



# CAR T-cell Therapy Neurotoxicity Grading and Management

## Immune Effector Cell-Associated Encephalopathy (ICE) Assessment Tool

- Orientation: orientation to year, month, city, hospital: 4 points
- Naming: ability to name 3 objects (eg, point to clock, pen, button): 3 points
- Following commands: ability to 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 (eg, "Our national bird is the bald eagle"): 1 point
- Attention: ability to count backwards from 100 by 10: 1 point

### ICE Scoring

7-9, grade 1  
3-6, grade 2  
0-2, grade 3  
0 due to patient unarousable and unable to perform ICE assessment, grade 4

## ASTCT Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) Consensus Grading for Adults

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 (patient is unarousable and unable to perform ICE)
Depressed level of consciousness	Awakens spontaneously	Awakens to voice	Awakens only to tactile stimulus	Patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse
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 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
Elevated ICP/cerebral edema	N/A	N/A	Focal/local edema on neuroimaging	Diffuse cerebral edema on neuroimaging; decerebrate or decorticate posturing; or Cranial Nerve VI palsy; or Papilledema; or Cushing's triad

## CAR T-cell Related Neurotoxicity Treatment

### Assessment and Supportive Care Recommendations (all grades)

- Neurologic assessment and grading at least twice a day to include cognitive assessment and motor weakness
- MRI of the brain with and without contrast (or brain CT if MRI is not feasible) for  $\geq$  grade 2 neurotoxicity
- Neurology consultation at first sign of neurotoxicity
- Conduct EEG for seizure activity for  $\geq$  grade 2 neurotoxicity
- Aspiration precautions; IV hydration
- Use caution when prescribing medications that can cause central nervous system (CNS) depression (aside from those needed for seizure prophylaxis/treatment)

Grade	No Concurrent CRS	Concurrent CRS
Grade 1	Supportive care	IV tocilizumab 8 mg/kg over 1 hour (not to exceed 800 mg/dose)
Grade 2	As with grade 1; 1 dose of IV dexamethasone 10 mg and reassess. Can repeat every 6-12 hours, if no improvement.	Anti-IL-6 therapy as per grade 1; consider transferring to ICU if neurotoxicity associated with grade $\geq$ 2 CRS
Grade 3	ICU care is recommended; IV dexamethasone 10 mg every 6 hours or IV methylprednisolone, 1 mg/kg every 12 hours; consider repeat neuroimaging (CT or MRI) every 2-3 days if patient has persistent grade $\geq$ 3 neurotoxicity	Anti-IL-6 therapy as per grade 1
Grade 4	ICU care, consider mechanical ventilation for airway protection; high-dose steroids; consider repeat neuroimaging (CT or MRI) every 2-3 days if patient has persistent grade $\geq$ 3 neurotoxicity; treat convulsive status epilepticus per institutional guidelines	Anti-IL-6 therapy as per grade 1