Chimeric Antigen Receptor (CAR) T-Cell Therapy

A Timeline of Events

1. Leukopheresis: Collection of Autologous T-Cells
   - Patient's blood is collected and then the leukocytes are separated out.
   - Adverse Events May Include:
     - Hypocalcemia
     - Anemia
     - Infection

2. Ex Vivo Manufacturing Process
   - CAR T-cells are stimulated and trained to recognize and destroy cancer cells expressing a certain antigen.

3. Conditioning
   - Chemotherapy is administered prior to infusion of CAR T-cells to lymphodeplete and prepare the body for the manufactured T-cells.
   - Adverse Events May Include:
     - Nausea / Vomiting
     - Fatigue
     - Cytopenias

4. Infusion of CAR T-Cells
   - Prepared and activated CAR T-cells are infused. The procedure is performed according to institutional protocol.
   - Adverse Events Are Rare and Usually Not Severe, but May Include:
     - Nausea / Vomiting
     - Hypotension

5. Acute Monitoring
   - Patient is monitored for any adverse events.
   - Adverse Events May Include:
     - Cytokine Release Syndrome
     - Immune Effector Cell-associated Neurotoxicity Syndrome (ICANS)
     - Tumor Lysis Syndrome
     - Cytopenias
     - Infection

ONS
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# Adverse Event Management and Resources

## Adverse Event Management

### CAR T Related Adverse Event

<table>
<thead>
<tr>
<th>Event</th>
<th>Management</th>
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</thead>
<tbody>
<tr>
<td>Cytokine Release Syndrome (CRS)*</td>
<td>Grades 1 and 2: Antipyretics, analgesics, antihistamines; empiric treatment for fever, supportive care as necessary.</td>
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<td>Grades 3 and 4: Oxygen supplementation as required; IV fluid and/or vasopressor support as required, *tocilizumab +/- corticosteroids; intensive care support with possible intubation.</td>
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<tr>
<td>Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)</td>
<td>Physical exam and neurologic assessment per institutional standard; Neurology consult, seizure precautions, and prophylactic antiepileptics; continuous pulse oximetry and cardiac telemetry monitoring; intensive care support for management of cerebral edema or intracranial pressure (ICP).</td>
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<tr>
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<td>Pharmacologic treatment: Corticosteroids and/or *tocilizumab in the setting of CRS.</td>
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<tr>
<td>Tumor Lysis Syndrome</td>
<td>Hydration; electrolyte and renal functioning monitoring; allopurinol and rasburicase.</td>
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<tr>
<td>Cytopenias</td>
<td>Transfusions as indicated; growth factors if not contraindicated; neutropenic and bleeding precautions.</td>
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<tr>
<td>Infection</td>
<td>Prophylactic antimicrobials per institutional guidelines; empiric treatment as required.</td>
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</tbody>
</table>

* Treatment of CRS based on grade. Several grading criteria exist, including CTCAE, Lee, Penn, ASTCT Consensus Grading, and CARTOX.

* Other IL-6 monoclonal antibodies may be used.

* Tocilizumab for ICANS is controversial and should only be used if patient is also experiencing associated CRS.

## ONS Resources

- Immuno-Oncology Learning Library | [www.ons.org/immuno-library](http://www.ons.org/immuno-library)
  - ONS CAR T-Cell Therapy Video | [www.ons.org/videos/car-t-cell-therapy-video](http://www.ons.org/videos/car-t-cell-therapy-video)

## References