

Understanding Neurological Events Associated With Immunotherapies



BACKGROUND

Neurological events are disorders affecting the central nervous system. These events have been reported in patients receiving T-cell–based immunotherapies.^{1,2}

These events vary widely and can include confusion, dizziness, dysesthesia, dysphasia, edema cerebral, encephalopathy, headache, seizures, and tremor.¹⁻³

These neurological events are generally reversible; however, severe, life-threatening, and fatal events have been reported.^{1,4}

The pathophysiology of these neurological events is not fully understood and likely multi-factorial.^{1,2} Some T-cell–based therapies cross the blood-brain barrier and have been seen in the cerebrospinal fluid, but it is not clear whether this is directly correlated with these events.^{4,5}

Patients receiving T-cell–based immunotherapies should be monitored closely for signs and symptoms of neurological events. Further studies are required to understand the underlying mechanisms associated with the observed events, identify risk factors, and determine optimal treatment strategies.

Definitions and Grading per NCI CTCAE³

Confusion: A disorder characterized by a lack of clear and orderly thought and behavior.	Dizziness: A disorder characterized by a disturbing sensation of lightheadedness, unsteadiness, giddiness, spinning, or rocking.	Dysesthesia: A disorder characterized by distortion of sensory perception, resulting in an abnormal and unpleasant sensation.
Grade 1	Grade 1	Grade 1
Mild disorientation	Mild unsteadiness or sensation of movement	Mild sensory alteration
Grade 2	Grade 2	Grade 2
Moderate disorientation; limiting instrumental ADL	Moderate unsteadiness or sensation of movement; limiting instrumental ADL	Moderate sensory alteration; limiting instrumental ADL
Grade 3	Grade 3	Grade 3
Severe disorientation; limiting self-care ADL	Severe unsteadiness or sensation of movement; limiting self-care ADL	Severe sensory alteration; limiting self-care ADL
Grade 4	Grade 4	Grade 4
Life-threatening consequences; urgent intervention indicated	–	–
Grade 5	Grade 5	Grade 5
–	–	–

ADL, activities of daily living; CTCAE, Common Terminology Criteria for Adverse Events; NCI, National Cancer Institute.

Definitions and Grading per NCI CTCAE (Continued)³

Dysphasia: A disorder characterized by impairment of verbal communication skills, often resulting from brain damage.	Edema cerebral: A disorder characterized by swelling due to an excessive accumulation of fluid in the brain.	Encephalopathy: A disorder characterized by a pathological process involving the brain.
Grade 1	Grade 1	Grade 1
Awareness of receptive or expressive characteristics; not impairing ability to communicate	–	Mild symptoms
Grade 2	Grade 2	Grade 2
Moderate receptive or expressive characteristics; impairing ability to communicate spontaneously	–	Moderate symptoms; limiting instrumental ADL
Grade 3	Grade 3	Grade 3
Severe receptive or expressive characteristics; impairing ability to read, write, or communicate intelligibly	New onset; worsening from baseline	Severe symptoms; limiting self-care ADL
Grade 4	Grade 4	Grade 4
–	Life-threatening consequences; urgent intervention indicated	Life-threatening consequences; urgent intervention indicated
Grade 5	Grade 5	Grade 5
–	Death	Death
Headache: A disorder characterized by a sensation of marked discomfort in various parts of the head, not confined to the area of distribution of any nerve.	Seizure: A disorder characterized by sudden, involuntary skeletal muscular contractions of cerebral or brain stem origin	Tremor: A disorder characterized by the uncontrolled shaking movement of the whole body or individual parts.
Grade 1	Grade 1	Grade 1
Mild pain	Brief partial seizure and no loss of consciousness	Mild symptoms
Grade 2	Grade 2	Grade 2
Mild pain; limiting instrumental ADL	Brief generalized seizure	Moderate symptoms; limiting instrumental ADL
Grade 3	Grade 3	Grade 3
Severe pain; limiting self-care ADL	New onset seizures (partial or generalized); multiple seizures despite medical intervention	Severe symptoms; limiting self-care ADL
Grade 4	Grade 4	Grade 4
–	Life-threatening consequences; prolonged repetitive seizures	–
Grade 5	Grade 5	Grade 5
–	Death	–

ADL, activities of daily living; CTCAE, Common Terminology Criteria for Adverse Events; NCI, National Cancer Institute.

References

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