

Bi-specific related Immune Effector-cell Associated Neurotoxicity Syndrome (ICANS) grading and management guidance



Withhold bispecific until resolution of symptoms and follow local disease specific ongoing management

American Society for Transplantation and Cellular therapy (ASTCT) ICANS GRADING D.W. Lee et al. / Biol Blood Marrow Transplant 25 (2019) 625638

Grade	Treatment	No concurrent CRS:	With concurrent CRS:
Grade 1 ICE Score 7-9 <ul style="list-style-type: none"> Awakens spontaneously 	<ul style="list-style-type: none"> Dexamethasone, 10 mg IV every 12 hours Consider non-sedating anti-seizure medication (e.g., levetiracetam) until resolution of ICANS 	<ul style="list-style-type: none"> Anti-cytokine therapy not recommended 	<ul style="list-style-type: none"> Treatment with dexamethasone Choose immunosuppressant alternatives to tocilizumab, if possible
Grade 2 ICE score 3-6 <ul style="list-style-type: none"> Awakens to voice 	<ul style="list-style-type: none"> Dexamethasone at 10-20 mg IV every 12 hours Consider non-sedating anti-seizure medication (e.g., levetiracetam) until resolution of ICANS. 	<ul style="list-style-type: none"> Anti-cytokine therapy not recommended 	<ul style="list-style-type: none"> Treatment with dexamethasone Choose immunosuppressant alternatives to tocilizumab, if possible
Grade 3 ICE score 0-2 <ul style="list-style-type: none"> Awakens only to tactile stimulus Any clinical seizure focal or generalized that resolves rapidly or nonconvulsive seizures on EEG that resolve with intervention Focal/local oedema on neuroimaging⁵ 	<ul style="list-style-type: none"> Dexamethasone 10-20 mg IV every 6 hours. If no response, initiate methylprednisolone 1000 mg/day. Consider non-sedating anti-seizure medication (e.g., levetiracetam) until resolution of ICANS. 	<ul style="list-style-type: none"> Anti-cytokine therapy not recommended 	<ul style="list-style-type: none"> Treatment with dexamethasone If no response, initiate methylprednisolone 1000 mg/day Choose immunosuppressant alternatives to tocilizumab, if possible
Grade 4 ICE score 0 <ul style="list-style-type: none"> 0 (patient is unarousable and unable to perform ICE) Patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse. Stupor or coma Life-threatening prolonged seizure (>5 min); or Repetitive clinical or electrical seizures without return to baseline in between Deep focal motor weakness such as hemiparesis or paraparesis Diffuse cerebral oedema on neuroimaging; decerebrate or decorticate posturing; or cranial nerve VI palsy; or 	<ul style="list-style-type: none"> Dexamethasone 10-20 mg IV every 6 hours. If no response, initiate methylprednisolone 1000 mg/day. Consider non-sedating anti-seizure medication (e.g., levetiracetam) until resolution of ICANS. 	<ul style="list-style-type: none"> Anti-cytokine therapy not recommended 	<ul style="list-style-type: none"> Treatment with dexamethasone If no response, initiate methylprednisolone 1000 mg/day Choose immunosuppressant alternatives to tocilizumab, if possible

If patient is arousable and able to perform Immune Effector Cell-Associated Encephalopathy (ICE) **Assessment:** Orientation (oriented to year, month, city, hospital = 4 points); Naming (name 3 objects, e.g., point to clock, pen, button = 3 points); Following Commands (e.g., "show me 2 fingers" or "close your eyes and stick out your tongue" = 1 point); Writing (ability to write a standard sentence = 1 point; and Attention (count backwards from 100 by ten = 1 point). If patient is unarousable and unable to perform ICE Assessment (Grade 4 ICANS) = 0 points. Riegler L et al. (2019)