Understanding CAR-T Therapy: A Guide for Oncology Nurses

What is CAR-T cell therapy? It is a treatment for relapsed or refractory cancers using patient-derived T cells that are genetically modified to target cancer antigens on the surface of malignant cells; CAR-T cell therapy has shown promise in patients in the leukemia, lymphoma, and myeloma settings.

### Treatment Process

1. **In Apheresis**
   - The white blood cells, including T cells, are separated out, and the rest of the blood is returned to the patient.

2. **In the Lab/Manufacturing Facility**
   - T cells are engineered using a lentiviral or retroviral vector.
   - An inactive virus is used to insert genes into the T cells.
   - The genes cause the T cells to make receptors, called CARS, on their surfaces.
   - Modified T cells (now called CAR-T cells) are multiplied.

3. **In the Clinic**
   - CAR-T cells are infused back into the patient’s bloodstream, typically after lymphodepleting chemotherapy; the CAR-T cells continue to multiply.

4. **In the Body**
   - The receptors are attracted to the targets on the surface of the cancer cells.
   - The CAR-T cells identify target antigens (e.g., CD19, BCMA) on the cancer cells and kill them; CAR-T cells may remain in the body for some time, thus preventing relapse.

CAR-T cell therapies are used or under investigation in which cancer settings?

### ALL (Anti–CD19-Targeted CAR-T Cell Therapy)

- **Tisagenlecleucel (CTL019)**
  - FDA approved
  - Patients aged ≤25 y with B-cell precursor ALL (refractory or in second or later relapse)

- **Axicabtagene ciloleucel (KTE-019)**
  - Phase 1/2
  - Adult/pediatric relapsed/refractory B precursor ALL after two or more lines of systemic therapy

- **Lisocabtagene maraleucel (JCAR017)**
  - Phase 1/2
  - Pediatric and young adult relapsed/refractory B cell ALL

### B-Cell NHL (Anti–CD19-Targeted CAR-T Cell Therapy)

- **Axicabtagene ciloleucel (KTE-019)**
  - FDA approved
  - Adult patients with relapsed/refractory large B-cell lymphoma after two or more lines of systemic therapy

- **Tisagenlecleucel (CTL019)**
  - FDA approved
  - Adult patients with relapsed/refractory large B-cell lymphoma after two or more lines of systemic therapy

- **Lisocabtagene maraleucel (JCAR017)**
  - Breakthrough therapy designation
  - Relapsed/refractory DLBCL (phase 2); relapsed/refractory CLL/SLL (phase 1/2)

### Myeloma (Anti–BCMA-Targeted CAR-T Cell Therapy)

- **bb2121**
  - Phase 1

- **bb21217**
  - Phase 1

- **LCAR-B38M**
  - Phase 1b/2

- **JCARH025**
  - Phase 1/2

- **P-BCMA-101**
  - Phase 1

- **MCARH171**
  - Phase 1

- **FCARH143**
  - Phase 1

Adult relapsed/refractory multiple myeloma

What is the role of the oncology nurse in the clinical application of CAR-T cell therapy?

- Expedite eligibility screening for CAR-T trial candidates and review documents to determine eligibility
- Communicate with patients and referring team regarding eligibility review and insurance approval and secure appointments for various procedures
- Provide patient education regarding CAR-T cells, treatment process, and safety management
- Establish patient care plan based on established guidelines for patient management
- Collect clinical trial and research data
- Follow patients in the inpatient and outpatient settings
- Closely monitor for and promptly respond to toxicities; CAR-T cell toxicity management requires complex nursing care
- Manage infusion of CAR-T cells
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- Follow patients in the inpatient and outpatient settings
- Closely monitor for and promptly respond to toxicities; CAR-T cell toxicity management requires complex nursing care
- Manage infusion of CAR-T cells

This Practice Aid has been provided as a quick reference to help learners apply the information to their daily practice and care of patients.

Managing Unique Toxicities Associated With CAR-T Cell Therapy: A Guide for Oncology Nurses

General Guidance

- **Determine toxicity**
- **Grade toxicity**
- **Manage toxicity**

### Cytokine Release Syndrome (CRS)

- **Symptoms:** constitutional flu-like symptoms, hypotension, tachycardia, cardiac events, hypoxia, renal insufficiency, multiple organ failure
- **Very frequently begins with fever, with severe CRS often progressing to unstable hypotension**
- **May require ICU-level care; can be fatal**

#### ASBMT Toxicity Criteria by Grade

<table>
<thead>
<tr>
<th>Grade</th>
<th>Temperature</th>
<th>Hypotension</th>
<th>Hypoxia</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>≥38°C</td>
<td>Not requiring vasopressors</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>≥38°C</td>
<td>Requiring a vasopressor ± vasopressin</td>
<td>Requiring low-flow nasal cannula or blow-by</td>
</tr>
<tr>
<td>3</td>
<td>≥38°C</td>
<td>Requiring high-flow nasal cannula, facemask, nonrebreather mask, or venturi mask</td>
<td>Requiring multiple vasopressors (but not vasopressin)</td>
</tr>
<tr>
<td>4</td>
<td>≥38°C</td>
<td>Requiring positive pressure (e.g., CPAP, BiPAP, intubation, and mechanical ventilation)</td>
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</tr>
</tbody>
</table>

- **Manage toxicities by clinical symptoms and progression**
- **Symptom management; maintenance of fluids; antipyretics, analgesics (often narcotics), antiemetics, blood products, O2, vasopressin early in treatment of hypotension, anti–IL-6 therapy (tocilizumab), corticosteroids; CPAP, ventilation; transfer to ICU**

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**Neurological Toxicities (ICANS)**

- Vary by CAR-T cell product
- Symptoms: aphasia, altered level of consciousness, impairment of cognitive skills, motor weakness, seizures, and cerebral edema
- Increase in ICP occurs—can progress to cerebral edema, which can be rapid in onset and life-threatening

<table>
<thead>
<tr>
<th>ASBMT Toxicity Criteria by Grade</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICE score (patients aged &gt;12 y)</td>
<td>7-9</td>
<td>3-6</td>
<td>0-2</td>
<td>0 (unable to perform ICE)</td>
</tr>
<tr>
<td>CAPD score (patients aged ≤12 y)</td>
<td>&lt;9</td>
<td>&lt;9</td>
<td>&lt;9</td>
<td>Unable to perform CAPD</td>
</tr>
<tr>
<td>Level of consciousness</td>
<td>Awakens spontaneously</td>
<td>Awakens to voice</td>
<td>Awakens only to tactile stimulus</td>
<td>Unarousable or arousable only with vigorous or repetitive tactile stimuli; stupor or coma</td>
</tr>
<tr>
<td>Seizure</td>
<td>N/A</td>
<td>N/A</td>
<td>Any clinical seizure (focal or generalized) resolving rapidly or nonconvulsive seizure on EEG that resolves with intervention</td>
<td>Life-threatening seizure &gt;5 min or repetitive clinical or electrical seizures with no return to baseline in between</td>
</tr>
<tr>
<td>Motor weakness</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>Deep focal motor weakness (e.g., hemiparesis, paraparesis)</td>
</tr>
<tr>
<td>ICP/Cerebral edema</td>
<td>N/A</td>
<td>N/A</td>
<td>Focal/local edema on neuroimaging</td>
<td>Decerebrate or decorticate posturing, cranial nerve VI palsy, papilledema, Cushing’s triad, diffuse cerebral edema on neuroimaging</td>
</tr>
</tbody>
</table>

- Supportive care; neurologic work-up; NPO as appropriate; neuroimaging; anxiolytics and/or antiepileptics (levetiracetam) as needed; anti-IL-6 therapy (tocilizumab or siltuximab); early use of corticosteroids
- Transfer to ICU
- Often self-resolving with the exception of cerebral edema, which is a medical emergency

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**B-Cell Aplasia**
- Expected result of successful CD19-specific CAR-T cell treatment
- Immunoglobulin replacement therapy may be given to prevent infection

**Tumor-Lysis Syndrome**
- Metabolic complications from breakdown of dying cells; can cause organ damage and may be life-threatening
- Monitor for hyperkalemia, hypocalcemia, and elevated uric acid; provide standard supportive therapy

**Anaphylaxis**
- Symptoms: hives, facial swelling, tingling hands, low blood pressure, hypoxia, and respiratory distress
- Thorough monitoring and immediate treatment are critical

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