# ENHANCING PATIENT CARE
## for CAR T-Cell Therapy in NHL:
Comprehensive Solutions for Your Community

## 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 end-organ 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 co-morbidities, consider early dexamethasone (10 mg x 1).<br>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<br>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<br>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<br>• IVIGs are usually given every 3–6 weeks or subcutaneously weekly<br>• IVIG doses start at 0.4 g/kg body weight and subcutaneous doses at 0.1–0.15 g/kg body weight<br>• Doses and intervals are adapted due to infections and serum IgG levels<br>• 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 methylprednisolone) | 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 consultation<br>• Low threshold for inpatient management (if outpatient at time of onset)<br>• Multidisciplinary team approach | Levetiracetam for seizure prophylaxis for the first 30 days |
| | Can be biphasic |
| | Early phase overlaps with CRS<br>• Often mild (grade 1/2) and short lived (2-4 days)<br>• May respond to tocilizumab |
| | Delayed phase may occur 2-4 weeks after CAR T-cell infusion<br>• May be more severe and prolonged<br>• Corticosteroids preferred therapy<br>• Tocilizumab generally not effective |

CRS, cytokine release syndrome; ICANS, Immune effector Cell Associated Neurotoxicity Syndrome; IVIGs, Intravenous immunoglobulins.
*High-burden, high-risk products; older; comorbidities, etc.
Chohan KL, et al. Curr Hematol Malig Rep. 2023 Apr;18(2):9-18 Topp M, et al. 2022 Feb 7. In: Kröger N, Gribben J, Chabannon C, et al., editors. The EBMT/EHA CAR-T Cell Handbook [Internet]. Cham (CH): Springer; 2022. Chapter 28.

## 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:

- Chemotherapeutic combination therapy
- CAR T-cell Therapies
- Non-covalent BTK inhibitors
- Phosphoinositide 3-kinase inhibitors
- Allogeneic stem cell transplant
- Lenalidomide monotherapy or ± rituximab
- Covalent BTK inhibitors
- BCL-2 Inhibitors
- Bispecific antibodies

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

TEAEs can range from mild to severe and can include:

- Nausea and vomiting
- Diarrhea
- Fatigue
- Cough
- Fever
- Rash
- Headache
- Infections
- Neuropathies
- Anemia
- Neutropenia
- Thrombocytopenia
- Tumor lysis syndrome
- Heart disease
- Atrial fibrillation
- Hypertension
- Bleeding
- Secondary cancers

NHLs, non-Hodgkin lymphomas; TEAEs, treatment-emergent adverse events.

NCCN Guidelines Version 2.2024. Diffuse Large B-Cell Lymphoma. NCCN Guidelines Version 2.2024. Follicular Lymphoma. NCCN Guidelines Version 2.2024. Mantle Cell Lymphoma. NCCN Guidelines Version 3.2024. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. U.S. Food & Drug Administration. Cellular & Gene Therapy Products.; U.S. Prescribing Information.