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Clinical Decision Tool Reviews

Review of Immune effector Cell-Associated Neurotoxicity Syndrome (ICANS)

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Abstract

The American Society for Transplantation and Cellular Therapy (ASTCT) developed this consensus grading system based on prior Common Terminology Criteria for Adverse Events (CTCAE) and Immune Effector Cells Therapy Toxicity Assessment and Management (CARTOX) grading systems. Grade of Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) should guide management.

I. HOW TO USE

When to Use

ICANS should be used for any adult patient receiving an immune effector cell engaging therapy. This should not be limited to only those receiving CAR T-cells. Clinicians should use a different grading system for children < 12 years old.

Pearls / Pitfalls

This grading tool helps standardize assessments of neurotoxicity given the subjectivity of other descriptions of encephalopathy. This consensus grading system by ASTCT was built using CTCAE v4.03, CTCAE v5.0, and CARTOX CAR T-cell-Related Encephalopathy Syndrome (CRES) grading systems.

Why to Use

Grading of ICANS guides management. This is the most recent consensus grading by a national organization.

II. NEXT STEPS

Advice

Neurologic assessment should be done prior to administration of immune effector cell engaging therapy and then daily afterwards while hospitalized. The ICANS tool should not be the sole basis for care, and clinicians should use judgment and full clinical evaluation to guide management.

Management

Per 2026 NCCN Guidelines for Management of CAR T-Cell-Related Toxicities, consider the following management approach:

- Grade 1 – supportive care +/- 1 dose of dexamethasone 10 mg IV
- Grade 2 – supportive care, 1 dose of dexamethasone 10 mg IV then reassess; repeat every 6-12 hours if no improvement
- Grade 3 – ICU care, dexamethasone 10 mg IV every 6 hours or methylprednisolone 1 mg/kg every 12 hours, consider adding anakinra 100 mg every 6 hours if not responsive to steroids or worsening symptoms, consider repeat CT head or MR brain every 2-3 days if persistent Grade 3 or higher neurotoxicity
- Grade 4 – ICU care, consider mechanical ventilation for airway protection, high-dose steroids, consider adding anakinra 100 mg every 6 hours if not responsive to steroids, consider repeat CT head or MR brain every 2-3 days if persistent Grade 3 or higher neurotoxicity, treat convulsive status epilepticus per institutional guidelines

Critical Actions

Evaluate for papilledema or other signs of high intracranial pressure (ICP) if grade 3 or grade 4 per NCCN

guidelines. Diagnostic LP can be obtained if high ICP is excluded to evaluate grade 3-4 neurotoxicity.

III. EVIDENCE

Evidence Appraisal

One study compared the grading of ICANS using ASTCT 2019 consensus grading and compared that to grading using other grading schemes. The ASTCT grading of ICANS had a higher percentage of Grade 3 than either CTCAE or CARTOX and lower percentage of Grade 4 than CARTOX.

Formula

- ICANS Grade 1 = ICE score 7-9 and awakens spontaneously
- ICANS Grade 2 = ICE score 3-6 or awakens to voice
- ICANS Grade 3 = ICE score 0-2, or
  - awakens only to tactile stimulus, or
  - any clinical seizure focal, or
  - generalized that resolves rapidly, or
  - nonconvulsive seizures on EEG that resolve with intervention, or
  - focal/local edema on neuroimaging
- ICANS Grade 4 = ICE score 0, or
  - unarousable, or
  - requires vigorous or repetitive tactile stimuli to arouse, or
  - stupor, or
  - coma, or
  - life-threatening prolonged seizure (> 5 min), or
  - repetitive clinical, or
  - electrical seizures without return to baseline in between, or
  - deep focal motor weakness such as hemiparesis, or
  - paraparesis, or
  - diffuse cerebral edema on neuroimaging or decerebrate, or
  - decorticate posturing, or
  - CN VI palsy or papilledema, or
  - Cushing's triad

ICE Scoring (sum)

- Orientation = max 4 points (orientation to year, month, city, hospital)
- Naming = max 3 points (name 3 objects – e.g., point to clock, pen, button)
- Following commands = max 1 point (follow simple commands, e.g., "show me 2 fingers" or "close your eyes and stick out your tongue")
- Writing = max 1 point (write a standard sentence, e.g., "Our national bird is the bald eagle")
- Attention = max 1 point (count backwards from 100 by 10)

Literature

Original/Primary & Validation

Lee DW 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. PMID 30592986.

Other References (including meta-analyses, CPGs, and impact analyses)

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