CAR T-CELL THERAPY: LYMPHOMA SERIES

EPISODE 1:

IT'S TIME TO UNDERSTAND CAR-T THERAPY FOR B-CELL LYMPHOMA: EARLIER INDICATIONS COMING TO A COMMUNITY NEAR YOU

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DOWNLOADABLE RESOURCES | REFERENCE SLIDES

Med Table Talk™ addresses clinical challenges with interprofessional perspectives to foster meaningful change

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Today's Discussion

- Overview of CAR-T therapy
- Benefits and risks versus those of other therapies
- Identifying patients who may be candidates for CAR-T
- Potentially practice-changing data from the recent hematology conference
  - **TRANSFORM, ZUMA-7, and BELINDA trials**

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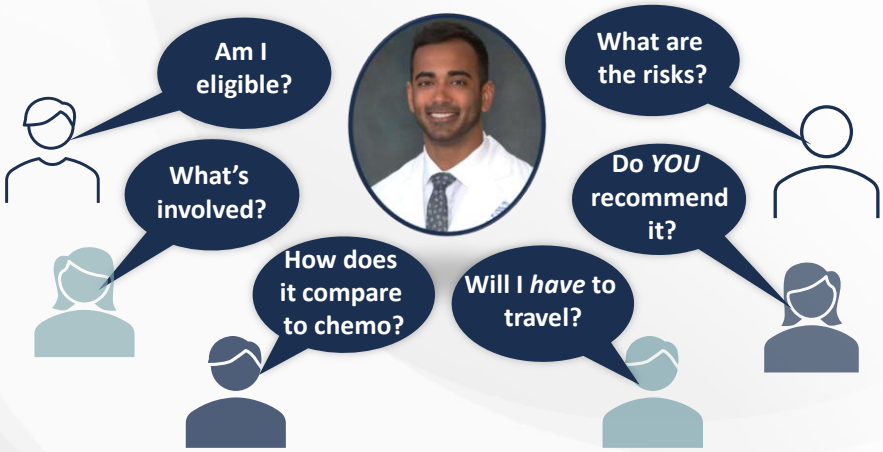
How Will You Respond When Your Patient Asks You About CAR-T Therapy?



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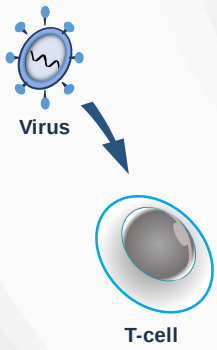
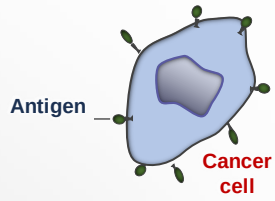
What Exactly Is Chimeric Antigen Receptor (CAR) T-CELL Therapy?





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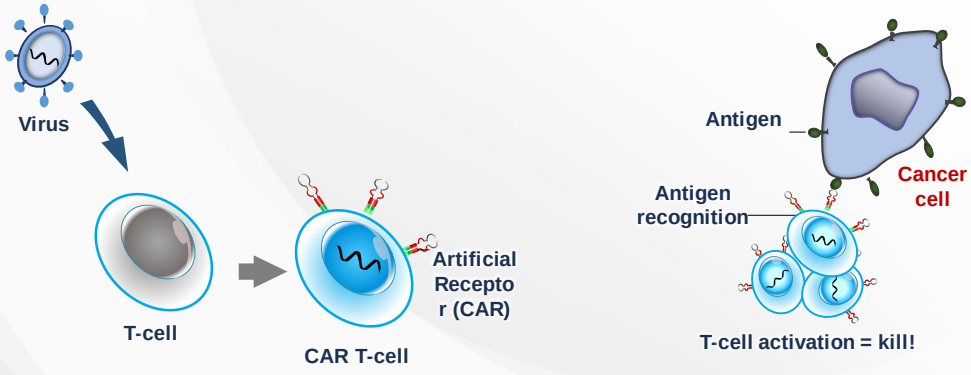

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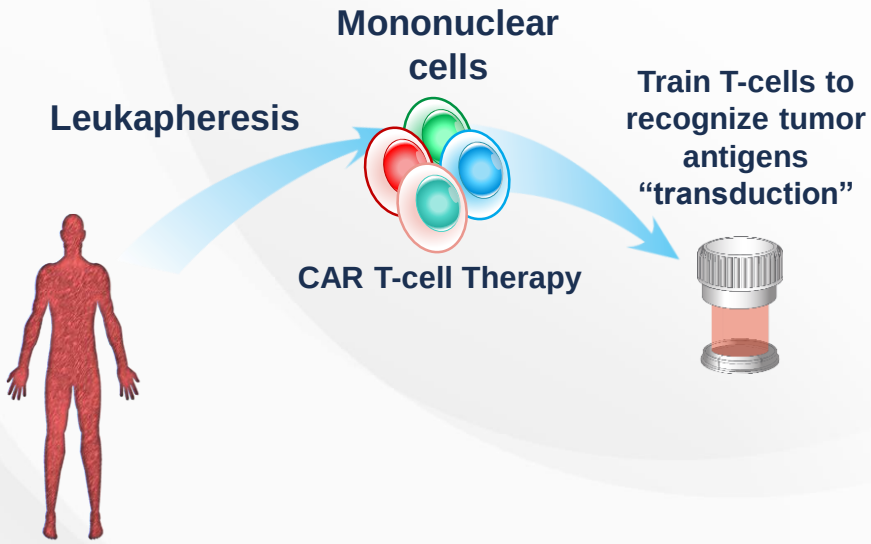
Manufacturing CAR T-Cells



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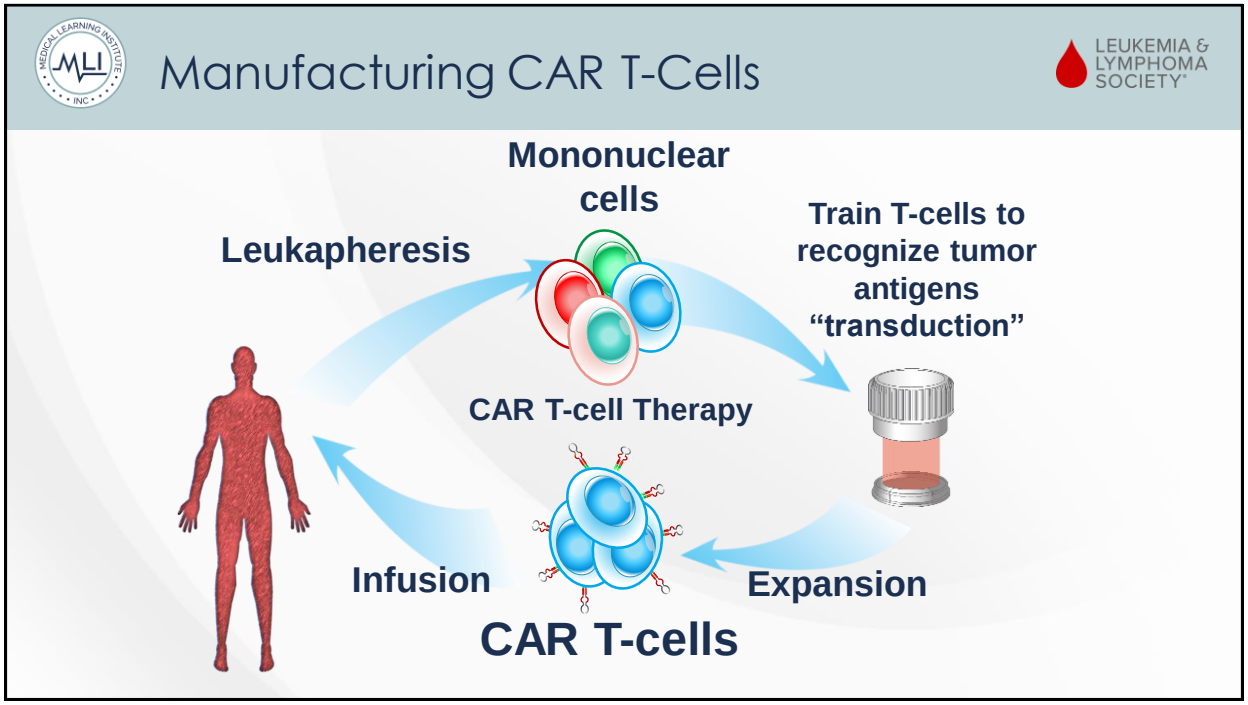
Manufacturing CAR T-Cells
LEUKEMIA & LYMPHOMA SOCIETY
Mononuclear cells
Leukapheresis
Train T-cells to recognize tumor antigens "transduction"
CAR T-cell Therapy
Infusion
Expansion
CAR T-cells

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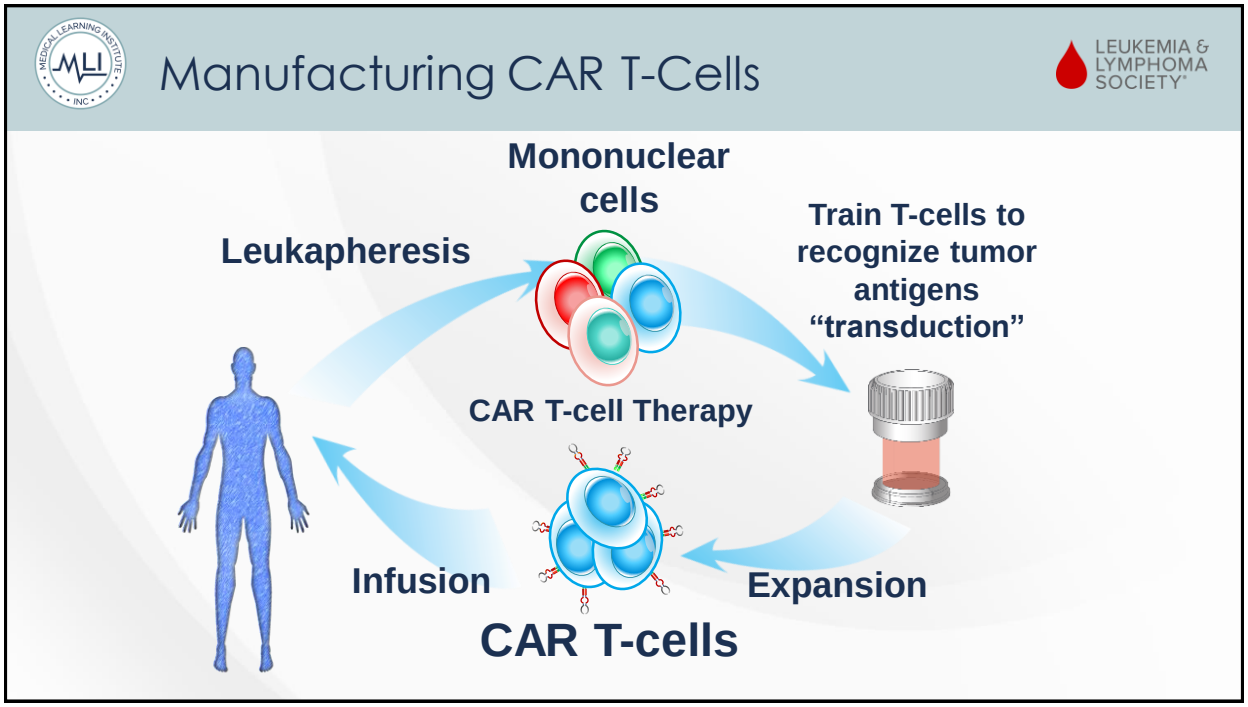
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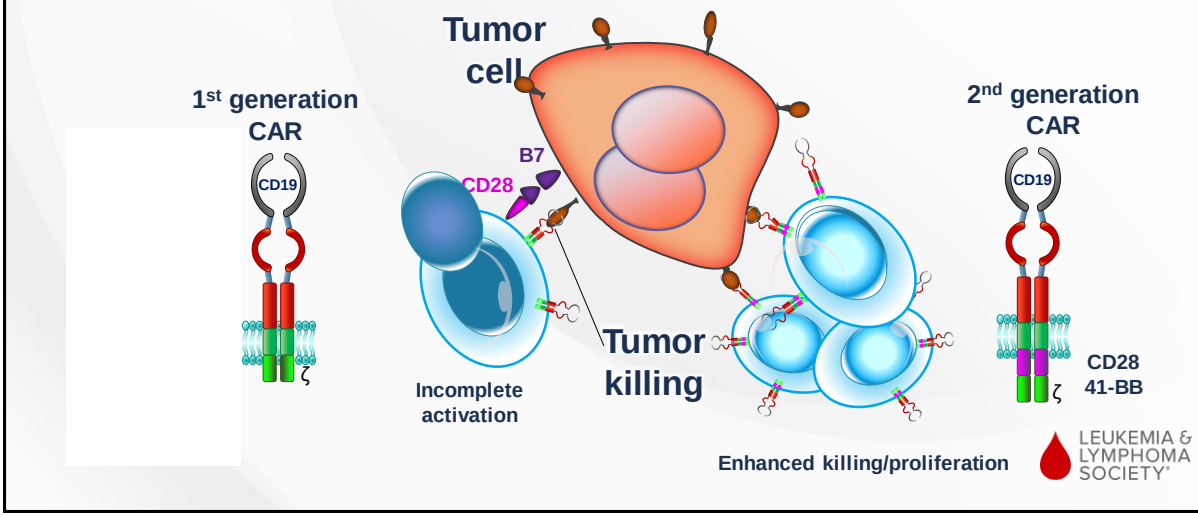
The Evolution of CAR T-Cells



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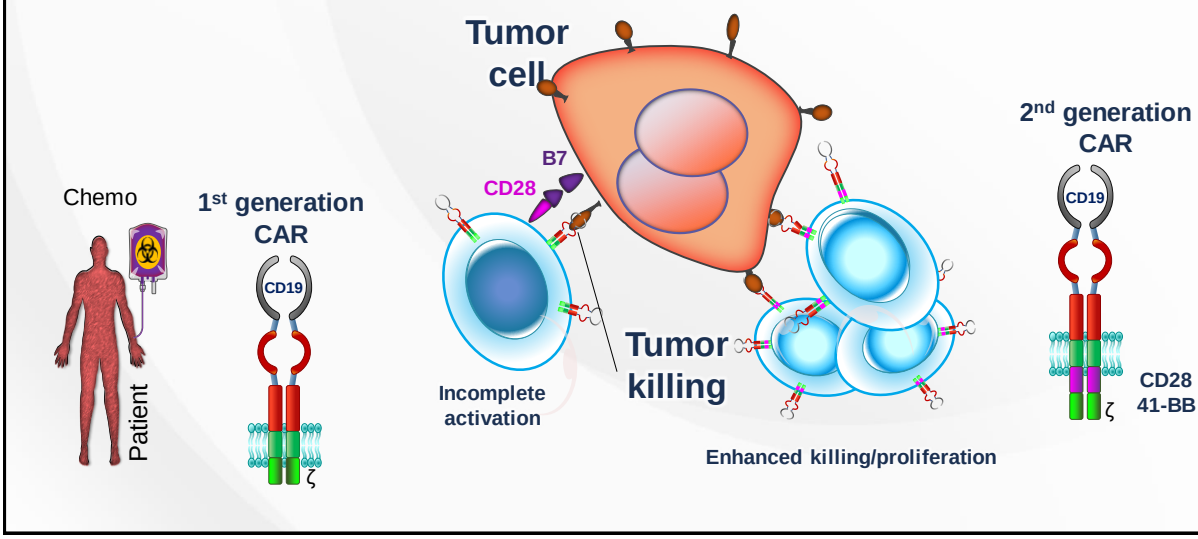
The Evolution of CAR T-Cells



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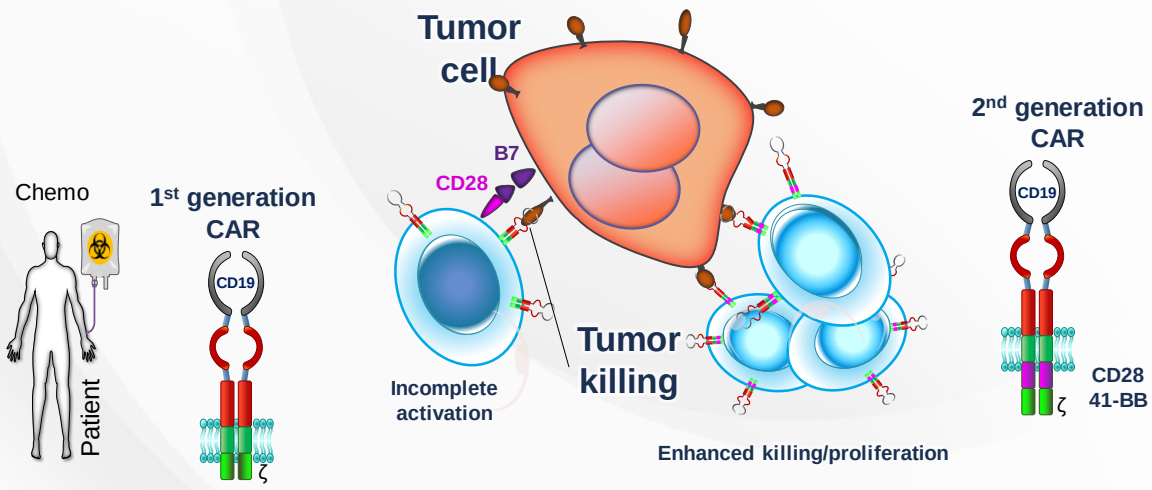

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Benefits Compared With Those Of Other Therapies

Benefits of CAR-T

- Personalized, targeted therapy designed to target a specific antigen (protein) on the cancer cell, thus usually does not cause some of the toxicities standard chemo does (eg, hair loss, mucositis, nausea)
  - Side effects are typically limited to the first few weeks after treatment
  - Less risk for long-term organ-related toxicity or secondary cancers
- Improved quality of life versus prolonged courses of chemotherapy
- Less stringent than an autologous or allogeneic transplant

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Risks Compared With Those Of Other Therapies

Risks specific to CAR-T

- CRS and neurotoxicity are relatively unique to CAR-T
- Products are not “one-size-fits-all”: this applies to manufacture and treatment
- Newer therapy, so long-term data are limited

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VIA STANDARD THERAPY	VIA CAR-T ROUTE
Diagnostic workup	Screening/insurance approval
Standard therapy: combination chemo +/- stem cell transplant	T-cell collection & manufacture
Investigational therapy or salvage therapy	Treatment & aftercare

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Short- And Long-Term Effects Of Traditional Cancer Therapy

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Safety First! Toxicity Related To CAR-T

Immediate

Rare

Day 1 to 4 weeks

- Cytokine release syndrome
- Neurotoxicity
- Cytopenias and infections
- Organ dysfunction

First year

B-cell aplasia requiring IVIG

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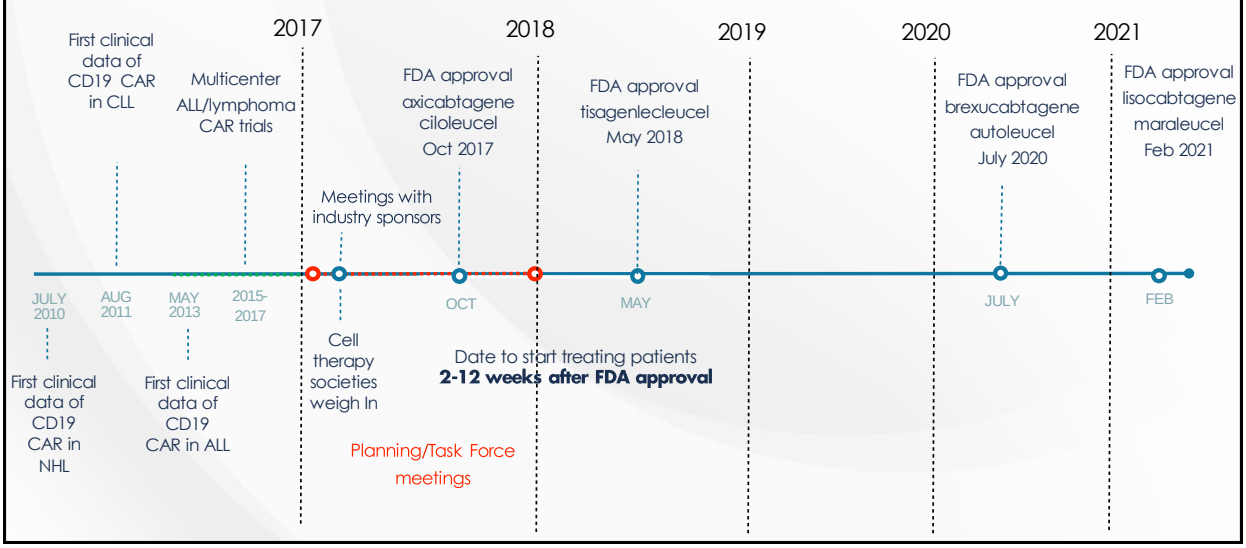
The Road TO CAR-T Approval for Lymphoma



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From Research Product To Commercial Product

	Research	Commercial
Patient expectation	• Public accepts limited access • Public expects strict eligibility criteria	• Public expects broad access, but CAR T-cells limited to certain centers • Public expects more flexible eligibility criteria, which is not exactly true for CAR T-cells
Patient volume	• Limited because of manufacturing constraints; 1-2 patients/month	• No limit to patients to be treated • 10-15 patients/month • Manufacturers can make 4,000 products a year
Logistics	• Less complex intake process • Involve production center • Only limited providers (protocol personnel)	• Complex intake process • Involve manufacturer, third-party payor, and Institution • Only limited providers in specialized units
Reimbursement	• Issues regarding investigational nature of product • Product is free	• Product very expensive: $300-500K plus care delivery • Issues with third-party payors • Significant financial risk for institutions (particularly with government payors)
Reporting requirements	• Protocol requirements and only to sponsor	• Sponsor requirements and FDA through CIBMTR • Similar to allogeneic HCT

CIBMTR, Center for International Blood & Marrow Transplant Research: https://www.cibmtr.org/Pages/index.aspx

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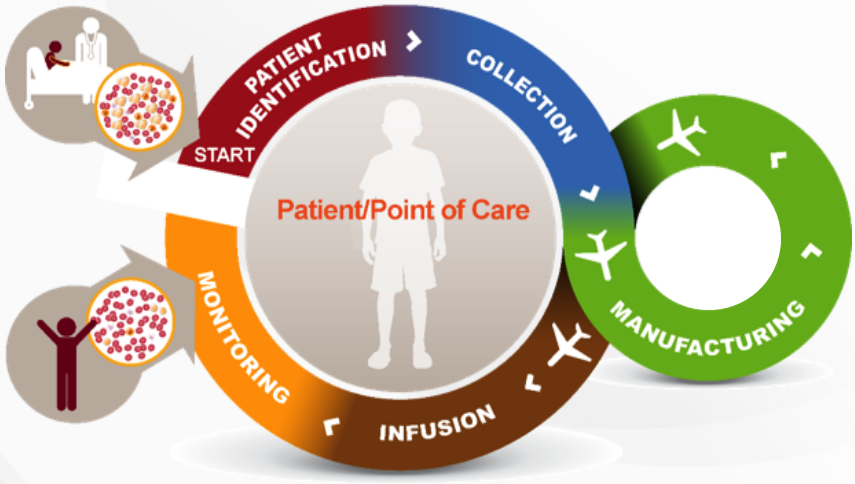
THE ROAD TO CAR-T



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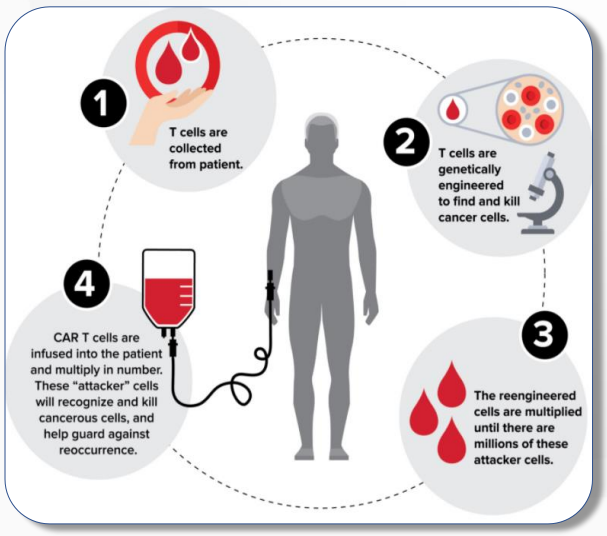
CAR-T Therapy: Turning The Body Into A Cancer Fighter



https://www.LLS.org/CARTtherapy Used with permission.

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CAR-T Products Approved For B-Cell Lymphoma

Product *	Approval	Indication
Axicabtagene ciloleucel or axi-cel (Yescarta™)	October 2017	**R/R large B-cell lymphoma after 2+ lines of therapy, including DLBCL not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B cell lymphoma, and DLBCL arising from follicular lymphoma; also indicated for adults with R/R follicular lymphoma after 2+ lines of therapy**
Tisagenlecleucel or tisa-cel (Kymriah™)	May 2018	**R/R large B-cell lymphoma after 2+ lines of therapy including DLBCL not otherwise specified, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma**
Brexucabtagene autoleucel or brexu-cel (Tecartus™)	July 2020	**R/R mantle cell lymphoma**
Lisocabtagene maraleucel or liso-cel (Breyanzi™)	February 2021	**R/R large B-cell lymphoma after 2+ lines of therapy including DLBCL not otherwise specified (including DLBCL arising from indolent lymphoma), high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and follicular lymphoma grade 3B**
Axi-cel and liso-cel likely to be approved for 2nd line	Q3-Q4 2022	**Likely: primary refractory or relapsing within 12 months based on Phase III trials**

*To comply with accreditation standards, we will use generic names throughout this educational activity. Brand names are provided in the table for the convenience of clinician-learners. R/R: relapsed/refractory; DLBCL, diffuse large B-cell lymphoma

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Upcoming Episodes

MED TABLE TALK

CAR T-CELL THERAPY
LYMPHOMA SERIES

EPISODE 2: What you MUST know as more lymphoma patients are on the road to CAR-T

EPISODE 3: Avoiding roadblocks in coordinating CAR-T therapy for B-cell lymphoma: Practical tips for community oncology clinicians

EPISODE 4: Opening the CAR(T) door to get your patients to therapy

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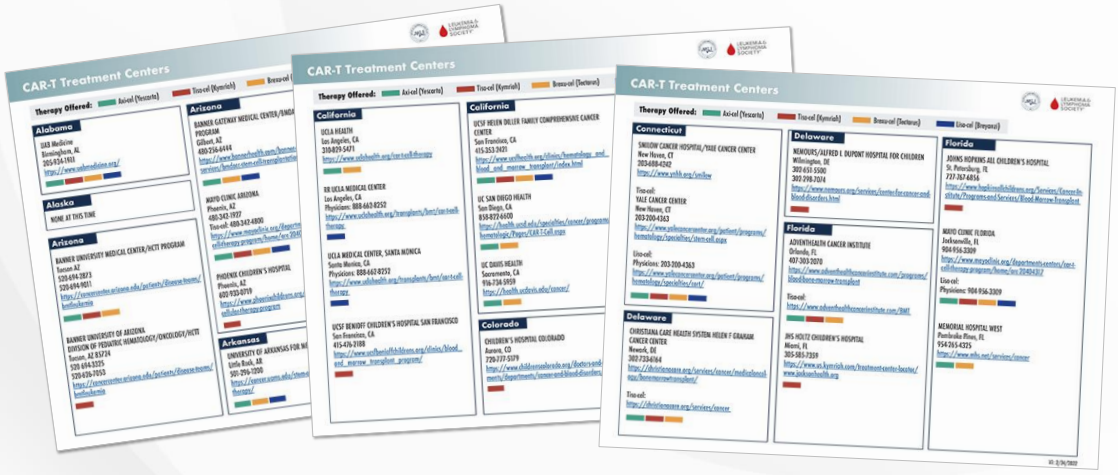
Directory Of CAR-T Centers By State



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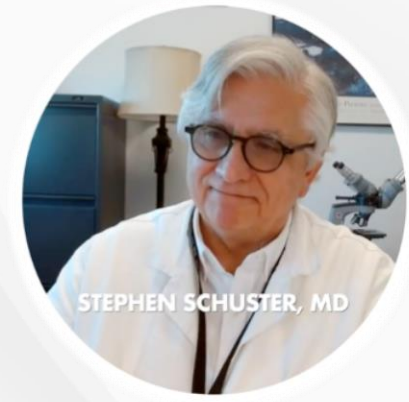
Special Guest



STEPHEN J. SHUSTER, MD

Robert and Margarita Louis-Dreyfus
Professor of CLL and Lymphoma

Professor of Medicine
University of Pennsylvania
Director of the Lymphoma Program and
Director of Lymphoma Translational Research
at the Abramson Cancer Center

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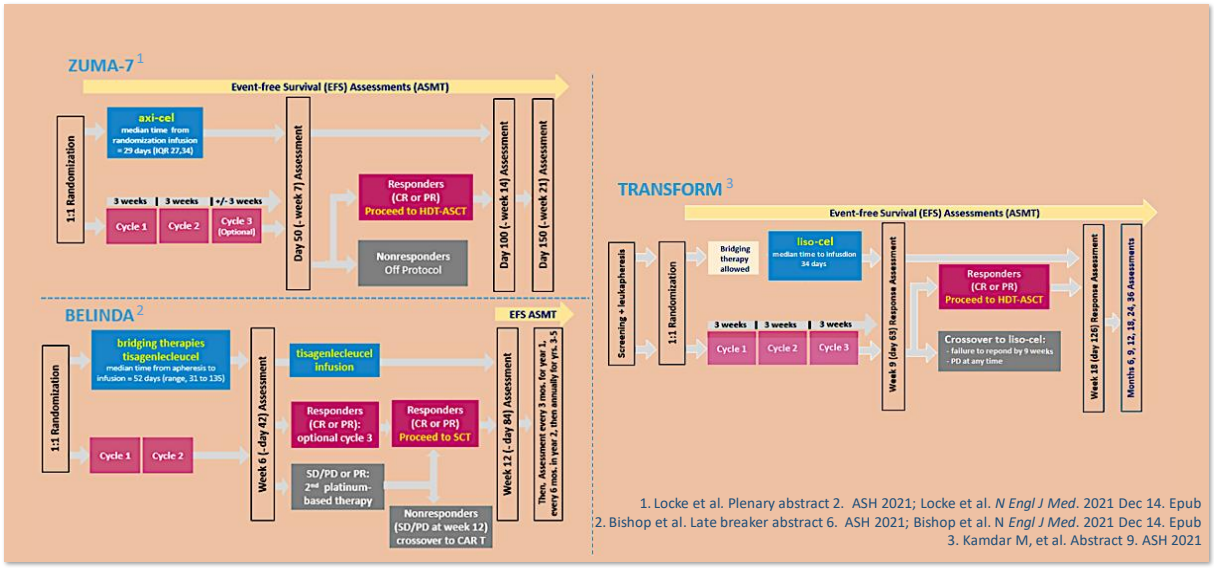
…AND THEN THERE WERE 3: ZUMA-7, BELINDA, AND TRANSFORM

RANDOMIZED TRIALS OF 3 CAR-T PRODUCTS VS STANDARD OF CARE



1. Locke et al. Plenary abstract 2. ASH 2021; Locke et al. *N Engl J Med*. 2021 Dec 14. Epub
2. Bishop et al. Late breaker abstract 6. ASH 2021; Bishop et al. N *Engl J Med*. 2021 Dec 14. Epub
3. Kamdar M, et al. Abstract 9. ASH 2021

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Take-home Messages

- CAR-T therapy is a personalized, targeted immunotherapy treatment that can be effective at inducing remission even in patients who have not responded to standard or salvage therapy
- The approved CAR-T therapies are equally efficacious
- Early identification and referral of patients who may be eligible for CAR-T therapy can help avoid some treatment obstacles

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Take-home Messages

- CAR T-cells have a unique risk profile that differs from standard or salvage lymphoma therapy
- Ongoing research is evaluating earlier use of CAR-T (prior to relapse or refractory disease), reducing toxicity, and improving access to this personalized therapy
- Ongoing collaboration between referring community oncologists and specialized centers can improve patients' experience

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The Leukemia & Lymphoma Society's
Information Specialists and Clinical Trial Support Centers

Information Specialists

Highly trained social workers, nurses, and health educators assist through treatment, financial, and social challenges

Phone: (800) 955- 4572
Website: LLS.org/IRC
Live chat: LLS.org/InformationSpecialists
Email: infocenter@LLS.org

Clinical Trial Support Center

Work one on one with an LLS clinical trial nurse navigator who will personally assist throughout the entire clinical trial process; a nurse navigator will help identify potential clinical trials and overcome the barriers to enrollment (navigators can help clinicians and patients)

For information about this free service, call an Information Specialist to be referred to the CTSC at (800) 955 4572, visit: www.LLS.org/CTSC, or complete a referral form at: www.LLS.org/CTSCreferral

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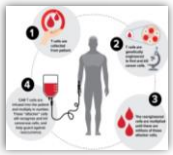
Resources For Community Clinicians

- Directory of CAR-T treatment centers
  (download from the activity website)
- Animations and key slides used during this episode
  (download from the activity website)
- Treating Blood Cancers: The LLS Podcast for Professionals
  CAR T-cell Therapy in 2022: What You Need to Know
  https://treatingbloodcancers.org/e51/
- LLS CAR T-Cell Therapy fact sheet for clinicians
  Facts About Chimeric Antigen Receptor (CAR) T-Cell Therapy
  https://www.LLS.org/booklet/facts-about-chimeric-antigen-receptor-car-t-cell-therapy
- LLS infographic
  How CAR-T Works
  https://www.LLS.org/CARTtherapy
- ASTCT slide deck
  https://www.astct.org/practice/practice-resources/cart-slides



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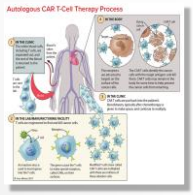
Patient Education Resources

- Chimeric Antigen Receptor (CAR) T-cell Therapy
  https://www.LLS.org/CARTtherapy
- Support for financial and other resources
  https://www.LLS.org/support
- CAR T-cell Therapy and Its Side Effects
  CAR T-cell Therapy in 2022: What You Need to Know
  https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy/car-t-cell1.html
- Chimeric Antigen Receptor T-Cell Therapy: How it Works
  https://www.LLS.org/treatment/types-treatment/immunotherapy/chimeric-antigen-receptor-car-t-cell-therapy
- LLS CAR T-Cell Therapy fact sheet for patients and caregivers
  Facts About Chimeric Antigen Receptor (CAR) T-Cell Therapy
  https://www.LLS.org/sites/default/files/2021-11/FS27_CART_Facts_11.21update.pdf



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