Quality of Life after CAR T-cell Therapy (Chimeric Antigen Receptor)

Celebrating a Second Chance at Life
Survivorship Symposium

April 27 – May 3, 2024

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at Harvard Medical School
CAR-T Cell Therapy: Longitudinal Quality of Life

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Outline

• The basics of CAR-T cell Therapy
• The patient journey during CAR-T cell therapy
• Psychosocial experience of patients undergoing CAR-T cell therapy
• CAR-T Cell therapy: living with immense prognostic uncertainty
• Early recovery and long-term effects after CAR-T cell Therapy
• Survivorship and beyond
CAR-T Overview

• Chimeric antigen receptor (CAR)-T cell therapy: A form of immunotherapy that uses the cells of the immune system to treat cancer

• 6 FDA approved products to treat lymphomas, leukemias, and multiple myeloma

• > 100 clinical trials in both solid and blood cancers
Chimeric antigen receptor (CAR)

Genetically engineered antigen-binding domain (like a latch to bind cancer cells)

Normal T-cell
CAR-T Overview

1. Leukapheresis
2. T-cell activation/transduction
3. Modified T-cell expansion
4. Chemotherapy
5. Modified T-cell infusion

*Cellular reprogramming and ex vivo expansion are conducted at a cell processing facility.

Courtesy of Marcela Maus
CAR-T Overview

- CAR-T cell therapy is currently approved to treat patients with relapsed/refractory blood cancers such as lymphoma and multiple myeloma

- Aggressive lymphomas: often eligible after 1 or 2 prior treatments

- Indolent lymphomas, leukemias and multiple myeloma: usually eligible after multiple prior treatments
**Patient Journey**

**Leukapheresis:** collection of patient’s cells (3-5 hours)

**Bridging therapy:**
Some patients require chemotherapy to control disease while waiting for CAR-T cell therapy (3-4 weeks)

**CAR-T treatment**
- 3 days chemo
- 1-2 week hospitalization
- Monitor for toxicities

**Early recovery**
- Close monitoring for first 30 days
- Monitor for toxicities
- Monitor for response

**Survivorship**
- Monitor long-term effects
- Transition to home
## CAR-T Toxicities

### Symptoms of Cytokine Release Syndrome (CRS)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>Low oxygen</td>
</tr>
<tr>
<td>Chills</td>
<td>Low blood pressure</td>
</tr>
<tr>
<td>Muscle aches</td>
<td>Joint aches</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Headache</td>
</tr>
<tr>
<td>Loss of appetite</td>
<td>Organ injury</td>
</tr>
</tbody>
</table>
# CAR-T Toxicities

## Symptoms of Neurologic Toxicity

<table>
<thead>
<tr>
<th>Confusion</th>
<th>Somnolence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trouble with speech or language</td>
<td>Agitation</td>
</tr>
<tr>
<td>Trouble with writing</td>
<td>Seizure</td>
</tr>
<tr>
<td>Tremors</td>
<td>Brain swelling</td>
</tr>
</tbody>
</table>
Other CAR-T Toxicities

• Low blood counts
• Low immunoglobulin (proteins that help body defend against infections) levels
• Infections
• Second cancers (rare)

## Symptoms During CAR-T

<table>
<thead>
<tr>
<th>Disease Symptoms</th>
<th>Moderate to Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>42.9%</td>
</tr>
<tr>
<td>Difficulty swallowing</td>
<td>14.3%</td>
</tr>
<tr>
<td>Cough</td>
<td>9.5%</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>9.5%</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>4.8%</td>
</tr>
<tr>
<td>Abdominal bloating</td>
<td>4.8%</td>
</tr>
<tr>
<td>Itching</td>
<td>4.8%</td>
</tr>
<tr>
<td>Light-headedness</td>
<td>4.8%</td>
</tr>
</tbody>
</table>

Whisenant, et al. Seminars in Oncology Nursing 2021
## Symptoms During CAR-T

<table>
<thead>
<tr>
<th>CAR-T Symptoms</th>
<th>Moderate to Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>61.9%</td>
</tr>
<tr>
<td>Lack of appetite</td>
<td>28.6%</td>
</tr>
<tr>
<td>Headache</td>
<td>28.6%</td>
</tr>
<tr>
<td>Chills</td>
<td>28.6%</td>
</tr>
<tr>
<td>Feeling confused</td>
<td>23.8%</td>
</tr>
<tr>
<td>Memory loss</td>
<td>14.3%</td>
</tr>
<tr>
<td>Pain</td>
<td>9.5%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>9.5%</td>
</tr>
<tr>
<td>Light-headedness</td>
<td>9.5%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>9.5%</td>
</tr>
</tbody>
</table>

Whisenant, et al. Seminars in Oncology Nursing 2021
Physical Symptoms During and After CAR-T

<table>
<thead>
<tr>
<th></th>
<th>Baseline (N = 98)</th>
<th>1 Week (N = 94)</th>
<th>1 Month (N = 86)</th>
<th>3 Months (N = 80)</th>
<th>6 Months (N = 72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe Symptoms</td>
<td>20%</td>
<td>14%</td>
<td>26%</td>
<td>28%</td>
<td>33%</td>
</tr>
<tr>
<td>Moderate Symptoms</td>
<td>47%</td>
<td>52%</td>
<td>40%</td>
<td>45%</td>
<td>39%</td>
</tr>
<tr>
<td>Mild or No Symptoms</td>
<td>33%</td>
<td>34%</td>
<td>35%</td>
<td>28%</td>
<td>28%</td>
</tr>
</tbody>
</table>

Psychological Symptoms Over Time

![Bar chart showing rates of clinically significant psychological distress](chart.png)

Rates of Clinically Significant Psychological Distress

- Baseline (N = 100)*: 30% Anxiety, 26% Depression, 29% PTSD Symptoms
- 1 Month (N = 86): 29% Anxiety, 41% Depression, 23% PTSD Symptoms
- 3 Months (N = 80): 21% Anxiety, 20% Depression, 25% PTSD Symptoms
- 6 Months (N = 72): 22% Anxiety, 18% Depression, 22% PTSD Symptoms

*N = 98 for PTSD Symptoms

Depression Symptoms Over Time

![Graph showing depression symptoms over time with data points at baseline, 1 week, 1 month, 3 months, and 6 months.](Johnson, et al. Blood Adv. 2023.)
Anxiety Symptoms Over Time

PTSD Symptoms Over Time

Prognostic Uncertainty: What Does the Future Hold?

• Increase in prognostic uncertainty in oncology with novel therapies, especially CAR-T cell therapy

• How to focus on living well and acknowledge risks?

You can’t do anything. You can’t plan anything, so you never know how long you are going to live. You might live another 20 years. It might be cured, but still the level of uncertainty is painful.

Jacobsen, J Palliat Med 2018; Lai-Kwon, J Cancer Survivorship 2021
Early Recovery after CAR-T

- Patients typically followed closely at CAR-T center until day 30-60
- Close monitoring for CRS and neurotoxicity during the first 30 days
- Often living away from home during first 30 days after CAR-T
- Residual physical and functional limitations early after treatment
- Fatigue common and persistent up to 6 months post-CAR-T
- Risk of infections after treatment (viral is biggest risk)
Quality of Life (QOL) During and After CAR-T

- QOL measured over time (higher is better)

- On average improving by 3-6 months after CAR-T and similar to US population average

- No group of patients were associated with negative QOL trajectory

Early Recovery after Liso-cel (Breyanzi) CAR-T for Lymphoma

Early Recovery after Liso-cel (Breyanzi) CAR-T for Lymphoma

Quality of Life with CAR-T Compared to Chemotherapy in Lymphoma
CAR-T in Blue versus Chemo in Red

EORTC QLQ-C30 global health status/QoL

<table>
<thead>
<tr>
<th>Study visit</th>
<th>Axi-cel</th>
<th>SOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>165</td>
<td>130</td>
</tr>
<tr>
<td>D50</td>
<td>163</td>
<td>125</td>
</tr>
<tr>
<td>D100</td>
<td>146</td>
<td>62</td>
</tr>
<tr>
<td>D150</td>
<td>110</td>
<td>56</td>
</tr>
<tr>
<td>M9</td>
<td>88</td>
<td>40</td>
</tr>
<tr>
<td>M12</td>
<td>79</td>
<td>33</td>
</tr>
<tr>
<td>M15</td>
<td>67</td>
<td>26</td>
</tr>
</tbody>
</table>

Early Recovery after Cilta-cel (Carvykti) CAR-T for Myeloma

Most patients reported improvement at day 100

Martin, et al. Lancet Haematology 2022
Survivorship after CAR-T

- Physical Effects
- Psycho-social Effects
- Cognitive Effects
- Recurrence & New Cancers
- Chronic Conditions
- Health Promotion
Survivorship Concerns

- Late Bacterial and Viral Infections
- Fungal Infections
- Pneumocystis Pneumonia
- Low Immunoglobulins (Proteins that help with battling infections)
- Impaired B-cell and T-cell Recovery
- Prolonged Cytopenias
- Late Neurological and Psychiatric Events
- Late Immune-related Adverse Events
- Subsequent Malignancies
Long Term Quality of Life After CAR-T for Leukemia in Pediatrics and Young Adults

Laetsch, et al. Journal of Clinical Oncology 2023
Survivorship Concerns

• Compared to general population, CAR-T survivors at 1-5 years post-CAR-T were not different in mean:
  • Quality of life scores
  • Physical health
  • Mental health

• 37.5% reported cognitive difficulties

Ruark et al. Transplant Cell Ther, 2019
Neurocognitive Outcomes 6 Months After CAR-T

- No difference in average scores 6 months after CAR-T compared to baseline
- No response to CAR-T was associated with worse neurocognitive outcomes

Barata et al. [Unpublished]

Perceived Cognition (N=70)

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Improved</th>
<th>Stable</th>
<th>Declined</th>
</tr>
</thead>
<tbody>
<tr>
<td>32.9</td>
<td>47.1</td>
<td>20</td>
<td></td>
</tr>
</tbody>
</table>

Composite Neurocognitive Score (N=26)

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Improved</th>
<th>Stable</th>
<th>Declined</th>
</tr>
</thead>
<tbody>
<tr>
<td>15.4</td>
<td>73.1</td>
<td>11.5</td>
<td></td>
</tr>
</tbody>
</table>
Effect on Caregivers

• Caregivers provide majority of care for CAR-T recipients
• Caregivers monitor for toxicities early in the recovery period
• Caregivers have a stressful job
• Chronic caregiving especially in the context of CAR-T
• Immense caregiving burden
• Impact on relationships
• Impact on caregiver health
• Financial burden is immense
Effect on Caregivers

Barata et al. Transplant Cell Ther. 2024.
Conclusions

• Generally, quality of life and symptom burden improve over time after CAR-T across blood cancers
• Quality of life decreases by two weeks after CAR-T but, on average, improves by 3-6 months after CAR-T
• CAR-T survivors have quality of life similar to the general population
• Physical and psychological symptoms improve, though can persist for a subset of patients
• Cognitive outcomes long-term appear good, based on research to date
• Caregivers of patients receiving CAR-T experience significant psychological symptoms
Questions?

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