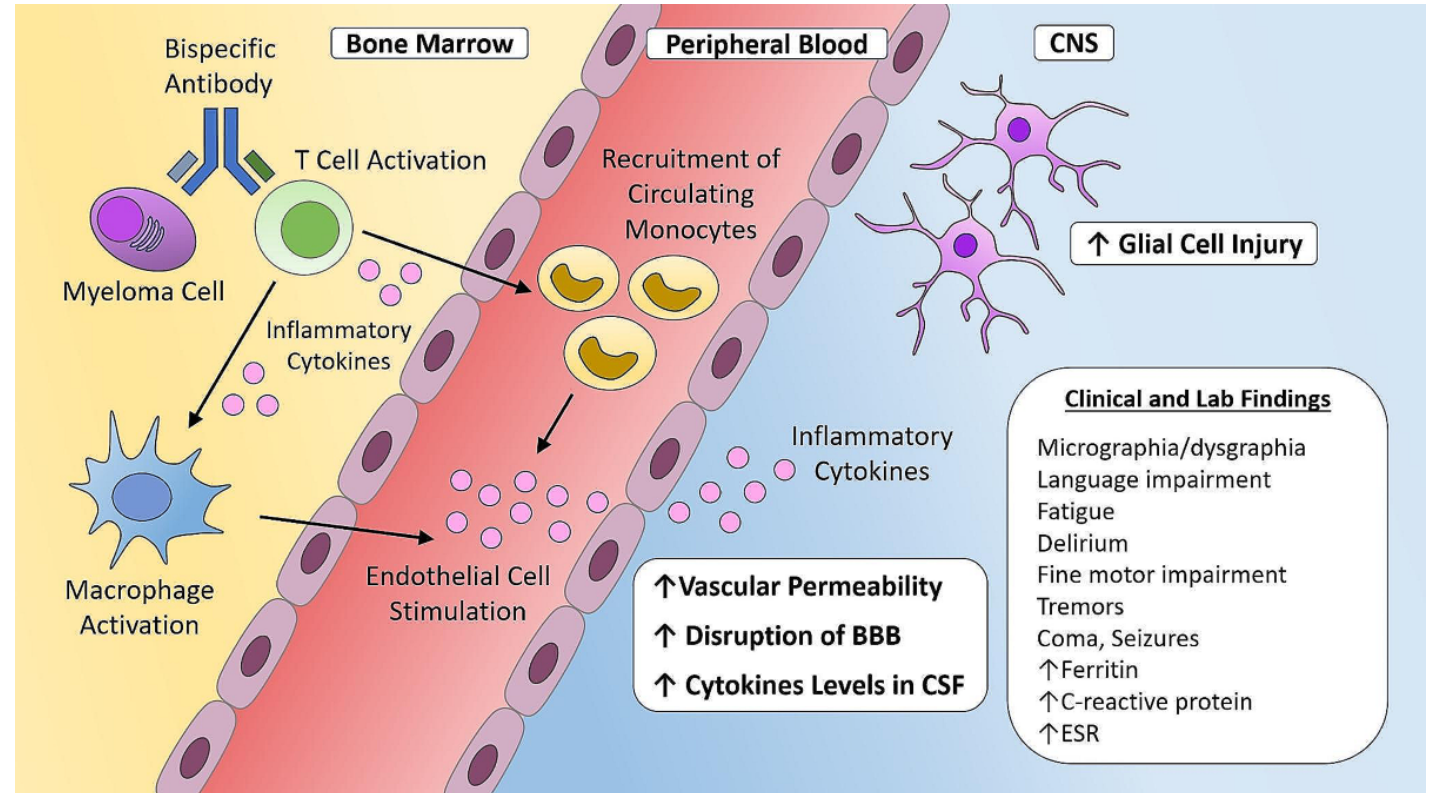
ECHO #5 will review how to treat and manage patients with infections!

PO = by mouth; PRN = as needed

Teclistamab-cqyv (Tecvayli) [prescribing information]. Janssen Biotech, Inc; March 2026; Elranatamab-bcmm (Elrexio) [prescribing information]. Pfizer Inc; July 2025; Talquetamab-tgvs (Talvey) [prescribing information]. Janssen Biotech, Inc; August 2023. Linvoseltamab-gcpt (Lynozytic) [prescribing information]. Regeneron Pharmaceuticals, Inc; July 2025.

Pathophysiology of Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)

- Neurological toxicity caused by the inflammatory cytokines released after BsAb therapy
 - Leads to disruption of the blood-brain barrier and accumulation of cytokines in the CNS
- ICANS is a diagnosis of exclusion



CRS often precedes ICANS—it is important to promptly recognize the signs and symptoms!

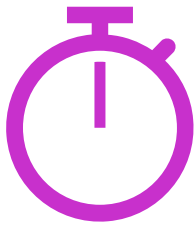
BBB = blood brain barrier; CNS = central nervous system; CSF = cerebrospinal fluid; ESR = erythrocyte sedimentation rate

Pan D, Richter J. *Curr Hematol Malig Rep.* 2024;19(6):237-245; Lee DW, et al. *Biol Blood Marrow Transplant.* 2019;25:625-638;

Risk Factors for ICANS



Concurrent CRS



Early treatment period (step-up dosing, or within the first few doses)



Pre-existing neurological conditions

Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25:625-638; Santomaso BD, et al. *J Clin Onc* 2021; 39: 3978-3992; Ludwig H, et al. *Lancet Oncol*. 2023;24: e255-69; VHA Guidance. Accessed April 15, 2026. https://www.va.gov/formularyadvisor/DOC_PDF/CRE_Bispecific_Antibody_CRIS_and_ICANS_Neurotoxicity_Guidance_Feb2024.pdf; Teclistamab-cqyv (Tecvayli) [prescribing information]. Janssen Biotech, Inc; March 2026; Elranatamab-bcmm (Elrexio) [prescribing information]. Pfizer Inc; July 2025; Talquetamab-tgvs (Talvey) [prescribing information]. Janssen Biotech, Inc; August 2023; Linvoseltamab-gcpt (Lynozzyfic) [prescribing information]. Regeneron Pharmaceuticals, Inc; July 2025.

Symptoms of ICANS



Trouble Concentrating



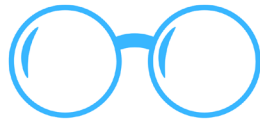
Confusion



Difficulty Writing



Fatigue/Lethargy



Vision Changes



**Slurred Speech/
Trouble Speaking**



Headache



Seizure/Tremors



Slower Movements

Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25:625-638; Santomasso BD, et al. *J Clin Oncol* 2021; 39: 3978-3992; Ludwig H, et al. *Lancet Oncol*. 2023;24: e255-69; VHA Guidance. Accessed April 15, 2026. https://www.va.gov/formularyadvisor/DOC_PDF/CRE_Bispecific_Antibody_CRS_and_ICANS_Neurotoxicity_Guidance_Feb2024.pdf; Teclistamab-cqyv (Tecvayli) [prescribing information]. Janssen Biotech, Inc; March 2026; Elranatamab-bcmm (Elrexio) [prescribing information]. Pfizer Inc; July 2025; Talquetamab-tgvs (Talvey) [prescribing information]. Janssen Biotech, Inc; August 2023; Linvoseltamab-gcpt (Lynozytic) [prescribing information]. Regeneron Pharmaceuticals, Inc; July 2025.

Timing of ICANS

BsAb	Median Time to ICANS Onset After Most Recent Dose	Median Duration of ICANS
Teclistamab monotherapy	4 days	3 days
Teclistamab + daratumumab	2 days	2 days
Elranatamab	3 days	2 days
Talquetamab	2.5 days	2 days
Linvoseltamab	1 day	2 days

VHA Guidance. Accessed April 15, 2026. https://www.va.gov/formularyadvisor/DOC_PDF/CRE_Bispecific_Antibody_CRS_and_ICANS_Neurotoxicity_Guidance_Feb2024.pdf; Teclistamab-cqyv (Tecvayli) [prescribing information]. Janssen Biotech, Inc; March 2026; Elranatamab-bcmm (Elrexio) [prescribing information]. Pfizer Inc; July 2025; Talquetamab-tgvs (Talvey) [prescribing information]. Janssen Biotech, Inc; August 2023; Linvoseltamab-gcpt (Lynozytic) [prescribing information]. Regeneron Pharmaceuticals, Inc; July 2025.

Incidence of ICANS

BsAb	Incidence of ICANS in Clinical Trials
Teclistamab monotherapy	6%
Teclistamab + daratumumab	1.1%
Elranatamab	3.3%
Talquetamab	9%
Linvoseltamab	8%

Teclistamab-cqyv (Tecvayli) [prescribing information]. Janssen Biotech, Inc; March 2026; Elranatamab-bcmm (Elrexfio) [prescribing information]. Pfizer Inc; July 2025; Talquetamab-tgvs (Talvey) [prescribing information]. Janssen Biotech, Inc; August 2023; Linvoseltamab-gcpt (Lynozyfic) [prescribing information]. Regeneron Pharmaceuticals, Inc; July 2025.

Consequences of Unrecognized ICANS

Severe cases of ICANS can lead to coma or cerebral edema if not caught and managed in a timely fashion

Patients may develop persistent neurologic problems, including residual cognitive or language deficits in some cases

- Patients may experience a severe functional decline in performing daily activities

Prompt recognition and treatment are essential

Teclistamab-cqyv (Tecvayli) [prescribing information]. Janssen Biotech, Inc; March 2026; Elranatamab-bcmm (Elrexio) [prescribing information]. Pfizer Inc; July 2025; Talquetamab-tgvs (Talvey) [prescribing information]. Janssen Biotech, Inc; August 2023; Linvoseltamab-gcpt (Lynozytic) [prescribing information]. Regeneron Pharmaceuticals, Inc; July 2025; Crombie JL, et al. *Blood*. 2024;143(16):1565-1575.



Assessment of ICANS (ICE Score)

- Grading utilizes the Immune Effector Cell Encephalopathy Score assessment tool (ICE)
 - Higher scores are typically indicative of a lower grade ICANS
- Patients are assessed (often every 8 hours) on the following:
 - Orientation (4 points): Year, month, city, hospital
 - Naming (3 points): Name 3 objects
 - Following Commands (1 point)
 - Writing (1 point): Ability to write a standard sentence
 - Attention (1 point): Count backwards from 100 by 10

Monitoring for ICANS in Inpatient and Intensive Care Settings (1/2)



Perform a **physical exam** and review of vitals

Give neurological examination using the **ICE score** and **neurotoxicity domain of ASTCT twice daily**

- Consider a neurology consult

Assess for signs of **increased intracranial pressure**

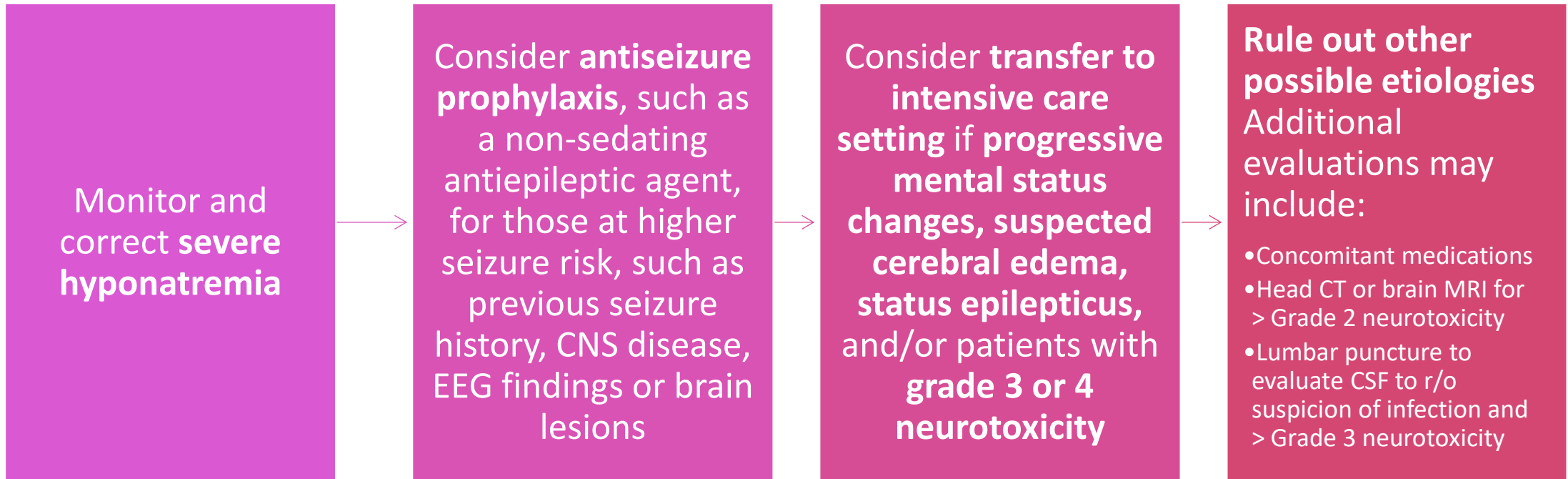
- Consider ophthalmology consult to perform fundoscopy

Order labs for **CBC, chem profile, PT, aPTT, fibrinogen, ferritin, and CRP**

aPTT = activated partial thromboplastin time; CBC = complete blood count; PT = prothrombin time

Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25:625-638; Santomasso BD, et al. *J Clin Onc* 2021; 39: 3978-3992; Ludwig H, et al. *Lancet Oncol*. 2023;24: e255-69; VHA Guidance. Accessed April 15, 2026. https://www.va.gov/formularyadvisor/DOC_PDF/CRE_Bispesific_Antibody_CRS_and_ICANS_Neurotoxicity_Guidance_Feb2024.pdf; Teclistamab-cqyv (Tecvayli) [prescribing information]. Janssen Biotech, Inc; March 2026; Elranatamab-bcmm (Elrexio) [prescribing information]. Pfizer Inc; July 2025; Talquetamab-tgvs (Talvey) [prescribing information]. Janssen Biotech, Inc; August 2023; Linvoseltamab-gcpt (Lynozytic) [prescribing information]. Regeneron Pharmaceuticals, Inc; July 2025.

Monitoring for ICANS in Inpatient and Intensive Care Settings (2/2)



Reserve intensive care setting for patients with worsening condition likely secondary to cerebral edema, status epilepticus and/or grade 3-4 ICANS/neurotoxicity

CT = computed tomography; EEG = electroencephalogram; MRI = magnetic resonance imaging

Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25:625-638; Santomasso BD, et al. *J Clin Oncol* 2021; 39: 3978-3992; Ludwig H, et al. *Lancet Oncol*. 2023;24: e255-69; VHA Guidance. Accessed April 15, 2026. https://www.va.gov/formularyadvisor/DOC_PDF/CRE_Bisppecific_Antibody_CRS_and_ICANS_Neurotoxicity_Guidance_Feb2024.pdf; Teclistamab-cqyv (Tecvayli) [prescribing information]. Janssen Biotech, Inc; March 2026; Elranatamab-bcmm (Elrexio) [prescribing information]. Pfizer Inc; July 2025; Talquetamab-tgvs (Talvey) [prescribing information]. Janssen Biotech, Inc; August 2023; Linvoseltamab-gcpt (Lynozytic) [prescribing information]. Regeneron Pharmaceuticals, Inc; July 2025.

ICANS Grading

Grade 1:

- Awakens spontaneously
- Fatigue
- ICE Score 7-9

Grade 2:

- Awakens to voice
- Delirious/somnolent
- ICE Score 3-6

Grade 3:

- Awakens to tactile stimulus
- Local edema on imaging
- Seizure that resolves with intervention
- ICE Score 0-2

Grade 4:

- Comatose
- Cerebral edema
- Life-threatening seizures
- Motor weakness
- ICE Score 0

Teclistamab-cqyv (Tecvayli) [prescribing information]. Janssen Biotech, Inc; March 2026; Elranatamab-bcmm (Elrexio) [prescribing information]. Pfizer Inc; July 2025; Talquetamab-tgvs (Talvey) [prescribing information]. Janssen Biotech, Inc; August 2023; Linvoseltamab-gcpt (Lynozytic) [prescribing information]. Regeneron Pharmaceuticals, Inc; July 2025.

Teclistamab, Elranatamab, and Talquetamab Guidance for Managing ICANS

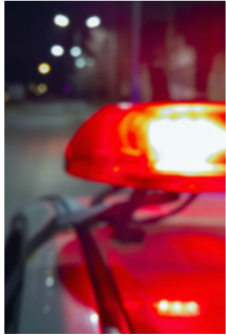
Grade	Action
1	<ul style="list-style-type: none">• Withhold BsAb until ICANS resolves• Monitor neurologic symptoms, and consider consultation with neurologist and other specialists• Consider non-sedating, anti-seizure medicines for seizure prophylaxis
2	<ul style="list-style-type: none">• Grade 1 actions• Administer dexamethasone 10 mg intravenously every 6 hours<ul style="list-style-type: none">— Continue dexamethasone use until resolution to Grade 1 or less, then taper• Monitor patients within proximity of a health care facility for 48 hours following the next dose and consider hospitalization
3	<ul style="list-style-type: none">• First occurrence of Grade 3: Grade 2 actions; Provide supportive therapy, which may include intensive care
	<ul style="list-style-type: none">• Recurrent Grade 3: Same as first occurrence of Grade 3 symptoms + Permanently discontinue BsAb
4	<ul style="list-style-type: none">• Recurrent Grade 3 actions• Consider instead of dexamethasone using methylprednisolone 1000 mg per day intravenously and continue methylprednisolone 1000 mg per day intravenously for 2 or more days

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Linvoseltamab Guidance for Managing ICANS

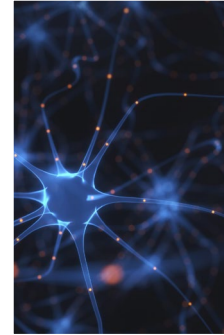
Grade	Action
1	<ul style="list-style-type: none">• Withhold BsAb until ICANS resolves or returns to baseline• Provide supportive therapy• Manage per current guidelines• Consider non-sedating, anti-seizure medicines for seizure prophylaxis
2	<ul style="list-style-type: none">• Grade 1 actions• Administer dexamethasone 10 mg intravenously every 6 hours<ul style="list-style-type: none">— Continue dexamethasone use until resolution to Grade 1 or less, then taper• Monitor patients within proximity of a health care facility for 24 hours following the next dose and consider hospitalization
3	<ul style="list-style-type: none">• Grade 2 actions• Consider neurology evaluation• Resume treatment with at a reduced dose and hospitalize for 24 hours after the administration of the dose• Permanently discontinue for recurrent Grade 3 ICANS
4	<ul style="list-style-type: none">• Recurrent Grade 3 actions

Caution With Tocilizumab



Tocilizumab can worsen ICANS by increasing systemic IL-6 levels in the CNS

- Tocilizumab binds to peripheral IL-6 receptors



Tocilizumab cannot cross the BBB and is therefore unable to neutralize the neurotoxic inflammatory cascade



Tocilizumab is not recommended for isolated ICANS and should only be used when the patient is experiencing concomitant CRS

Real-Time Management of ICANS

Without CRS

Grade 1:

- Supportive care
- IV hydration
- Aspiration precautions
- Consider non-sedating, anti-seizure medicines for seizure prophylaxis
- Consider neurology consult

Grade 2:

- Supportive care as Grade 1
- Administer dexamethasone 10 mg IV x 2 (or equivalent) and reassess
- Repeat every 6-12 hours if no improvement
- Rapidly taper once symptoms improve

Grade 3:

- Supportive care as Grade 2
- Transfer to ICU
- Continuous corticosteroids (every 6-12 hours or equivalent) and anti-epileptic drugs

Grade 4:

- Consider mechanical ventilation for airway protection
- Administer high-dose methylprednisolone IV 1000 mg one to two times daily for 3 days; if no improvement, can increase to two to three times daily
- Continue corticosteroids until Gr 1, then taper as appropriate

With CRS

Above care + tocilizumab 8mg/kg IV over 1 hour. Repeat every 8 hours as needed. Limit to maximum of 3 doses/24-hr period.

- Above care + Gr 1 CRS care
- Transfer to ICU

- Above care + Gr 1 CRS care

- Above care + Gr 1 CRS care

Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25:625-638; Santomasso BD, et al. *J Clin Onc* 2021; 39: 3978-3992; Ludwig H, et al. *Lancet Oncol*. 2023;24: e255-69; VHA Guidance. Accessed April 15, 2026.

https://www.va.gov/formularyadvisor/DOC_PDF/CRE_Bispecific_Antibody_CRS_and_ICANS_Neurotoxicity_Guidance_Feb2024.pdf

What did you learn?



Which monitoring approach best aligns with ASTCT recommendations for early detection of ICANS in patients receiving bispecific antibodies?

- A. Baseline and daily ICE-based neurologic assessments during risk period
- B. Routine brain MRI at baseline and at set intervals
- C. Continuous EEG monitoring for all patients
- D. Symptom-triggered neurologic assessments only



Role of the Pharmacy

- Review patient's home medication regimen
 - Consider holding or modifying sedating medications for 1-2 days following step-up doses
 - Clinically-significant drug interactions with BsAbs are rare
- Manage inventory of both BsAbs and tocilizumab
 - Ensure quick access to tocilizumab for cases where it's needed
- Collaboration in development of institutional protocols for ICANS management



Key Takeaways

- Anticipate ICANS, especially in patients with CRS, and ensure appropriate inpatient monitoring for initial doses
- Grade ICANS promptly using standardized criteria to guide management decisions
- Initiate timely treatment with corticosteroids and an anti-epileptic medication
- Use mitigation strategies, including step-up dosing, premedication, and treatment holds/resumption per protocol to reduce severity and recurrence



Ask the Audience!

Please unmute or use the chat feature to discuss with your colleagues.

What are your top 3 concerns on recognizing, assessing, and managing ICANS in your clinical practice?



Case Studies

Please come off mute or use the chat feature to discuss with your colleagues and ask questions about your patient cases.

Remember Our Case From Session 3!

- 81-year-old male with history of R-ISS stage III IgG Lambda MM
- Experienced Grade 3 CRS
 - Patient started on **empiric cefepime 2 g IV q8h**
 - Started on **vasopressin 0.03 units/min IV to maintain MAP >65** and **norepinephrine 0.2–0.4 mcg/kg/min IV to maintain MAP >65**
 - Continued **prophylactic acyclovir**
 - Over the next 2 days:
 - » s/p **tocilizumab 800 mg IV × 1 dose** (dose #1) at 21:47 PM → **ongoing hypotension**
 - » s/p **tocilizumab 800 mg IV × 1 dose** (dose #2) at 11:30 AM the following day (< 48 hours later)
 - **Infectious workup broadened**: EBV, *Rickettsia*, *Ehrlichia/Anaplasma*, *Babesia*, and *Francisella tularensis* testing → all negative
 - Patient escalated to **cefepime, metronidazole, and vancomycin**
 - **Vasopressor support** was subsequently **discontinued**, and patient was eventually **de-escalated from antibiotics**

EBV = Epstein-Barr virus; IgG = immunoglobulin G; MAP = mean arterial pressure; MM = multiple myeloma; q8h = every 8 hours; R-ISS = Revised International Staging System; s/p = status post

What Happened Next?

- **Also had altered mental status PRIOR to tocilizumab:**
 - 1/24 ammonia level: 11 (normal)
 - 1/24 CT head: no evidence of intracranial mass, hemorrhage, or acute territorial infarction
 - EMV 15, upon assessment, however, reported intermittent situational confusion/hallucinations
 - Frequent reorientation
 - **Dexamethasone 10mg IV every 6 hours for grade 1 ICANS**
 - » **Worsened mental status**
- **ICE Score: 7/10**
 - Orientation to year, month, city, hospital: 3
 - Name 3 objects: 3
 - Follow commands: 1
 - Ability to write a standard sentence: 0
 - Count backward from 100 by ten: 0

CT = computed tomography; EMV = eye, motor, verbal response score



What Treatments Were Initiated?

- **Dexamethasone 10mg IV every 6 hours for grade 1 ICANS over the next 3 days for persistent grade 1 ICANS**
- **EEG: consistent with moderate diffuse cerebral dysfunction (moderate encephalopathy)**
 - No seizures or interictal epileptiform activity
 - The tremulousness and jerking of the head, face, and arms had no ictal EEG correlation and are non-epileptic in nature
 - **Recommended discontinuing cefepime and using an alternative antibiotic**



What Treatments Were Initiated?

- Cefepime changed to meropenem
- **MR head: Small acute ischemic infarcts in the bilateral cerebellar hemispheres and the right occipital lobe as above**
 - No subacute intracranial hemorrhage
- **Following day: ICE score 9/10 (grade 1 ICANS)**
- **Patient continues to receive teclistamab with at least VGPR by biochemical monitoring (patient opted not to repeat BM Bx) and continues monthly dosing of teclistamab**

EEG = electroencepalogram

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