

# CAR T-cell Therapy for Lymphoma: What's Involved, Potential Outcomes

**Celebrating a Second Chance at Life  
Survivorship Symposium**

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# CAR T-cell Therapy for Lymphoma: What's Involved, Potential Outcomes

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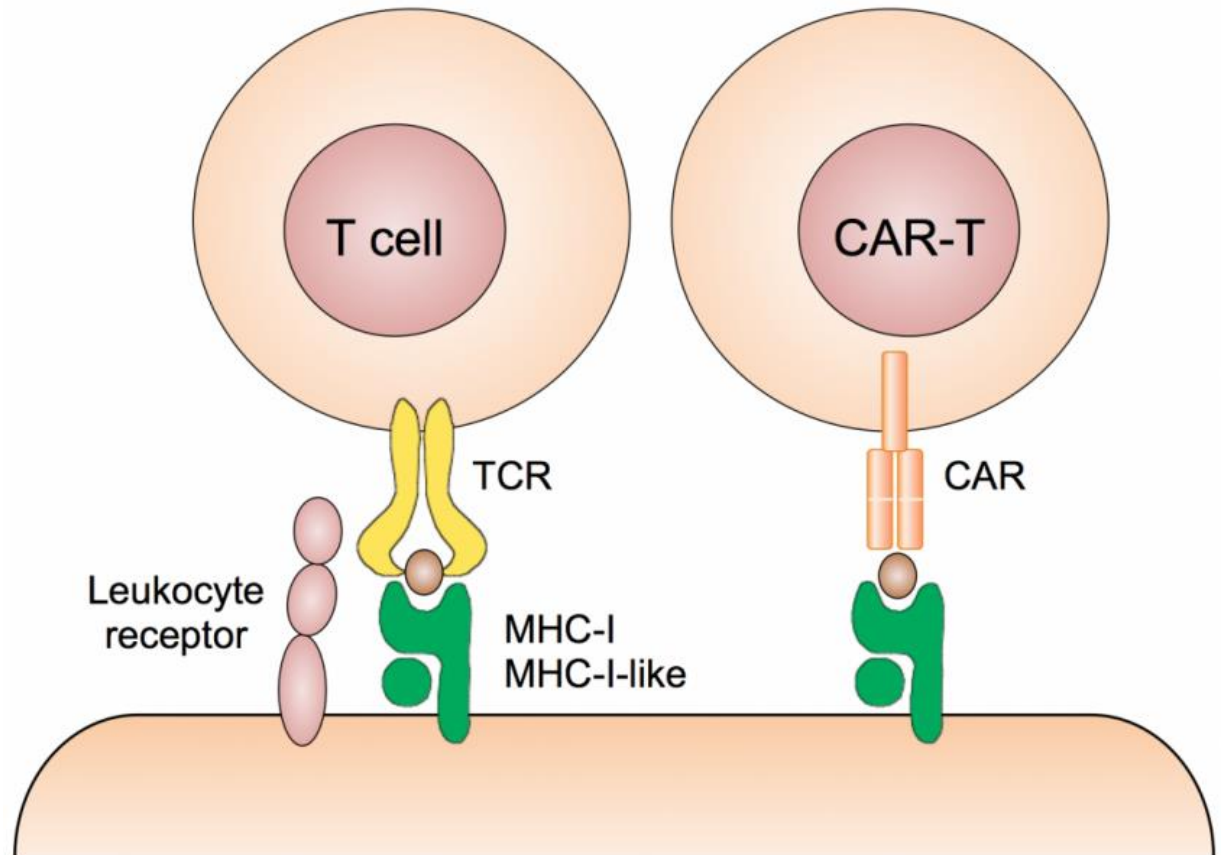


# Learning Objectives

- At the conclusion of the workshop, attendees should understand the following:
  - Rationale for using CAR T-cell therapy to treat patients with various types of lymphoma.
  - Who's a candidate for CAR T-cell therapy.
  - Steps involved in undergoing CAR T-cell therapy
  - Potential short- and long-term risks associated with CAR T-cell therapy
  - Potential outcomes after CAR T-cell therapy: does it cure cancer?

# What is CAR T-cell Therapy?

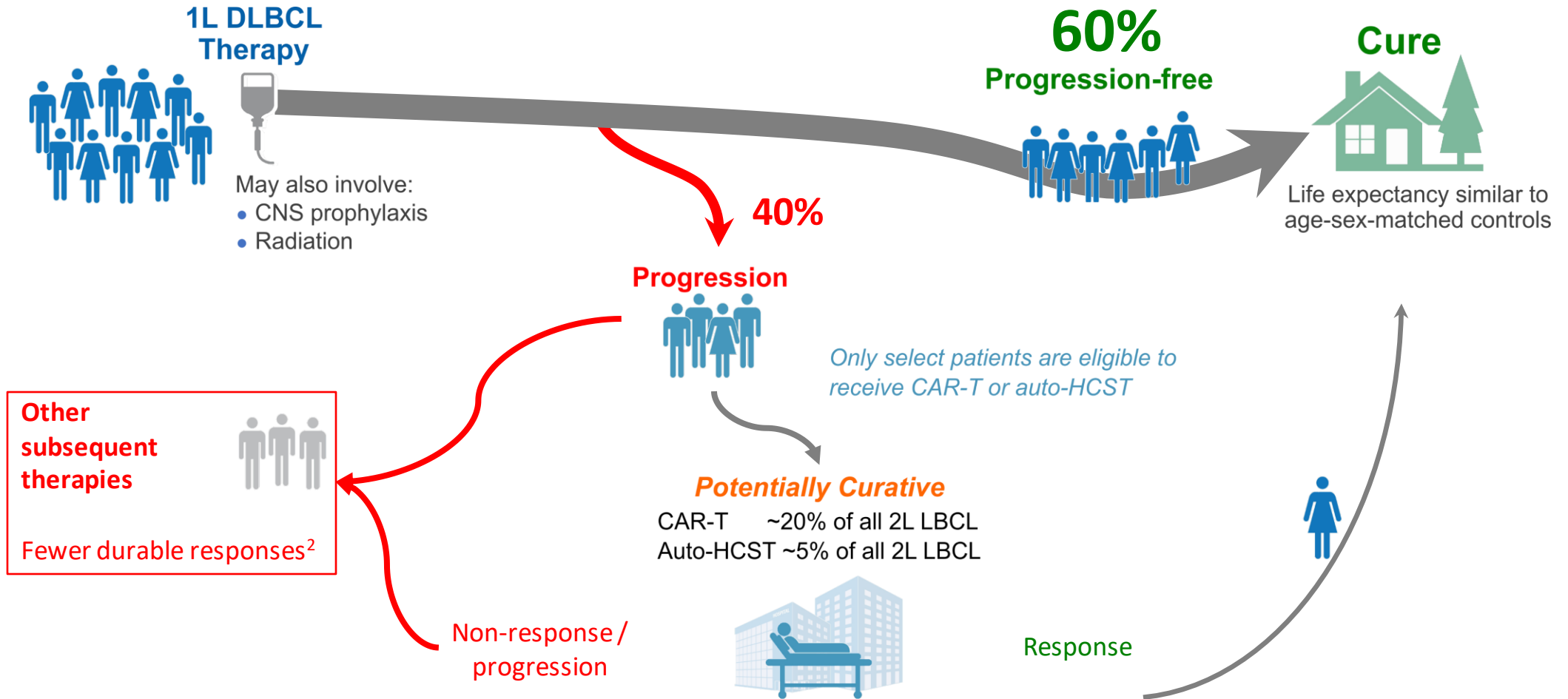
- Chimeric Antigen Receptor (CAR) T-cells are cells engineered to attack cancer cells without need for “presentation” to T-cells
- Works when cancer is not responding to chemotherapy



# Who is a candidate for CAR-T cell therapy?

1. Patients with diffuse large B-cell lymphoma (aggressive B-cell lymphoma)
  - a) Relapsed after 2 lines of therapy (including autologous transplant)
  - b) Relapsed within a year of first line of therapy or didn't respond
2. Patients with
  - a) follicular lymphoma after 2 lines of therapy
  - b) mantle cell lymphoma after 1 lines of therapy
3. Patients with B-cell acute lymphoblastic leukemia after 1 line of therapy
4. Patients with myeloma after 4 lines of therapy

# Diffuse large B-cell lymphoma: Patient Journey

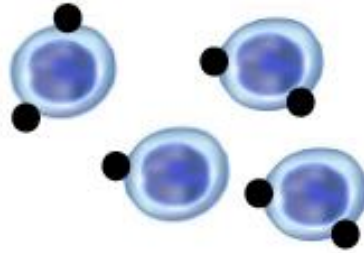


# How are CAR-T cells made?

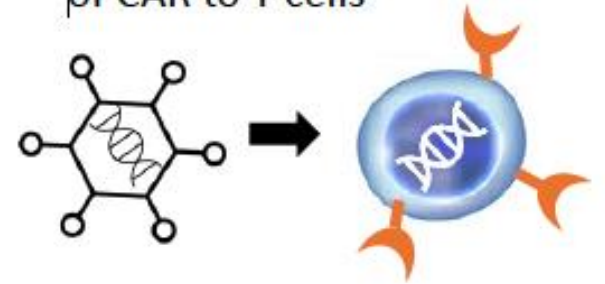
Step 1: T-cell collection  
(leukapheresis)



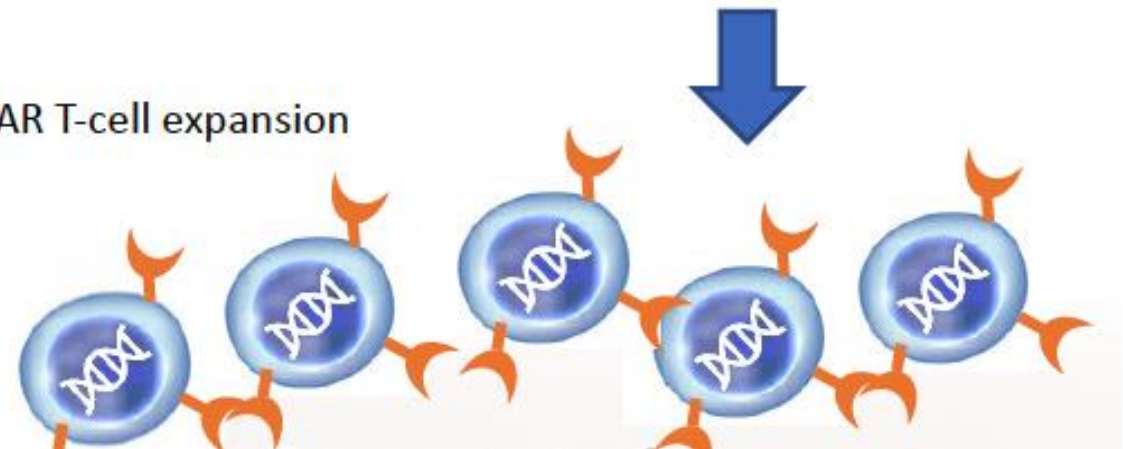
Step 2: T-cell selection +  
activation + enrichment



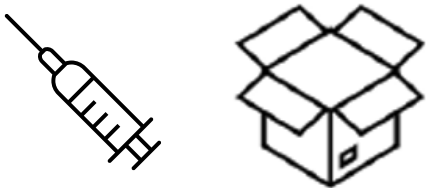
Step 3: viral vector transfer  
of CAR to T-cells



Step 4: CAR T-cell expansion



Step 5: CAR T-cell administration





# Typical CAR-T patient journey

1. Referral to a CAR-T treatment center (varies)
2. Insurance approval, production request, health/fitness evaluation (10-21 days)
3. T-cell collection (7-14 days)
4. “Manufacturing” at company to modify and grow T-cells (10-28 days; could be longer with “manufacturing failure”)
5. “Bridging therapy” may be needed while waiting
6. Low dose “lymphodepleting” chemotherapy (fludarabine and cyclophosphamide) usually outpatient (3 days)
7. Infusion of cells (inpatient or outpatient) – product is thawed and infused over 30 min with pre-medication
8. Monitoring for toxicities 14-28 days



# Early Toxicities of CAR-T cells (initial 4 weeks)

- Cytokine release syndrome
- Neurotoxicity (ICANS = Immune Effector Cells associated neurotoxicity syndrome)
- Infections
- Macrophage activation syndrome (bone marrow failure)
- Close monitoring is needed
- If not in the hospital, need to stay close to the treatment center and be seen every day for the first 2 weeks
- Remote monitoring technology being used in some centers

# Cytokine release syndrome (CRS)

- Happens due to rapid expansion of T-cells
- More common with more disease prior to CAR-T
- More common with certain CAR-T products
- Big 3 symptoms: fever, low blood pressure, shortness of breath
- Patients carry patient card
- Treated with steroids and tocilizumab
- Resembles influenza or acute COVID19
- Severe cases require ICU admission

# Neurotoxicity

- Also known as ICANS: Immune effector cell-associated neurotoxicity syndrome
- Due to cytokines crossing blood-brain barrier
- Presents with tremors, forgetfulness, difficulty with comprehension, confusion and seizures (like a “stroke”)
- You will get frequent standardized assessments
- More common with certain CAR-T products
- Treated with high doses of steroids
- Reversible in most cases however may need ICU admission
- There can be secondary effects: “deconditioning”

# Neurotoxicity Assessments (ICE Score)

| Parameter  | Score (Points) |
|--|----------------|
| Orientation: year, month, city, hospital   | 4              |
| Naming: ability to name 3 objects (eg, point to clock, pen, button)  | 3              |
| Following commands: ability to follow simple commands (eg, “show me 2 fingers” or “close your eyes and stick out your tongue”) | 1              |
| Writing: ability to write a standard sentence (eg, “our national bird is the bald eagle”)                                      | 1              |
| Attention: ability to count backwards from 100 by 10   | 1              |

Scoring:

**10**, no impairment

**7-9**, grade 1 ICANS

**3-6**, grade 2 ICANS

**0-2**, grade 3 ICANS

**0** due to patient unarousable and unable to perform ICE assessment, grade 4 ICANS

# Neurotoxicity Assessments (Handwriting)

Day 4  
9 am

I love Shawnee, KS.

MMSE score  
29/30

Day 5  
01:30 PM

Shawnee is a ~~place~~  
a town

27/30

Toci 8 mg/kg

Day 5  
03:30 PM

I'm sure  
177.

27/30

Day 6  
9 am

I miss my kids.

29/30

# Delayed toxicities (30+ days)

- Long term loss of B-cells; may need long term IV immunoglobulins (IVIg)
- Low blood counts; “neutropenia” (needing filgrastim; Neupogen or similar)
- Need long term antiviral, pneumocystis (PCP/PJP), and may need short term anti-fungal and antibacterial
- Need to repeat vaccinations
- COVID19 vaccination needs to be repeated
- 7% risk of non-melanoma skin cancer
- 5% risk of myelodysplastic syndrome (MDS)
- Long-lasting neurotoxicity “brain fog”

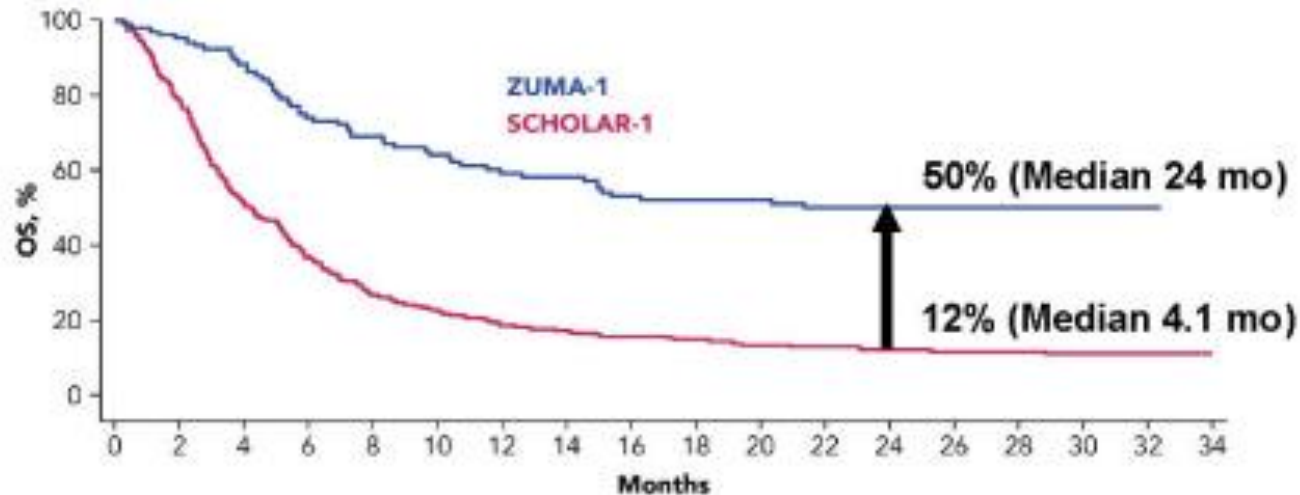
# Current FDA-approved CAR-T products

| Generic Name              | Brand Name | Target Antigen | Targeted Disease                          | Patient Population   |
|---------------------------|------------|----------------|---|--|
| Tisagenlecleucel          | Kymriah    | CD19           | B-cell acute lymphoblastic leukemia (ALL) | Children and young adults with refractory or relapsed B-cell ALL <b>ALL age up to 25 years</b> |
|                           |            |                | B-cell non-Hodgkin lymphoma (NHL)         | Adults with relapsed or refractory B-cell NHL <b>DLBCL or FL 2+ lines</b>                      |
| Axicabtagene ciloleucel   | Yescarta   | CD19           | B-cell non-Hodgkin lymphoma (NHL)         | Adults with relapsed or refractory B-cell NHL <b>DLBCL 1+ line (relapse &lt;12 m)</b>          |
|                           |            |                | Follicular lymphoma                       | Adults with relapsed or refractory follicular lymphoma <b>FL 2+ lines</b>                      |
| Brexucabtagene autoleucel | Tecartus   | CD19           | Mantle cell lymphoma (MCL)                | Adults with relapsed or refractory MCL <b>MCL 1+ line</b>                                      |
|                           |            |                | B-cell acute lymphoblastic leukemia (ALL) | Adults with refractory or relapsed B-cell ALL <b>ALL relapsed any age</b>                      |
| Lisocabtagene maraleucel  | Breyanzi   | CD19           | B-cell non-Hodgkin lymphoma (NHL)         | Adults with relapsed or refractory B-cell NHL <b>DLBCL 1+ line (relapse &lt;12 m)</b>          |
| Idecabtagene vicleucel    | Abecma     | BCMA           | Multiple myeloma                          | Adults with relapsed or refractory multiple myeloma <b>MM 4+ lines</b>                         |
| Ciltacabtagene autoleucel | Carvykti   | BCMA           | Multiple myeloma                          | Adults with relapsed or refractory multiple myeloma <b>MM 4+ lines</b>                         |



# Outcomes of CAR-T Therapy in Aggressive B-cell Lymphoma

## Standardized OS Comparison: ZUMA-1 vs. SCHOLAR-1 (historical)



Neelapu et al. *N Eng J Med* 2017  
Locke et al. *Lancet Oncol* 2019  
Neelapu et al. ASH 2019

- Improvement in median overall survival from 4 months to 24 months; about 50% of patients can be cured by CAR-T therapy compared to 12% of historic controls

# Outcomes of CAR-T therapy in lymphomas; snapshot

| Product                 | Company  | Patients                   | Response Rate | Median Survival (1 year) | CRS (% total/severe) | ICANS (% total/severe) |
|-------------------------|----------|----------------------------|---------------|--------------------------|----------------------|------------------------|
| Axi-Cel<br>(Yescarta)   | Kite     | DLBCL 2 <sup>nd</sup> line | 83%           | 76%                      | 92/6%                | 61/21%                 |
|                         |          | DLBCL 3 <sup>rd</sup> line | 82%           | 64%                      | 93/13%               | 64/28%                 |
|                         |          | FL 3 <sup>rd</sup> line    | 94%           | 93%                      | 78/15%               | 56/6%                  |
| Tisa-Cel<br>(Kymriah)   | Novartis | DLBCL 3 <sup>rd</sup> line | 52%           | 49%                      | 58/22%               | 21/12%                 |
|                         |          | FL 3 <sup>rd</sup> line    | 86%           | 67%                      | 48/0%                | 11/3%                  |
| Liso-cel<br>(Beryanzi)  | BMS      | DLBCL 2 <sup>nd</sup> line | 79%           | 79%                      | 49/1%                | 12/4%                  |
|                         |          | DLBCL 3 <sup>rd</sup> line | 73%           | 58%                      | 42/2%                | 30/10%                 |
| Brexu-Cel<br>(Tecartus) | Kite     | MCL 2 <sup>nd</sup> line   | 93%           | 78%                      | 91/15%               | 63/31%                 |

DLBCL=diffuse large B-cell lymphoma; FL=follicular lymphoma; MCL=mantle cell lymphoma  
CRS=cytokine-release syndrome; ICANS=immune-effector cell neurotoxicity syndrome

# Thank you!



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# Questions?



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