



Advancing RRMM Care Through Communities of Practice: Educating Community-Based Hematologic/Oncologic Teams on the Use of BCMA-Directed BsAbs

**Prevention, Monitoring, and Management of Adverse Events Associated
With BCMA-Directed Bispecific Antibodies in Multiple Myeloma**

Led by



Produced in collaboration with



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Faculty

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Disclosures and Off-Label Discussion

Dr. Sara Scott is a consultant for GSK, Johnson & Johnson Innovative Medicine, Pfizer Inc., and Sanofi.

The discussion includes the consideration of tocilizumab for CRS prophylaxis, which is in the National Comprehensive Cancer Network (NCCN) guideline, but this use is off-label. Anakinra is also not FDA approved for the treatment of CRS or ICANS, but it is commonly integrated into guidelines.



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Learning Objectives

Upon completion, participants should be able to:

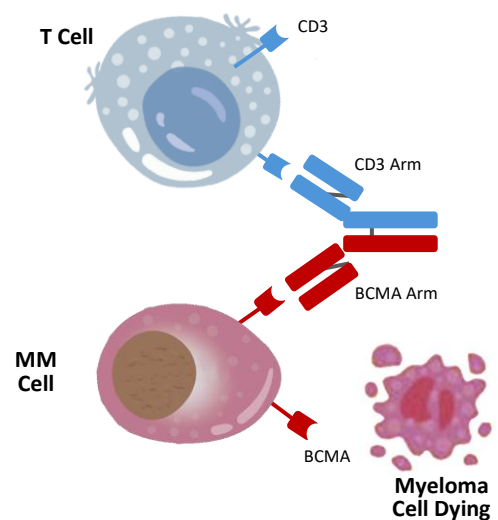
- Describe the diagnosis, risk factors, prevention, and management of cytokine release syndrome and immune effector cell–associated neurotoxicity syndrome
- Recognize infectious complications associated with BCMA-directed BsAbs and implement strategies for their prevention
- Establish and follow workflows and lines of communication for monitoring and managing BCMA-directed BsAb treatment-related adverse events



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BCMAxCD3 BsAb Mechanism of Action

- BCMA is expressed on both normal and malignant plasma cells
- Preferentially expressed on mature B lymphocytes
 - Minimizes on-target, off-tumor toxicity
- BCMA plays an essential role in pathophysiology of MM
 - Overexpression is associated with proliferation and survival of MM cells
 - Role in immunosuppressive bone marrow microenvironment
- T-cell target: CD3
- BsAbs targeting BCMA
 - Teclistamab-cqyv
 - Elranatamab-bcmm
 - Linvoseltamab-gcpt
 - Investigational use only: ABBV-383 (etentamig), HPN217



Maus MV, et al. *Clin Cancer Res.* 2013;19:1917-9; Shah N, et al. *Leukemia.* 2020;34:985-1005; Sanchez E, et al. *Clin Cancer Res.* 2016;22:3383-97; Cho S, et al. *Front Immunol.* 2018;9:1821; IMF Current FDA-Approved Medications. <https://www.myeloma.org/multiple-myeloma-drugs>.

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Toxicities of BCMAxCD3 BsAbs

Cytokine Release Syndrome (CRS)

Neurologic Toxicity

Infection

Cytopenias

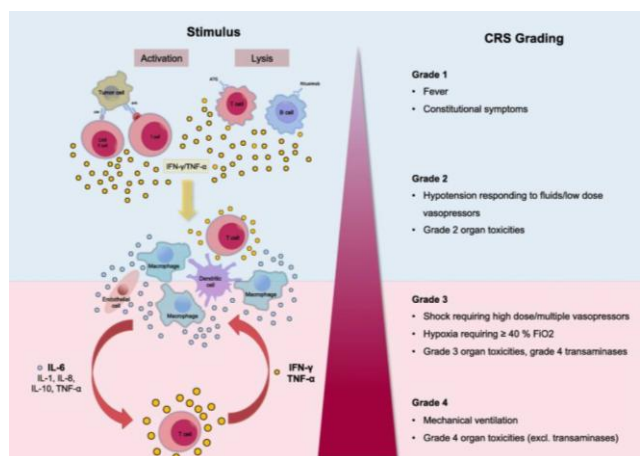


Ludwig H, et al. *Lancet Oncol.* 2023;24:e255-69.

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Cytokine Release Syndrome

- Risk factors not well defined
- Prevention
 - Step-up doses
 - Premedication including corticosteroids
 - Prophylactic tocilizumab
- Treatment options
 - Symptom management (eg, antipyretic)
 - Corticosteroids
 - Tocilizumab
 - Severe: anakinra, investigational agents
 - Supportive care: fluids, pressors, supplemental oxygen



Shimabukuro-Vornhagen A, et al. *J Immunother Cancer.* 2018;6:56;
Markouli M, et al. *Curr Oncol.* 2023;30:6330-52;
Rodriguez-Otero P, et al. *Lancet Oncol.* 2024;25:e205-16.



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Incidence and Timing of CRS

	All grade, n/N (%)	Grade ≥ 3, n/N (%)	Median time to onset (range)	Median duration (range)
Teclistamab	119/165 (72.1)	1/165 (0.6)	2 days (1-6)	2 days (1-9)
Elranatamab	71/123 (57.7)	0 (0)	2 days (1-9)	2 days (1-19)
Linvoseltamab (200 mg)	51/117 (44)	1/117 (0.9)	14.8 hours (0-117)	16.5 hours (1-144)

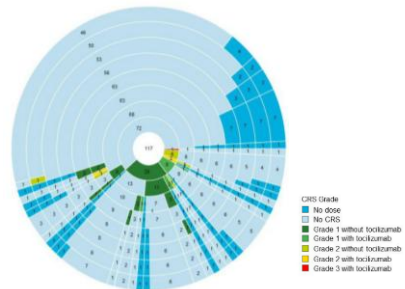
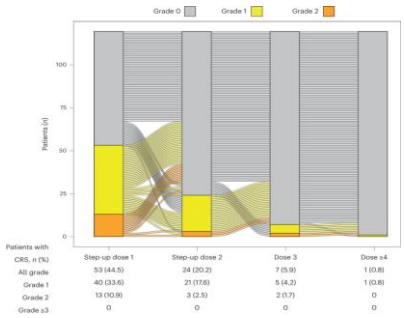
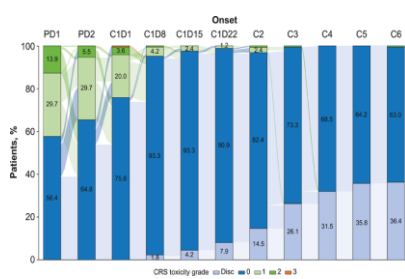


Table adapted from: Rodríguez-Otero P, et al. *Lancet Oncol.* 2024;25:e205-16. Martin TG, et al. *Cancer.* 2023;129:2035-46; Lesokhin AM, et al. *Nat Med.* 2023;29:2259-67; Bumma N, et al. *J Clin Oncol.* 2024;42:2702-12.

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Sample CRS Protocol

Prevention Strategies

- Premedication per product label
- Step-up dosing per product label
- Consider prophylactic tocilizumab prior to step-up dose 1

Workup

- Vital sign evaluation every 4-8 hours
- Infectious workup: blood cultures, initiate antibiotics
- Assess for concurrent neurotoxicity and other alternate diagnoses
- Review medications including last dose of antipyretic, steroid, or anticytokine

Treatment

- Grade 1: antipyretic, consider oral dexamethasone or tocilizumab
- Grade 2: antipyretic, tocilizumab; supportive care with IV fluids or oxygen as appropriate and consider steroids
- Grade 3+: same as grade 2 with additional supportive care such as vasopressors or increased supplemental oxygen; transfer care to ICU as appropriate; consider high-dose steroids or salvage therapy (ie, anakinra)

Monitoring

- Resolution of vital sign changes or other symptoms
- Follow up infectious workup and discontinue antibiotics as appropriate
- Resume therapy with next dose of BsAb per package insert



Rodríguez-Otero P, et al. *Lancet Oncol.* 2024;25:e205-16.

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Neurotoxicity

- Most common include headache, peripheral neuropathy, and immune effector cell–associated neurotoxicity syndrome (ICANS)
- ICANS incidence 3%-8% depending on product
- Risk factors not well defined
- Treatment options
 - Corticosteroids
 - Tocilizumab (if concurrent CRS)
 - Antiseizure prophylaxis
 - Anakinra

	All grade, n/N (%)	Grade ≥ 3, n/N (%)	Median time to onset (range)	Median duration (range)
Teclistamab	5/165 (3)	0 (0)	4 days (2-8)	3 days (1-20)
Elranatamab	4/123 (3.4)	0 (0)	2.5 days (1-4)	2 days (1-6)
Linvoseltamab (200 mg)	9/117 (7.7)	3/117 (2.6)	1 day (1-4)	2 days (1-11)

Markouli M, et al. *Curr Oncol*. 2023;30:6330-52; Rodriguez-Otero P, et al. *Lancet Oncol*. 2024;25:e205-16; Moreau P, et al. *N Engl J Med*. 2022;387:495-505; Van de Donk N, et al. IMS 2023. Abstract OA-51;

Garfall AL, et al. ASCO 2024. Abstract 7540; Lesohkin AM, et al. *Nature Med*. 2023;29:2259-67; Tomason M, et al. *Blood*. 2023;142:3385; Mohty M, et al. EHA 2024. Abstract P932; Bumma N, et al. *J Clin Oncol*. 2024;42:2702-12; Voorhees PM, et al. *Blood*. 2022;140:4401-4.



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Immune Effector Cell–Associated Encephalopathy (ICE) Score

Topic	Tasks	Score
Orientation	Orientation to year, month, city, hospital	4 points
Naming	Name 3 objects	3 points
Following commands	Follow simple commands (eg, “show me 2 fingers” or “close your eyes and stick out your tongue”)	1 point
Writing	Ability to write a standard sentence	1 point
Attention	Count backward from 100 by 10	1 point



Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;35:625-38.

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ICANS Grading

Neurotoxicity Domain	Grade 1	Grade 2	Grade 3	Grade 4
ICE score^a	7-9	3-6	0-2	0 (patient is unarousable)
Depressed level of consciousness^b	Awakens spontaneously	Awakens to voice	Awakens only to tactile stimulus	Patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse; stupor or coma
Seizure	N/A	N/A	Any clinical seizure focal or generalized that resolves rapidly or nonconvulsive seizures on EEG that resolve with intervention	Life-threatening prolonged seizure (> 5 minutes), repetitive clinical or electrical seizures without return to baseline in between
Motor findings^c	N/A	N/A	N/A	Deep focal motor weakness such as hemiparesis or paraparesis
Elevated ICP/cerebral edema	N/A	N/A	Focal/local edema on neuroimaging ^d	Diffuse cerebral edema on neuroimaging, decerebrate or decorticate posturing, cranial nerve VI palsy, papilledema, or Cushing's triad

ICANS grade is determined by the most severe event not attributable to any other cause.

^aA patient with an ICE score of 0 may be classified as grade 3 ICANS if awake with global aphasia, but a patient with an ICE score of 0 may be classified as grade 4 ICANS if unarousable.

^bAttributable to no other cause (eg, no sedating medication).

^cTremors and myoclonus associated with immune effector cell therapies may be graded according to CTCAE V.5.0, but they do not influence ICANS grading.

^dIntracranial hemorrhage with or without associated edema is not considered a neurotoxicity feature and is excluded from ICANS grading. It may be graded according to CTCAE V.5.0.



Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;35:625-38.

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Sample ICANS Protocol

Workup

- Complete ICE assessment every 8-12 hours
- If ICANS occurs, evaluate for concurrent CRS
- Consider brain imaging, EEG, or CSF evaluation depending on severity and treatment course
- Consider neurology consultation

Treatment

- Grade 1: observation
- Grade 2+: initiate systemic corticosteroids (dose and frequency dependent on grade)
- Administer tocilizumab if concurrent CRS
- Consider nonseizure prophylaxis (eg, levetiracetam 500 mg twice daily)
- Manage symptoms and escalate care to ICU as appropriate; consider alternate therapy for refractory cases

Monitoring

- Continue ICE assessments until resolution
- Taper steroids once ICANS has resolved (ie, ICE 10)
- Continue antiseizure prophylaxis for 30 days
- Resume therapy with next dose of BsAb per package insert



Rodriguez-Otero P, et al. *Lancet Oncol*. 2024;25:e205-16.

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REMS Programs

- Programs for all 3 FDA-approved products
- Purpose: to mitigate the risk of CRS and neurologic toxicity, including ICANS
- Ensure prescribers are aware of importance of monitoring for the signs and symptoms of CRS and neurologic toxicity
- REMS requires prescriber and pharmacy enrollment



Tecvayli and Talvey REMS. Janssen Biotech, Inc. Updated 2024. Accessed 9/4/2025. <https://www.tec-talrems.com/#Main>
Elrexio REMS. Pfizer Inc. Updated 2024. Accessed 9/4/2025. <https://www.elrexiorems.com/#Main>
Lynozofic REMS. Regeneron Pharmaceuticals. Updated 2025. Accessed 9/4/2025. <https://www.lynozyficrems.com/#Main>

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Step-Up Dosing to Mitigate CRS/ICANS

	Teclistamab	Elranatamab	Linvoseltamab
Step-up dosing with premedication	Days 1, 4, 7	Days 1, 4, 8	Days 1, 8, 15
Hospitalization recommended	Step-up doses and first full dose	Step-up doses	Step-up doses
REMS	✓	✓	✓
Route of administration	Subcutaneous	Subcutaneous	Intravenous

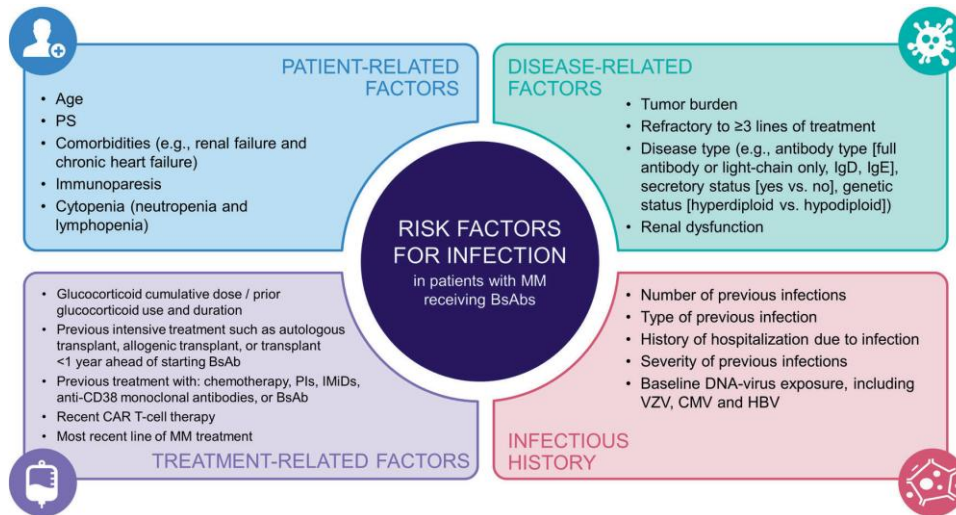
Premedication includes acetaminophen, an H1-antihistamine, and corticosteroids.



Tecvayli (teclistamab). Prescribing information. Janssen Biotech Inc; February 2024. Elrexio (elranatamab). Prescribing information. Pfizer Inc; August 2023. Lynozofic (linvoseltamab). Prescribing information. Regeneron Pharmaceuticals, Inc; July 2025.

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Risk Factors for Infection



Raje N, et al. *Blood Cancer J.* 2023;13:116.

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Consensus Recommendations for the Monitoring, Prophylaxis, and Treatment of Infections

Viral
• Valacyclovir or acyclovir prophylaxis • Screen for HBV prior to treatment initiation • Consider CMV and EBV monitoring • Vaccination as appropriate
<i>Pneumocystis jirovecii</i> pneumonia
• Recommend prophylaxis for all patients
Bacterial
• Consider fluoroquinolone prophylaxis at treatment initiation and when ANC < 500/mm³ • Vaccination as appropriate
Fungal
• Consider prophylaxis for ANC < 500/mm³
Other Supportive Care
• IVIG for IgG < 400 mg/dL or patients with history of recurrent infections • G-CSF as needed for ANC < 1,000/mm³



Raje N, et al. *Blood Cancer J.* 2023;13:116; Rodriguez-Otero P, et al. *Lancet Oncol.* 2024;25:e205-16.

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Cytopenia Management

- Often seen early in therapy and resolves with continued treatment
- Neutropenia
 - Filgrastim as needed
 - Consider holding therapy for $ANC \leq 500/\text{mL}$
 - Levofloxacin and fluconazole for $ANC \leq 500/\text{mL}$
- Thrombocytopenia
 - Consider addition of thrombopoietin receptor agonist for grade ≥ 4
 - Consider holding therapy until platelets $> 50,000$
- Anemia
 - Consider transfusions and erythropoietin-stimulating agents as needed
- Consider extended dosing intervals when resuming



Rodríguez-Otero P, et al. *Lancet Oncol.* 2024;25:e205-16.