

AE Profile of CAR T-cell and Symptom Management

CRS: Associated with symptoms that can range from mild to life-threatening, with progression from mild infusion reactions and fever to constitutional symptoms including hypotension, capillary leak, and endorgan dysfunction.

Grade	Management	Notes
Grade 1	Observe	Early fever (within 72 hrs) or significant comorbidities can consider early tocilizumab
Grade 2	Tocilizumab 8 mg/kg (Consider alternative agents after 2 doses) *No more than 3 doses in a 24 hr period or 4 doses in total	For patients with early fevers or significant comorbidities, consider early dexamethasone (10 mg x 1). Patients not responding to tocilizumab should could initiation of dexamethasone (10mg q12-24 hrs)
Grade 3	Tocilizumab 8 mg/kg (Consider alternative agents after 2 doses) *No more than 3 doses in a 24 hr period or 4 doses in total	Dexamethasone (10mg q12-24 hrs) with tocilizumab initial tocilizumab For patients refractory to dexamethasone can increase to 20mg q6-12 hrs
Grade 4	Tocilizumab 8 mg/kg (Consider alternative agents after 2 doses) *No more than 3 doses in a 24 hr period or 4 doses in total	In dexamethasone refractory patients, consider high dose methylprednisolone 2mg/kg x 12 hrs For refractory patients consider alternative therapies

Always look for infections and treat infectious complications, especially in patients with neutropenia

B cell aplasia: Long-term hypogammaglobulinaemia or agammaglobulinaemia are commonly seen in patients after CAR-T cell treatment

Management

Closely monitor immunoglobulin levels as well as acute, chronic, and silent infections to prevent organ damage and maintain long-term quality of life

Maintain serum immunoglobulin levels > 400 µg/l in adults and age-adapted normal ranges for children

- IVIGs are usually given every 3-6 weeks or subcutaneously weekly
- IVIG doses start at 0.4 g/kg body weight and subcutaneous doses at 0.1–0.15 g/kg body weight
- Doses and intervals are adapted due to infections and serum IgG levels
- · After reaching a steady state, serum IgG levels should be controlled at least every 3 months

Additional studies are needed to better understand optimal management of B cell aplasia

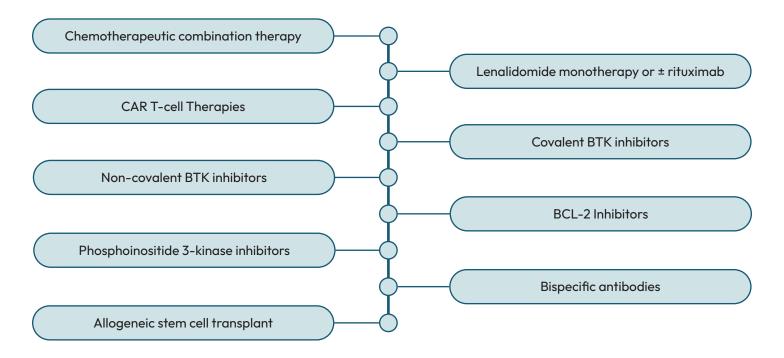
ICANS: Can range from encephalopathy to seizures, obtundation, and possible death; neurological events may occur independently of CRS-related toxicities.

Grade	Neurotoxicity	CRS + Neurotoxicity
Grade 1	Supportive care (± steroids)*	Supportive care (± tocilizumab)
Grade 2	Steroids (dexamethasone or methylprednisc	olone)Tocilizumab + steroids (dexamethasone)
Grade 3	Steroids (dexamethasone)	Tocilizumab + steroids (dexamethasone)
Grade 3	High-dose steroids (methylprednisolone) ICU/critical care	Tocilizumab + high-dose steroids (methylprednisolone) ICU/critical care

Management	ICANS Pearls
Neurology consultationLow threshold for inpatient	Levetiracetam for seizure prophylaxis for the first 30 days
management (if outpatient at time of onset)	Can be biphasic
Multidisciplinary team approach	Early phase overlaps with CRS Often mild (grade 1/2) and short lived (2-4 days) May respond to tocilizumab
	Delayed phase may occur 2-4 weeks after CAR T-cell infusion • May be more severe and prolonged • Corticosteroids preferred therapy • Tocilizumab generally not effective

Drug Classes for the Treatment of R/R NHL

Some of the drugs used in combination or in monotherapy for the treatment of R/R NHLs conditions include:



Other Reported AEs for non-CAR T-cell Treatment of NHLs

TEAEs can range from mild to severe and can include:



