[Clinic or Hospital Logo]

SOP #	[Number]
Effective	[Date]
Approved	[Date]
Next Review	[Date]
Owner	[Name]
Department	[Name]
Tags	[Tags]
Applicability	[Name of sites]

Adult Monitoring and Management of Neurotoxicity Associated with Bispecific T-Cell Engagers

Where Did This Resource Come From?	
Clinic/Hospital Type	Rural, Small Community Cancer Center
What's Unique?	• N/A

1. Purpose

To provide a framework for the monitoring and management of neurotoxicity in patients receiving bispecific T-cell engager (BTCE) therapy in the inpatient setting.

2. Scope

This policy is applicable to all clinical staff at [insert site name].

3. Definitions

- **Bispecific T-Cell Engager (BTCE)**: Synthetic proteins that bind two distinct antigens: one targets the CD3 protein on T cells, and the other targets a specific cancer antigen, redirecting T cells to activate an antitumor immune response.
- **Cytokine Release Syndrome (CRS):** A potentially severe inflammatory response that occurs when immune effector cell therapy leads to the release of cytokines into the bloodstream. This syndrome causes symptoms such as fever, hypotension, hypoxia, chills, tachycardia, dyspnea, nausea, rash, headache, and myalgia.
- **Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS):** A disorder characterized by a pathologic process involving the central nervous system (CNS) following any immune therapy that results in the activation or engagement of endogenous or infused T cells and/or other immune effector cells.
- **Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS):** A neurological complication caused by inflammation in the central nervous system following immune

effector cell therapy. Symptoms can range from mild, such as headache and confusion, to severe, including seizures and coma, which may be life-threatening.

- **Neurotoxicity**: Side effects that impact the nervous system, including those caused by immunotherapy.

4. Workup[2]

- Complete history and physical exam
- Review medications including last dose of antipyretic therapy, steroids, and/or anti-cytokine therapy
- Determine ICE score (see below) on all patients with neurologic symptoms
- Assess for alternate cause of symptoms; consider performing CT head, EEG, MRI, or lumbar puncture, as appropriate
- Assess for concurrent symptoms of CRS (fever, hypoxia, and hypotension); treatment of CRS can occur concurrently, if appropriate
- If concern for neurological AEs exists, patient should be evaluated in outpatient center or Emergency Department (ED). If symptoms worsen (e.g. somnolence, worsening confusion, weakness, etc.), patients should be promptly referred to the ED
- *Routine* neurologic testing for patients who are asymptomatic with normal neurological examination at baseline is not required

ICE Scoring:

Orientation to year, month, city, hospital	4 points
Naming 3 objects	3 points
Following simple commands	1 point
Writing standard sentence	1 point
Attention to count backward from 100 by 10	1 point

5. Management[2]

Grade	ICE Score	Level of Consciousness	Seizure	Motor Findings	Neuroimaging	Management
Grade 1	7-9	Awakens spontaneously	N/A	N/A	N/A	• Consider observation or close monitoring in outpatient setting • Consider dexamethasone 10 mg x 1
Grade 2	3-6	Awakens to voice	N/A	N/A	N/A	• Admit patient to hospital • Dexamethasone 10 mg IV q 12 hrs, followed by taper once grade ≥ 1
Grade 3	0-2	Awakens to tactile stimulus	Any clinical seizure that resolves rapidly	N/A	Local edema	• Monitor in ICU setting • Neurology consult • Dexamethasone 10 mg IV q 6 hrs, followed by taper once grade ≥ 1 • Use antiepileptics for seizure management as needed • Consider adding anakinra 100 mg q 12h if symptoms persist beyond 24 hrs; continue until resolution
Grade 4	0	Unarousable or requires vigorous or	Life-threatening prolonged	Deep focal motor weakness	Diffuse cerebral edema	• Monitor in ICU setting • Neurology consult

		repetitive tactile stimuli	seizure (>5 min) or repetitive seizures without return to baseline			• Dexamethasone 10 mg IV q 6 hrs, followed by taper once grade ≥ 1 • Use antiepileptics for seizure management as needed • Consider adding anakinra 100 mg q 12 hrs if symptoms persist beyond 24 hours, continue until resolution

6. Records and Documentation

- Document any neurologic toxicity in electronic medical record including adverse event grade, ICE score, medications, neurology consultation (if applicable), and any ICU stays.

7. References

1. Lee DW, Santomasso BD, Locke FL, et al. ASTCT Consensus Grading for Cytokine Release Syndrome and Neurologic Toxicity Associated with Immune Effector Cells. *Biol Blood Marrow Transplant*. 2019;25(4):625-638. doi:10.1016/j.bbmt.2018.12.758.
2. Crombie JL, Graff T, Falchi L, et al. Consensus Recommendations on the Management of Toxicity Associated with CD3xCD20 Bispecific Antibody Therapy. Blood. 2024;143(16):1565-1575.

8. Appendices

[Include any additional information that supports the SOP, such as flowcharts, diagrams, or checklists.]

9. Revision History

Version #	Date	Description of Changes	Reviewed / Approved By