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# Operationalizing Early-Line CAR T Cell Therapy in R/R DLBCL: From Evidence to Clinical Practice

**Matthew Lunning, DO, FACP**
*Chief, UNMC Division of Hematology*
*Professor, UNMC Division of Hematology*
*UNMC Assistant Vice Chancellor of Clinical Research*
*Omaha, Nebraska*

**Samuel Yamshon, MD**
*Perlmutter Cancer Center*
*NYU Langone Health*
*New York City, New York*

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# Disclosures

- **Matthew Lunning, DO, FACP:** Consultant—AbbVie, ADC Therapeutics
- **Samuel Yamshon, MD:** Advisory Board—Abbvie, ADC Therapeutics, Bristol Myers Squibb, Genmab, Incyte, Ipsen, Pfizer; consultant—Bristol Myers Squibb, Ipsen; grant/research support—Ipsen

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# Learning Objectives

- Evaluate clinical evidence supporting the evolving role of CAR T-cell therapy across lines of treatment in R/R DLBCL
- Apply evidence-based strategies for patient selection, referral timing, and treatment sequencing to optimize the use of CAR T-cell therapy in patients with R/R DLBCL across diverse clinical settings
- Implement multidisciplinary approaches to safely deliver CAR T-cell therapy, including recognition and management of treatment-related toxicities and integration into real-world clinical workflows

R/R = relapsed/refractory; DLBCL = diffuse large B-cell lymphoma.

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# Overview of R/R DLBCL and Evolving Treatment Paradigm

**Matthew Lunning, DO, FACP**

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# Setting the Stage in DLBCL



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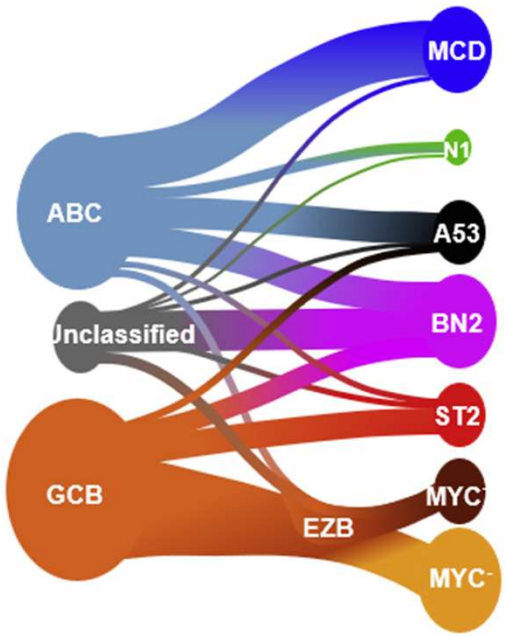
# Setting the Stage in DLBCL




DHT = double-hit translocation; HLH = hemophagocytic lymphohistiocytosis; smIPI = stage-modified International Prognostic Index.

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# Not Just One Disease




| Prevalence | 5-year OS | Genetic themes | Genetically related lymphomas | Gene expression signatures | Potential therapeutic targets |
|---|---|---|---|---|---|
| 8.7% | 40% (All)<br>37% (ABC) | My-T-BCR-dependent NF-κB<br>Immune evasion-MHC class I<br>Cell survival – BCL2 expression<br>Altered B Cell differentiation<br>G1-S cell cycle/p53 checkpoint BCR: IgM >> IgG: $IgV_H4\text{-}34^{**}$ | Primary extranodal DLBCL<br>Transformed WM | B-cell activation<br>NF-κB<br>IRF4<br>Myc<br>Proliferation | BCR-dep. NF-κB<br>P13 kinase<br>mTORC1<br>BCL2-BCLX-MCL<br>JAK1<br>IRAK4<br>IRF4 |
| 1.7% | 27% (All)<br>22% (ABC) | NOTCH1 signaling<br>Altered B cell differentiation<br>BCR: IgM > IgG | NOTCH1-mutant CLL | NOTCH<br>Quiescence<br>Plasma cell<br>T cell-myeloid-FDC | NOTCH1<br>Immune checkpoint |
| 5.8% | 63% (All)<br>33% (ABC)<br>100% (GCB) | *TP53* inactivation damage<br>Aneuploidy<br>Immune evasion – *B2M* loss<br>BCR: IgM >> IgG: $IgV_H4\text{-}34^{**}$ | – | p53<br>Immune low | BCR-dep. NF-κB |
| 13.3% | 67% (All)<br>76% (ABC)<br>100% (GCB)<br>38% (UC) | NOTCH2 signaling<br>Altered B cell differentiation<br>BCR-dependent NF-κB<br>Immune evasion – *CD70* loss<br>Proliferation – Cyclin D3<br>BCR: IgM >> IgG: $IgV_H4\text{-}34^{**}$ | MZL<br>Transformed MZL | B cell activation<br>NF-κB<br>NOTCH<br>Proliferation | BCR-dep. NF-κB<br>P13 kinase<br>mTORC1<br>BCL2<br>NOTCH2 |
| 6.4% | 84% (All)<br>81% (GCB) | JAK/STAT3 signaling<br>NF-κB<br>*P2RY8 – GNA13* inactivation<br>Altered B cell differentiation<br>BCR: IgM >> IgM | NLPHD<br>THRLBCL | GC B cell<br>P13K signaling<br>JAK2 signaling<br>Glycolysis<br>Stromal | P13 kinase<br>JAK2 |
| 5.9% ($MYC^+$)<br>17.6% ($MYC^-$) | 48% ($MYC^+$)<br>82% ($MYC^-$) | Chromatin modification<br>Anti-apoptosis<br>P13 kinase signaling<br>*S1PR2 – GNA13* inactivation<br>Altered $T_{FH}$ interactions<br>MYC (EZB-$MYC^+$)<br>BCR: IgM >> IgM | FL<br>Transformed FL<br>BL (EZB-$MYC^+$) | GC LZ ($MYC^-$)<br>GC IZ ($MYC^-$)<br>BCL6 ($MYC^+$)<br>TCF3 (both)<br>$T_{FH}$ cells ($MYC^-$)<br>Stromal ($MYC^-$)<br>Immune low ($MYC^+$) | P13 kinase<br>mTORC1<br>EZH2<br>BCL2-MCL1 |

OS = overall survival; ALL = acute lymphoblastic leukemia; ABC = activated B-cell; GCB = germinal center B-cell; UC = unclassified; WM = Waldenström macroglobulinaemia; CLL = chronic lymphocytic leukemia; MZL = marginal zone lymphoma; NLPHD = nodular lymphocyte predominance Hodgkin's disease; THRLBCL = T-cell/histiocyte-rich large B-cell lymphoma; FL = follicular lymphoma; BL = Burkitt lymphoma.

Dreyling M, et al. *Hemasphere*. 2022;6(6):e726.

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# Head to Head…Never

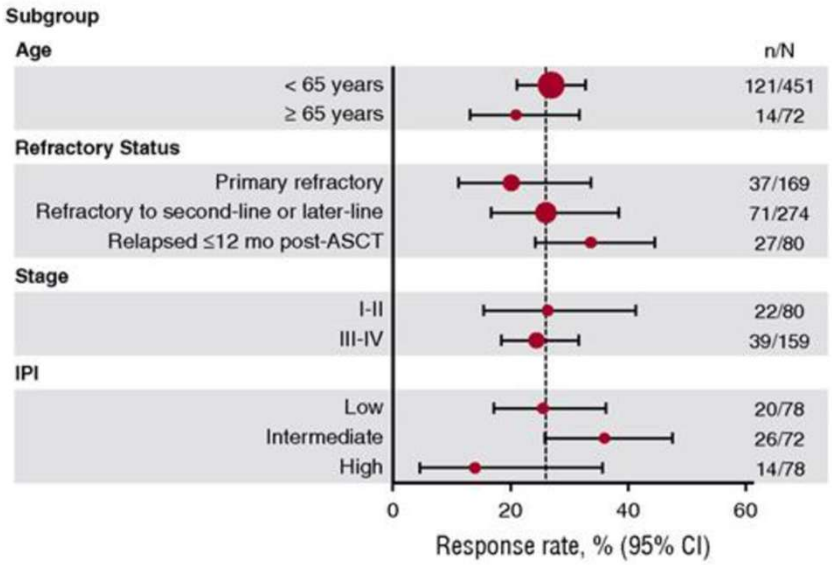
| | POLARIX | frontMIND |
|---|---|---|
| **Experimental Arm** | Pola-R-CHP (N=440) | Tafa+Len+R-CHOP (N=443) |
| **Control Arm** | R-CHOP (N=439) | R-CHOP (N=447) |
| **Schedule** | Pola D=1 each cycle x 6 cycles | Tafa D=1, 8, 15 each cycle x 6 cycles<br>Len D= 1-10 |
| **Population** | **IPI 2-5** | **IPI 3-5** |
| **Med follow-up** | 64.1 mos | 35.2 mos |
| **Med Age** | 65 | 65 |
| **PFS, HR**<br>**ABC subtype**<br>**GCB subtype**<br>**Unclassified**<br>**Unknown** | **0.73 (0.57, 0.95) @** mFU 28.2 mo<br>0.4 (0.2-0.6)<br>1.0 (0.7-1.5)<br>1.9 (0.8-4.5)<br>0.7 (0.4-1.2) **(25% unknown)** | **0.75 (0.59-0.96)** @ mFU 35.2 mos<br>0.59 (0.36-0.95)<br>0.69 (0.40-1.19)<br>0.58 (0.24-1.41)<br>**Not reported (47% unknown)** |
| **2-year PFS rate** | **ITT IPI 2-5:** 76.7%<br>**IPI 3.5:** 75.2% | **IPI 3-5:** 71.1% |
| **5-year PFS rate** | **IPI 2-5:** 64.9%<br>**IPI 3-5:** 63.2% | – |
| **mOS,**<br>**OS rates** | **HR 0.94 (0.65-1.37) @ mFU 28.2 mo**<br>2-year OS: 88.7%<br>5-year OS: 82.3% | **HR 0.85 (0.63-1.14)** @ mFU 35.2 mos<br>2-year OS: 84.1%<br>3-year OS: 81.1% |
| **ORR (CR)** | 95.9% (86.6%) | 80.4% (65.2%) |

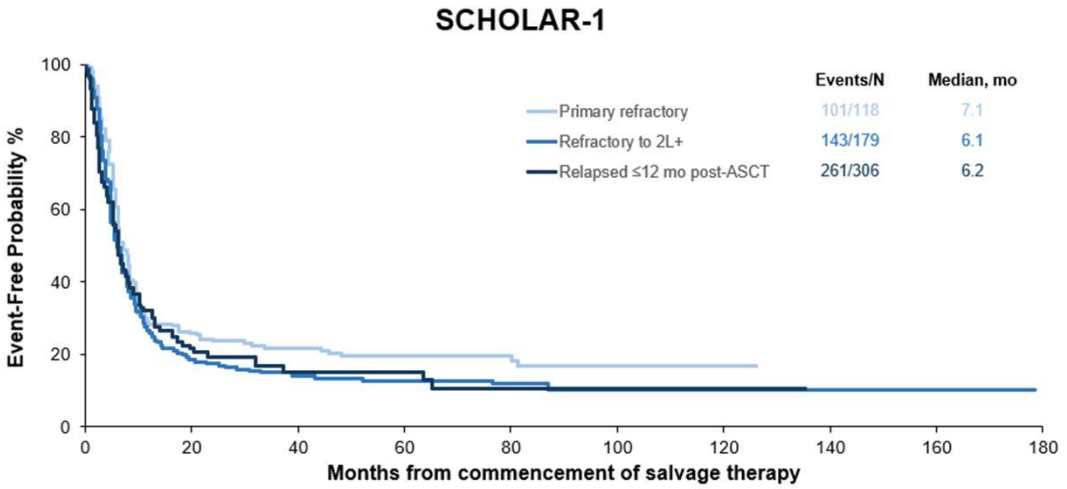
ITT = intention-to-treat; PFS = progression-free survival; mOS = median OS; ORR = objective response rate; pola-R-CHP = polatuzumab, rituximab, cyclophosphamide, doxorubicin, prednisolone; R-CHOP = rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone.

Morschhauser F, et al. *J Clin Oncol*. 2025;43(35):3698-3705. Lenz G, et al. *Lancet*. 2026;407(10547):2528-2541.

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# What Happens at Relapse…Old Data?



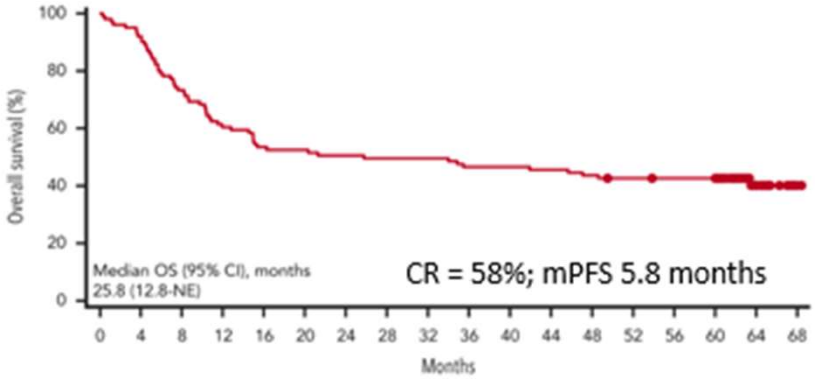




Crump M, et al. *Blood*. 2017;130(16):1800-1808.

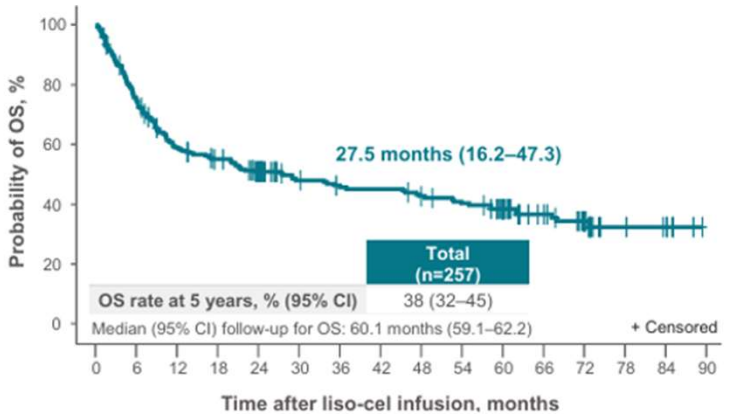
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# CAR T Comes to The Table

ZUMA-1




TRANSCEND




CR = complete response.
Neelapu SS, et al. *Blood*. 2023;141(19):2307-2315. Abramson JS, et al. *Blood*. 2026;148(11):1388-1393.

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# CAR T Moves to the Head of the Table

| Trials | CAR-T | Bridging Allowed | Median PFS/EFS (CAR-T) | Median PFS/EFS (SOC) | Outcome |
|---|---|---|---|---|---|
| ZUMA-7 | Axi-cel | No | 14.7 mo | 3.7 mo | **Positive** |
| TRANSFORM | Liso-cel | Yes | 10.1 mo | 2.3 mo | **Positive** |
| BELINDA | Tisa-cel | Yes | 3.0 mo | 3.0 mo | **Negative** |

EFS = event-free survival; SOC = standard of care.

Locke FL, et al. *N Engl J Med*. 2022;386(7):640-654. Kamdar M, et al. *Lancet*. 2022;399(10343):2294-2308. Bishop MR, et al. *N Engl J Med*. 2022;386(7):629-639.

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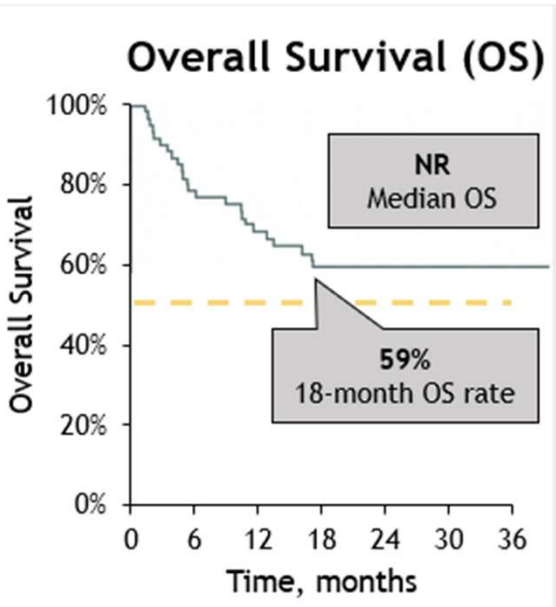
# CAR T Moves into Broader Populations

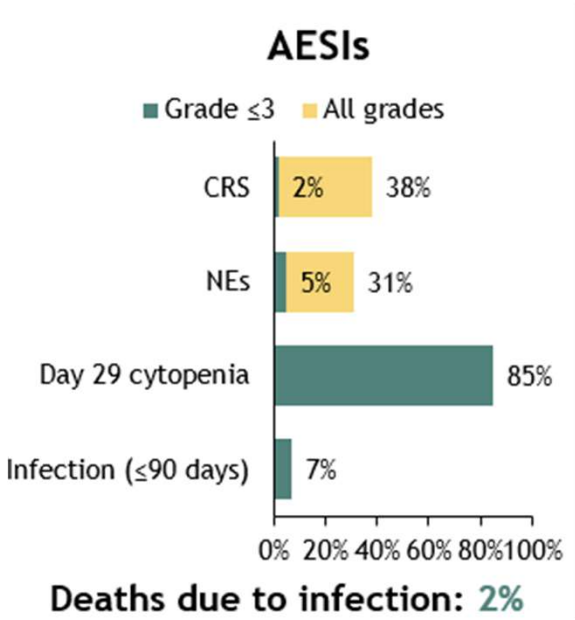
**mFU: 24.3 months**

**Liso-cel** as 2L treatment in patients with R/R LBCL who were deemed ineligible for HDT-ASCR (N = 61)

**ORR/CR: 80/54%**

| HDT-ASCR ineligibility criteria | Liso-cel, % (N = 61) |
|---|---|
| Age ≥ 70 years | 79 |
| ECOG PS 2 | 26 |
| CrCl < 60 mL/min | 25 |
| DLCO ≤ 60% | 7 |
| LVEF < 50% | 2 |



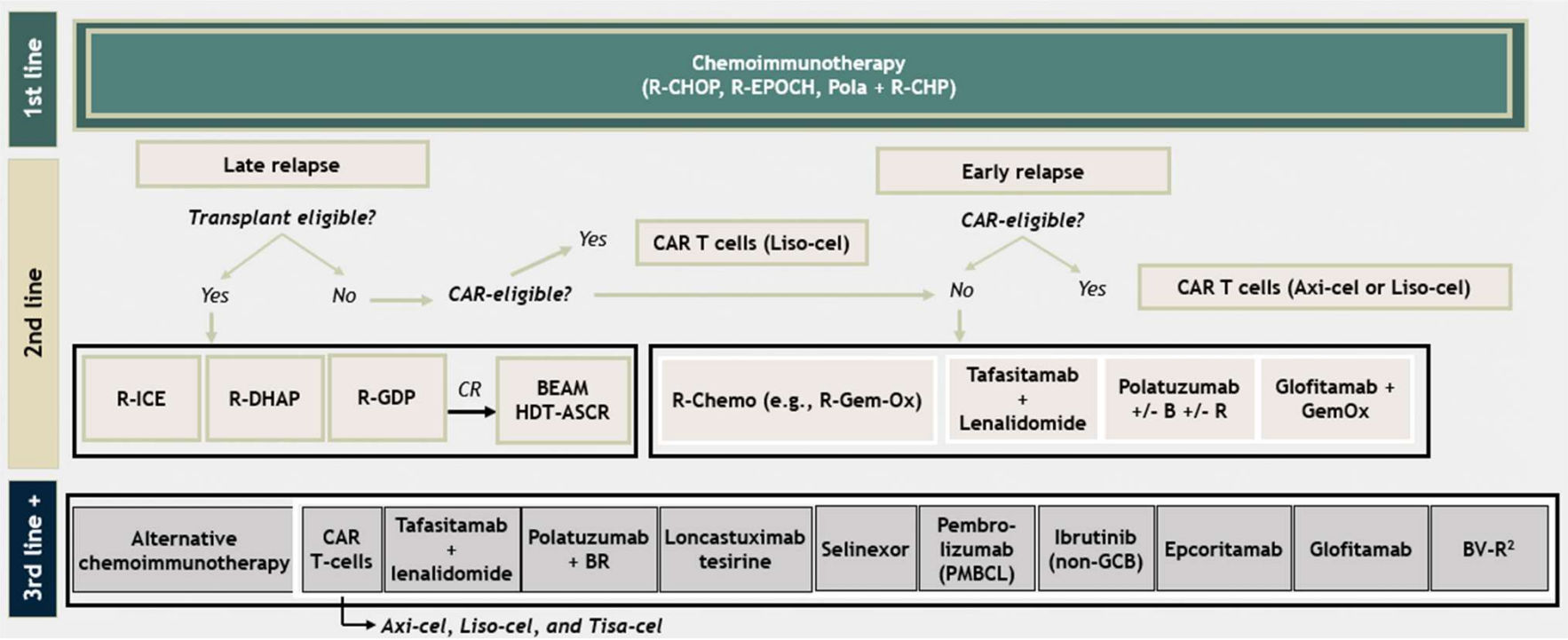




HDT = high-dose therapy; ASCR = autologous stem cell rescue; mFU = median follow-up; ECOG PS = Eastern Cooperative Oncology Group performance status; CrCl = creatinine clearance; DLCO = diffusing capacity of the lungs for carbon monoxide; LVEF = left ventricular ejection fraction; AESI = adverse event of special interest; CRS = cytokine release syndrome; NE = neurologic events.

Seghal A, et al. *Lancet Oncol*. 2022;23(8):1066-1077.

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# 2026 A New Flow



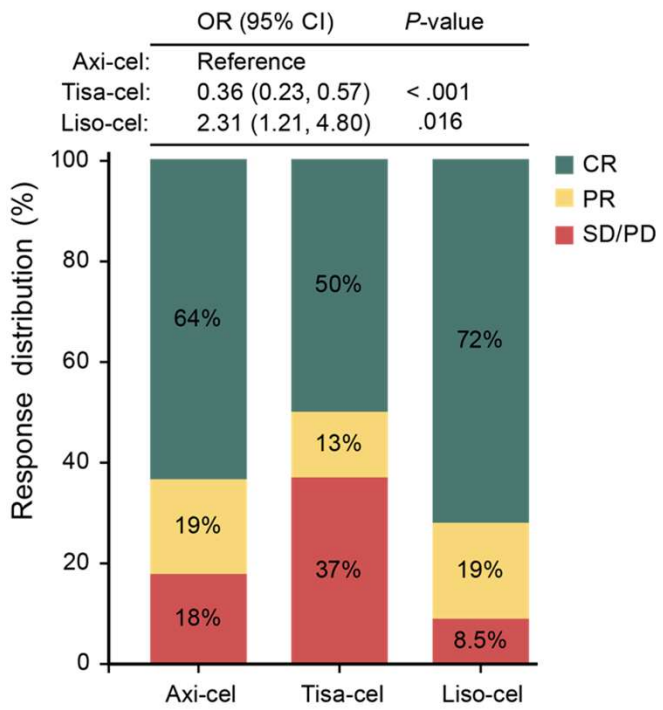

R-EPOCH = rituximab, etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin; R-ICE = rituximab, ifosfamide, carboplatin, etoposide; R-DHAP = rituximab, dexamethasone; high-dose cytarabine, cisplatin; R-GDP = rituximab, gemcitabine, dexamethasone, cisplatin; BEAM = carmustine, etoposide, cytarabine, melphalan; BR = bendamustine, rituximab; PMBCL = primary mediastinal B-cell lymphoma; BV = brentuximab vedotin.

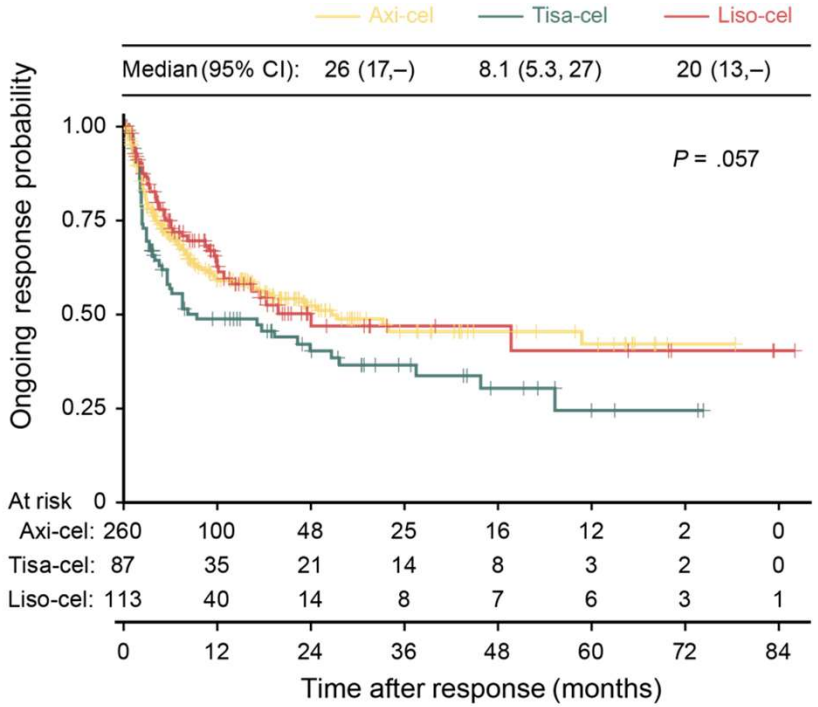
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# CAR T-Cell Therapies: Evidence Driving a New Standard in R/R DLBCL

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# Clinical Trials Get Therapies Approved, Then We Learn

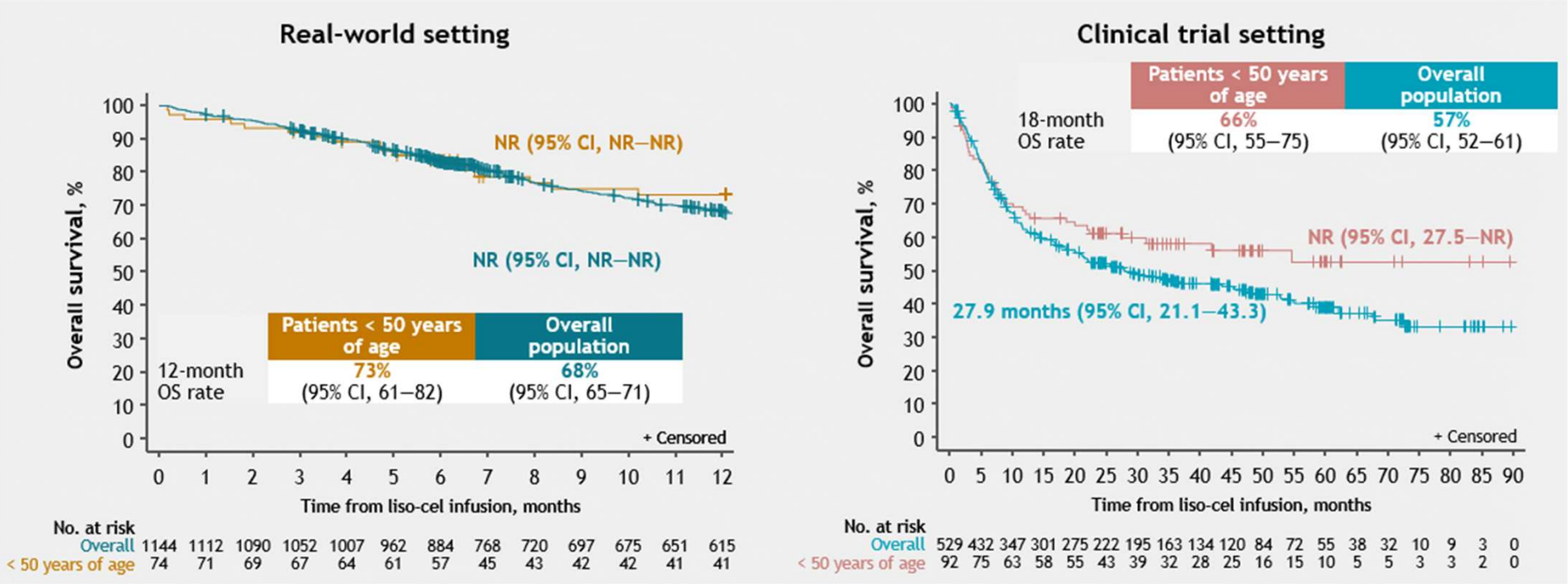



PR = partial response; SD = stable disease; PD = progressive disease.
Deschênes-Simard X, et al. *Blood Adv*. 2025;9(21):5571-5584.

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# Getting Rid of Age as a Barrier




NR = not reached.

Sheikh IN, et al. *Transplant Cell Ther*. 2026;32(2 Suppl):S166.

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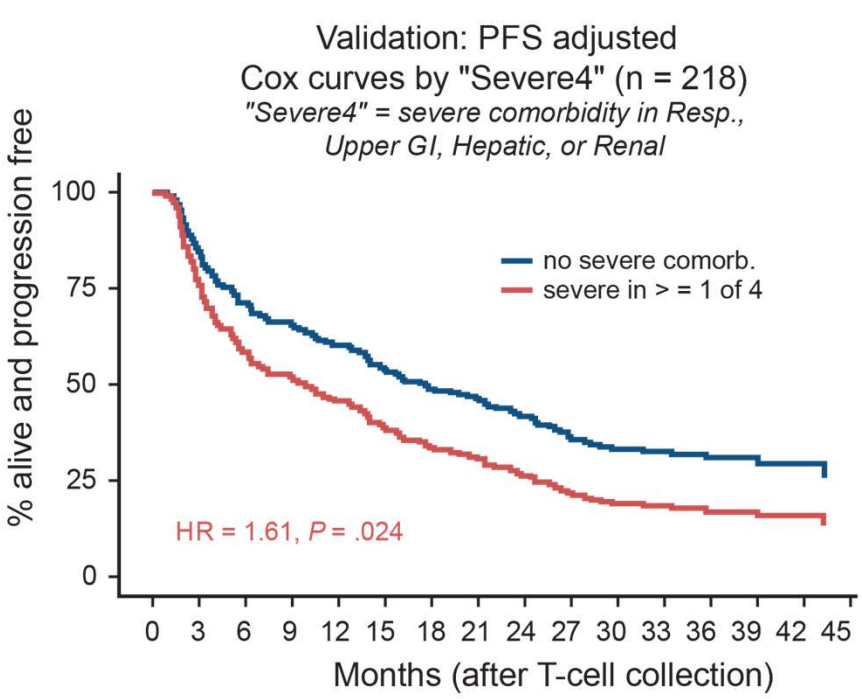
# Do Comorbidities Matter?

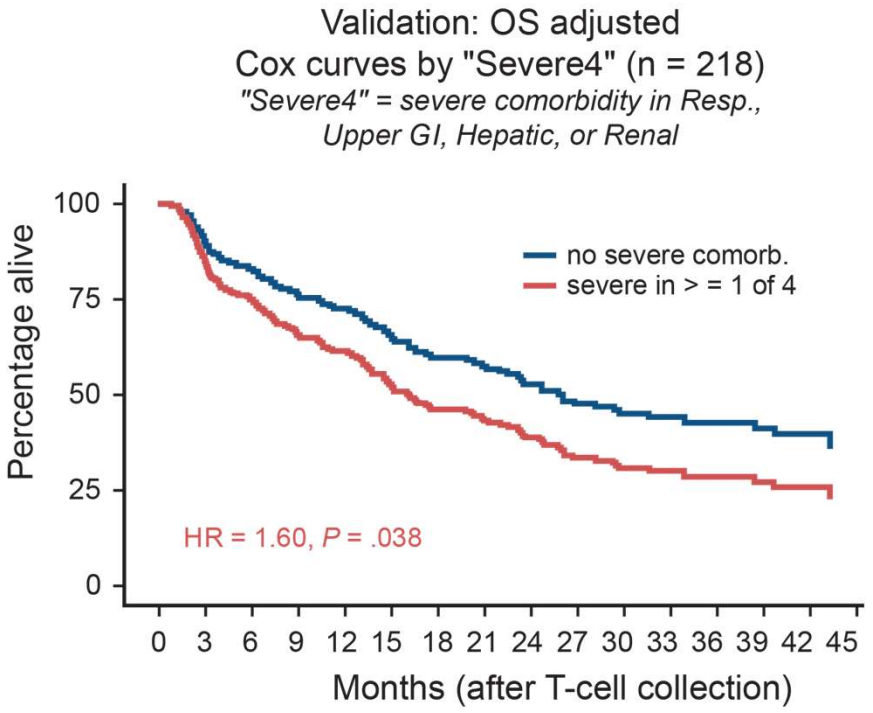
| Characteristics | PFS | | OS | |
|---|---|---|---|---|
| | HR (95% CI) | *P Value* | HR (95% CI) | *P Value* |
| **CIRS ≥7 or CIRS-3+** | 1.70 (0.94-3.06) | 0.08 | 2.39 (1.10-5.20) | 0.03 |
| **Age, 1-year increase** | 0.86 (0.96-1.06) | 0.15 | 0.82 (0.65-1.04) | 0.10 |
| **Previous therapy, 1-unit increase** | 0.87 (0.71-1.06) | 0.17 | 0.90 (0.71-1.13) | 0.35 |
| **ECOG PS, 1-unit increase** | 1.43 (0.99-2.05) | 0.05 | 1.63 (1.06-2.51) | 0.03 |
| **HGBL*** | 0.87 (0.46-1.63) | 0.66 | 0.97 (0.45-2.09) | 0.94 |
| **Complex cytogenetics*** | 1.15 (0.58-2.26) | 0.69 | 1.10 (0.45-2.67) | 0.84 |
| **GCB vs non-GCB*** | 0.99 (0.59-1.66) | 0.96 | 1.08 (0.58-2.02) | 0.81 |
| **Axi-cel vs Tisa-cel** | 0.60 (0.34-1.05) | 0.07 | 0.61 (0.31-1.20) | 0.15 |

CIRS = chronic inflammatory response syndrome; HGBL = high-grade B-cell lymphoma.
Kittai AS, et al. *Transplant Cell Ther*. 2021;27(1):46-52.

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# Which Comorbidities Matter



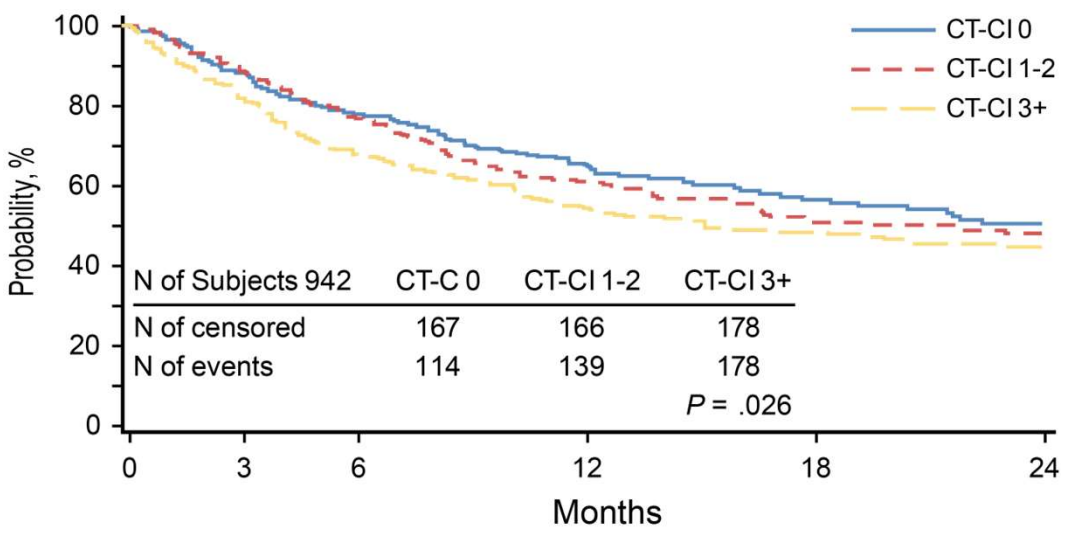




GI = gastrointestinal.
Shouse G, et al. *Blood Adv*. 2023;7(14):3516-3529.

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# Which Comorbidities Matter

| Comorbidity | N=951 | HR | Score |
|---|---|---|---|
| **Diabetes** | 139 | 1.20 | 1 |
| **History of cerebrovascular accident** | 25 | 1.17 | 1 |
| **Body mass index <20** | 70 | 1.39 | 1 |
| **Pulmonary disease, severe** | 116 | 1.28 | 1 |
| **Renal disease, moderate to severe** | 18 | 1.27 | 1 |
| **Hepatic disease, mild** | 80 | 1.48 | 1 |
| **Infection requiring therapy at infusion** | 32 | 1.95 | 2 |
| **Hepatic disease, moderate to severe** | 19 | 3.84 | 3 |

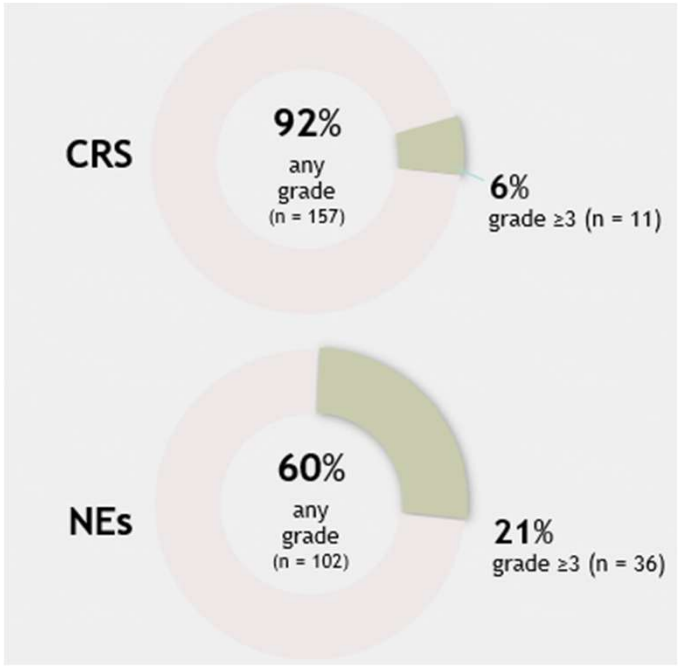



Greenbaum U, et al. *Blood Adv*. 2026;10(1):217-227.

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# Short of a CAR vs CAR Trial: Toxicity Matters

ZUMA-7



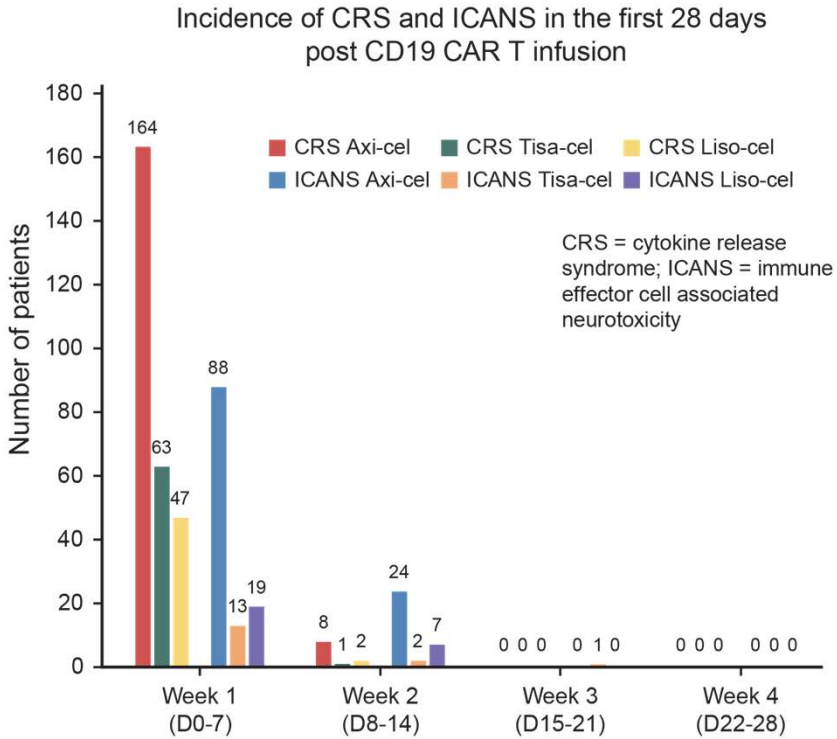

TRANSFORM




Locke FL, et al. *N Engl J Med*. 2022;386(7):640-654. Kamdar M, et al. *Lancet*. 2022;399(10343);2294-2308.

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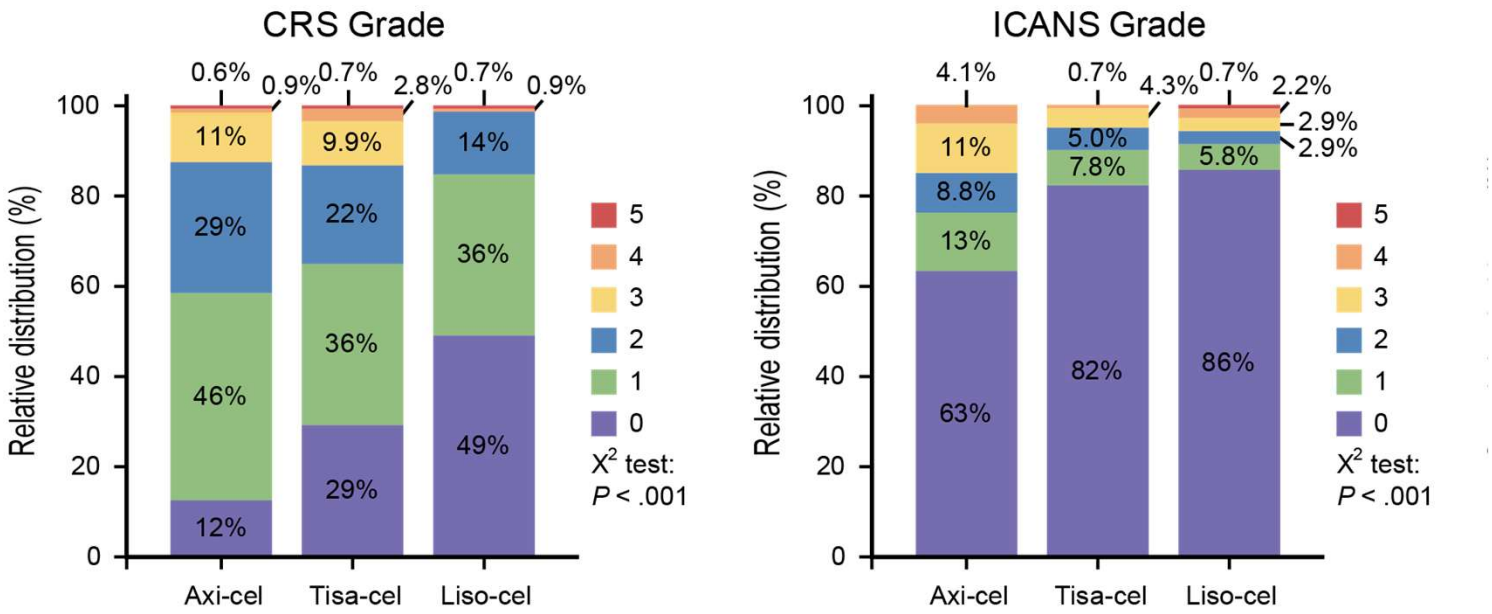
# When Is All the Excitement?




ICANS = immune effector cell-associated neurotoxicity syndrome.
Ahmed N, et al. *Blood Adv*. 2024;8(20):5346-5354.

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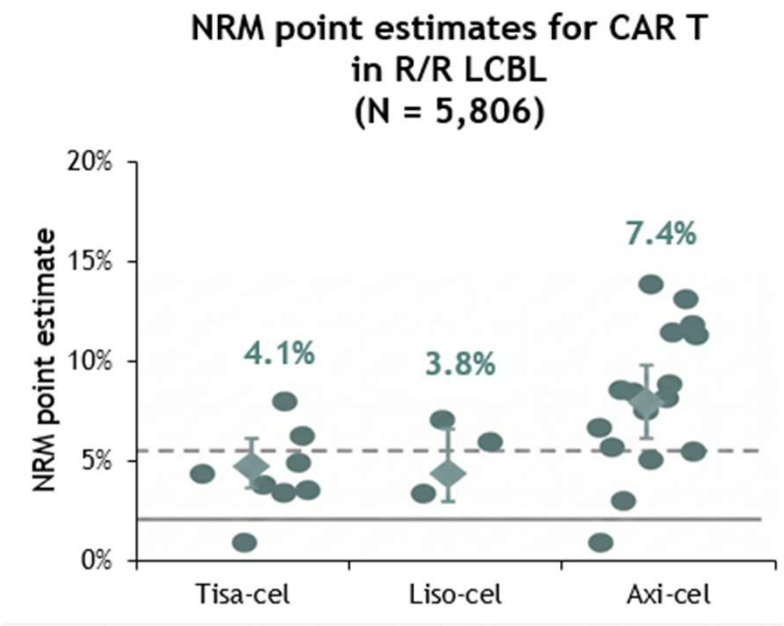
# Where Is All the Excitement?

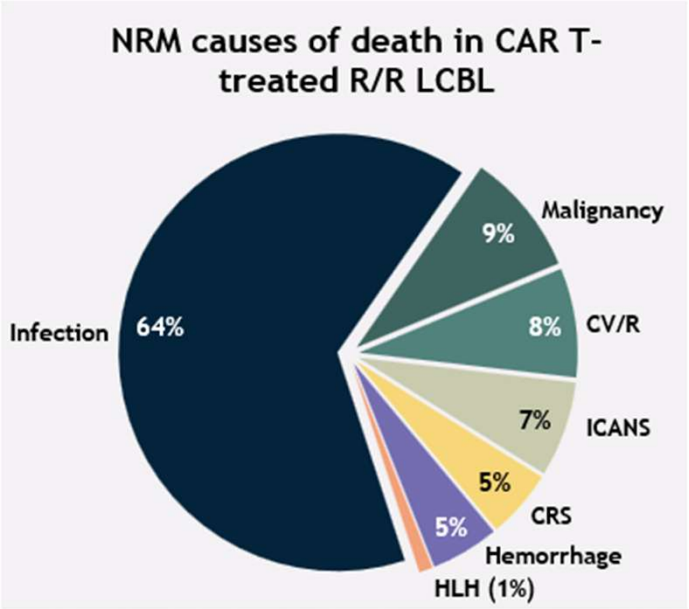



Deschênes-Simard X, et al. *Blood Adv*. 2025;9(21):5571-5584.

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# Where Is the Trouble—Non-Relapse Mortality?



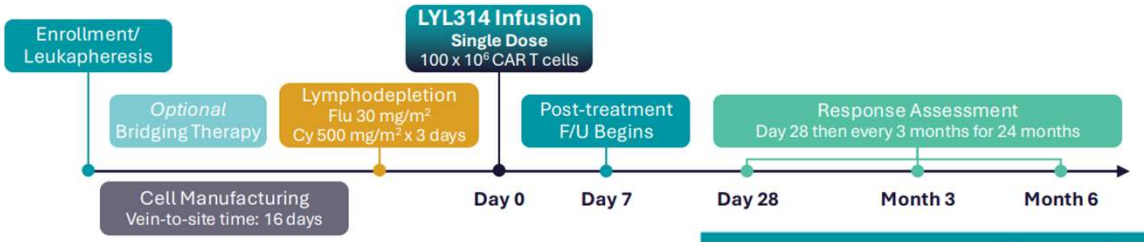

NRM = non-relapse mortality.
Cordas dos Santos DM, et al. *Nat Med*. 2024;30(9):2667-2678.

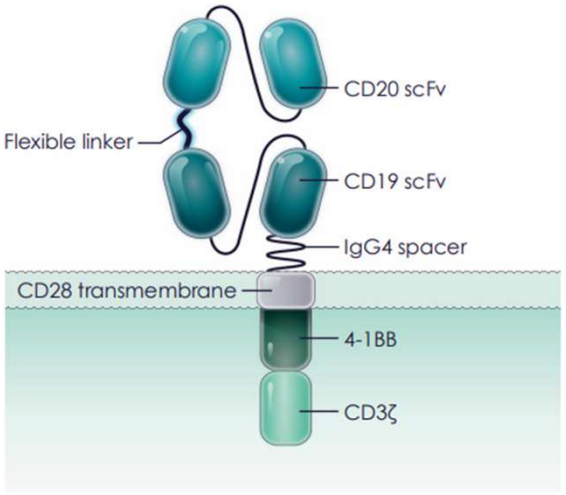
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# On the Horizon

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# What's Coming…Ronde-Cel




CD62L selected

| Characteristics | 3L+ N = 34 | 2L N = 17 |
|---|---|---|
| Median (range) age, years | 65 (21, 87) | 69 (44, 85) |
| ≥ 65 years, n (%) | 18 (53%) | 12 (71%) |
| ≥ 75 years, n (%) | 7 (21%) | 6 (35%) |
| Male, n (%) | 23 (68%) | 10 (59%) |
| White, n (%) | 24 (71%) | 10 (59%) |
| ECOG 1, n (%) | 24 (71%) | 12 (71%) |
| IPI score 3 or 4, n (%) | 13 (38%) | 8 (47%) |
| Stage IV disease at study entry, n (%) | 14 (41%) | 11 (65%) |
| LBCL histology n (%) | | |
| DLBCL | 21 (62%) | 10 (59%) |
| HGBCL | 4 (12%) | 2 (12%) |
| tFL | 5 (15%) | 3 (18%) |
| Primary refractory, n (%) | 16 (47%) | 14 (82%) |
| Elevated (above normal) LDH, n (%) | 16 (47%) | 5 (29%) |
| Median lines of prior therapy (range) | 2 (2-6) | 1 |
| Bulky disease (≥ 5 cm), n (%) | 8 (24%) | 6 (35%) |
| Median SPD (range) cm² | 13 (1.5-180.1) | 17 (4.5-92.8) |
| Double-/triple-hit status, n (%) | 5 (15%) | 5 (29%) |
| Received bridging therapy, n (%) | 18 (53%) | 9 (53%) |

scFv = single-chain variable fragment; tFL = transformed FL; LDH = lactate dehydrogenase; SPD = sum of products of diameters.
Merchant A, et al. Presented at: 19th International Conference on Malignant Lymphoma (ICML); 2025.

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# What's Coming…Ronde-Cel

| Best Overall Response (3L+) | N = 25 |
|---|---|
| **Overall Responses, n (%)** | **22 (88%)** |
| **Complete Responses, n (%)** | **18 (72%)** |
| Partial Response, n (%) | 4 (16%) |
| Stable Disease, n (%) | 1 (4%) |
| Median follow up, months (maximum) | 9 (17) |
| Median duration of response | Not reached |

| Best Overall Response (2L) | N = 11 |
|---|---|
| **Overall Responses, n (%)** | **10 (91%)** |
| **Complete Responses, n (%)** | **7 (64%)** |
| Partial Response, n (%) | 3 (27%) |
| Stable Disease, n (%) | 1 (9%) |
| Median follow up, months (maximum) | 5 (10) |
| Median duration of response | Not reached |

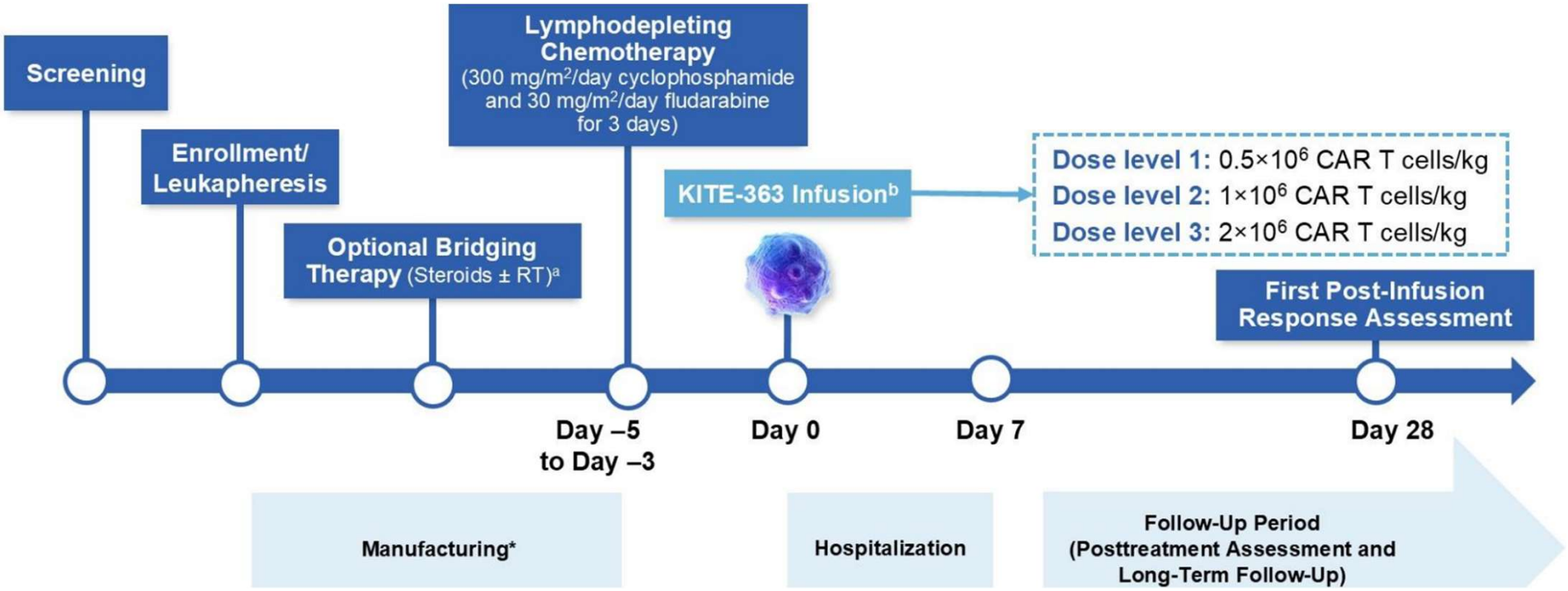
| Adverse Event, n (%) | N = 51 |
|---|---|
| **CRS** | |
| Grade 1 | 11 (22%) |
| Grade 2 | 18 (35%) |
| Grade ≥ 3 | 0 (0%) |
| Median time to onset, days (range) | 4 (1-13) |
| Median time to resolution, days (range) | 3 (1-8) |

| Adverse Event, n (%) | N = 51 |
|---|---|
| **ICANS** | |
| Grade 1 | 3 (6%) |
| Grade 2 | 1 (2%) |
| Grade ≥ 3 | 7 (14%) |
| Median time to onset, days (range) | 7 (4-11) |
| Median time to resolution, days (range) | 5 (2-10) |
| Median time to resolution to Grade < 3, days (range) | 2 (1-4) |

Merchant A, et al. Presented at: 19th International Conference on Malignant Lymphoma (ICML); 2025.

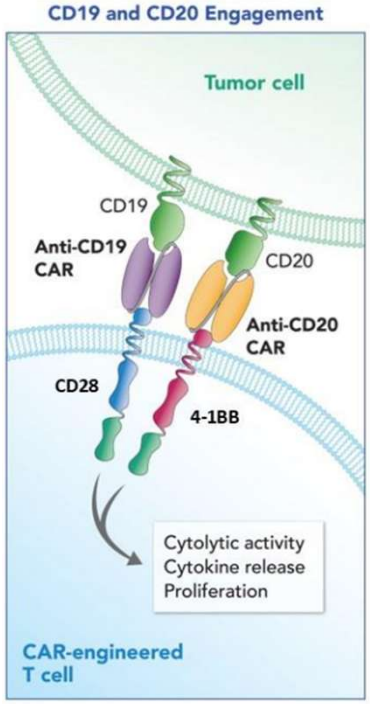
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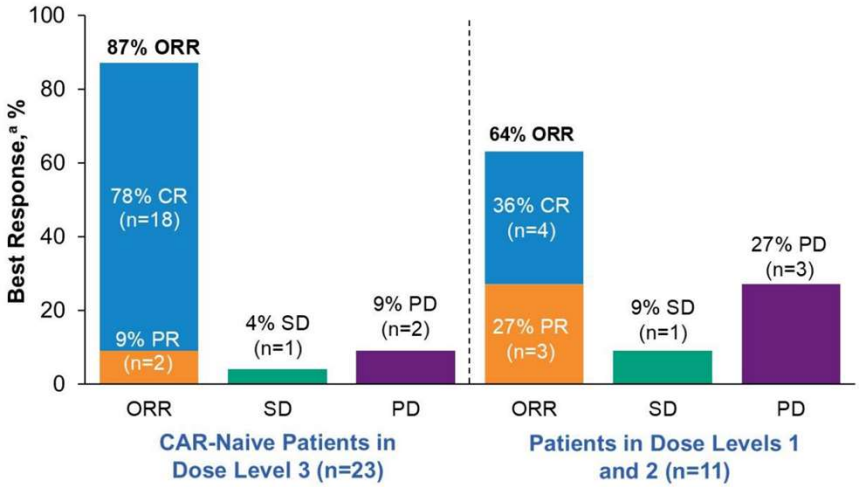
# What's Coming…KITE-363



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# What's Coming…KITE-363



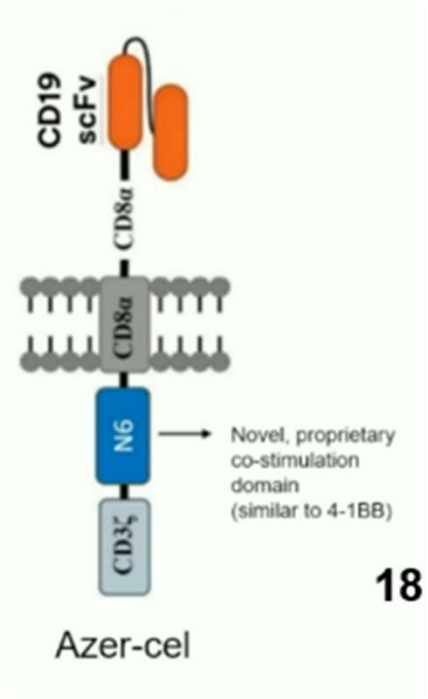




| Parameter | Dose Levels 1 & 2 (N=11) CRS | Dose Levels 1 & 2 (N=11) ICANS | Dose Level 3 (N=26) CRS | Dose Level 3 (N=26) ICANS |
|---|---|---|---|---|
| **Any grade, n (%)[a]** | 7 (64) | 1 (9) | 24 (92) | 12 (46) |
| Grade 1/2 | 7 (64) | 0 | 23 (88) | 10 (38) |
| Grade 3 | 0 | 1 (9) | 1 (4) | 2 (8) |
| Grade 4 | 0 | 0 | 0 | 0 |
| Grade 5 | 0 | 0 | 0 | 0 |
| **Median time to onset (range), days** | 6 (2-8) | 6 (6-6) | 3.5 (2-9) | 6.0 (2-13) |
| **Median duration of event (range), days** | 3 (1-10) | 6 (6-6) | 5.0 (2-11) | 4.5 (1-13) |
| **AE management, n (%)** | | | | |
| Tocilizumab | 5 (45) | 0 | 23 (88) | 0 |
| Corticosteroids | 3 (27) | 1 (9) | 17 (65) | 10 (38) |
| Anakinra | 0 | 1 (9) | 1 (4) | 4 (15) |

AE = adverse event.
Dahiya S, et al. *J Clin Oncol*. 2025;43(16 Suppl):7003.

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# Azer-Cel + IL-2




- AAV vector-based allo CAR 19 (TRAC locus)
- Expansion cohort w/low dose IL-2 (1M IU d1-14)
  - DLBCL:
    - 2 or more lines
    - relapsed after autologous CD19 CAR T
- Primary objective: ORR | Secondary objectives: CRR, DOR, PFS, OS, Safety
- Conditioning: Flu 30mg/m$^2$ x 3 and Cy 750mg/m$^2$ x 3

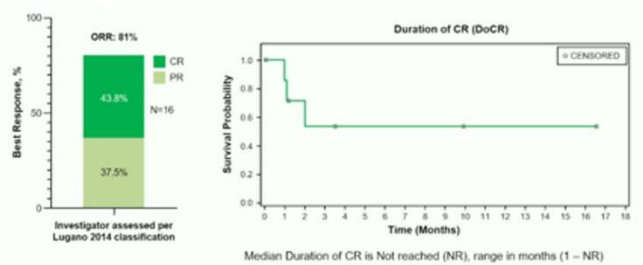
**18 DLBCL pts (11 *de novo*, 3 T-FL, 4 other)**

- **Median LOT = 4 (CAR T: 100%, BsAb: 44%)**
- **Response to auto CAR T < 6 months: 11 (61%)**

AAV = adeno-associated virus; CRR = complete response rate; DOR = duration of response; LOT = line of therapy; BsAb = bispecific antibody.
Gupta S, te al. *Blood*. 2025;146(Suppl 1):267.

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# Azer-Cel + IL-2




- **Azer-cel peak D+7 to 14**
- **Azer-cel observed beyond day 180**
- **MRD undetectable in 4/5 patients in CR**
- **<u>Safety</u>**
  - **Hematologic toxicity (100% G3+)**
  - **33% G3+ infections**
  - **CRS: 13 (72%) G1-2, no G3+**
  - **ICANS: 3 (17%) G1-2, 2 grade 3**

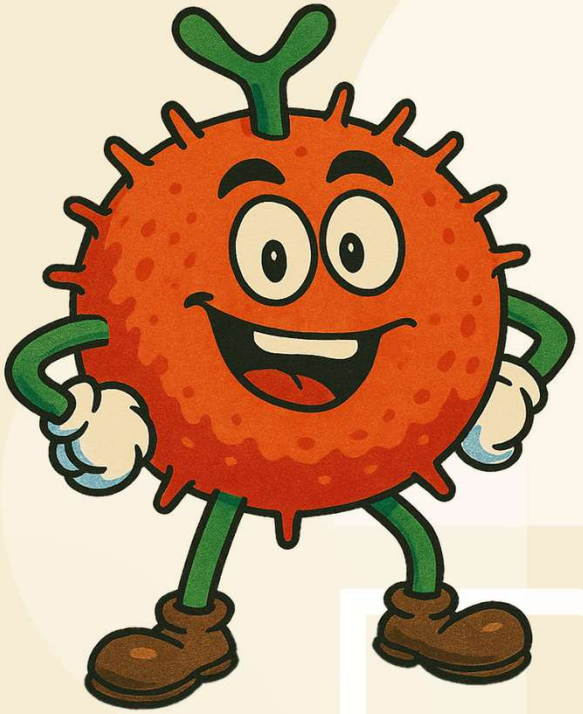
MRD = measurable residual disease.
Gupta S, te al. *Blood*. 2025;146(Suppl 1):267.

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# Integrating CAR T into Clinical Practice

**Samuel Yamshon, MD**

*Perlmutter Cancer Center*
*NYU Langone Health*
*New York City, New York*



# CAR T Is Very Effective in the Second Line…

## ZUMA-7

**axi-cel**

**HR 0.40** event-free survival vs salvage chemo + ASCT

- Bridging: steroids only
- Overall survival benefit (HR 0.73)

## TRANSFORM

**liso-cel**

**HR 0.38** event-free survival vs salvage chemo + ASCT

- Bridging chemotherapy allowed (63%)
- 3-year OS 63% vs 52%, despite crossover

ASCT = autologous stem cell transplantation.

Locke FL, et al. *N Engl J Med*. 2022; 386(7):640-654. Westin JR, et al. *N Engl J Med*. 2023;389(2):148-157. Kamdar M, et al. Lancet. 2022; Kamdar M, et al. *J Clin Oncol*. 2025;43(24):2671-2678.

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# …But Most Eligible Patients Never Get CAR T



**2 in 10**
receive CAR T

**8 in 10**
do not

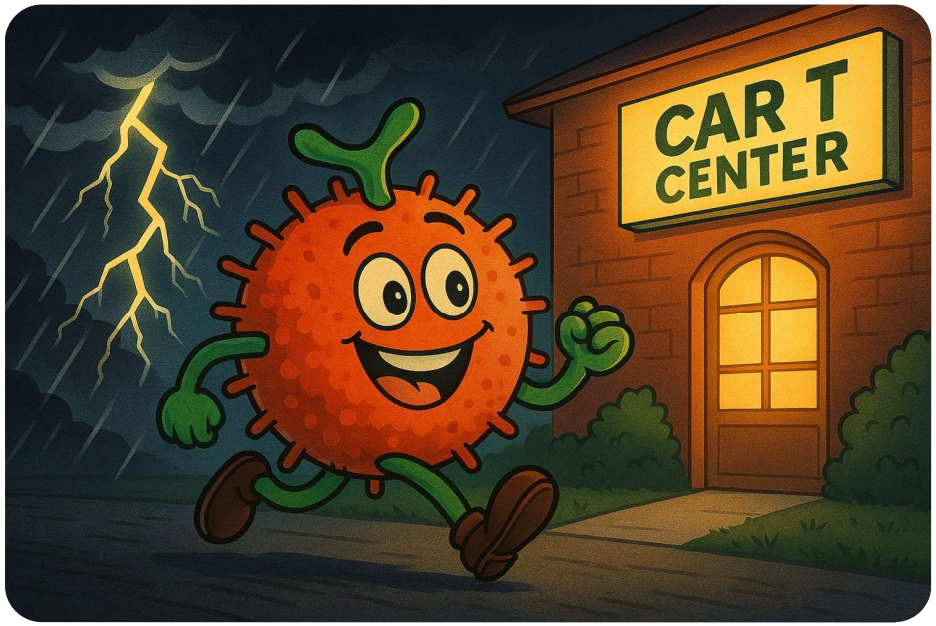
**Never referred**
never discussed, or assumed ineligible

**Referred too late**
the disease outpaced the process

**Couldn't get there**
distance, caregiver, coverage

Hoffmann MS, et al. *Transplant Cell Ther*. 2023;29(7):440-448.

# How Do Patients Get to a CAR T Center?




## Five things stand in the way

**Late referral**
after several lines, when disease is moving fast

**Assumed ineligibility**
age, comorbidity, "too frail"

**Distance**
travel and weeks away from home

**Caregiver**
someone who can be there around the clock

**Cost and coverage**
authorization, lodging, lost income

Hoffmann MS, et al. *Transplant Cell Ther*. 2023;29(7):440-448.

# A Critical Gap: How We Interpret Eligibility

| | Common perception at referral | | How a CAR T center sees it |
|---|---|---|---|
| **Age** | Under 75, sometimes under 65 | → | **No upper limit** |
| **Comorbidities** | Ineligible | → | **Optimize, co-manage, treat through** |
| **Performance status** | ECOG 0-1 | → | **ECOG 0-3** |
| **Disease** | Only the highest-risk relapse | → | **Any eligible relapse** |
| **Timing** | After other options have failed | → | **As early as eligible** |
| **Social support** | Only with ideal support in place | → | **Help build a caregiver plan** |

ECOG = Eastern Cooperative Oncology Group.
Adapted from Hoffmann MS, et al. *Transplant Cell Ther.* 2023;29(7):440-448. Shadman M, et al. *Transplant Cell Ther*. 2026;32(3):277-287.

# Transplant-Ineligible ≠ CAR T-Ineligible

**PILOT** enrolled patients with at least one of:

- **Age ≥70**
- **ECOG PS 2**
- **CrCl <60 mL/min**
- **DLCO ≤60%**
- **LVEF <50%**
- **AST/ALT >2× ULN**

Second-line liso-cel, no transplant planned

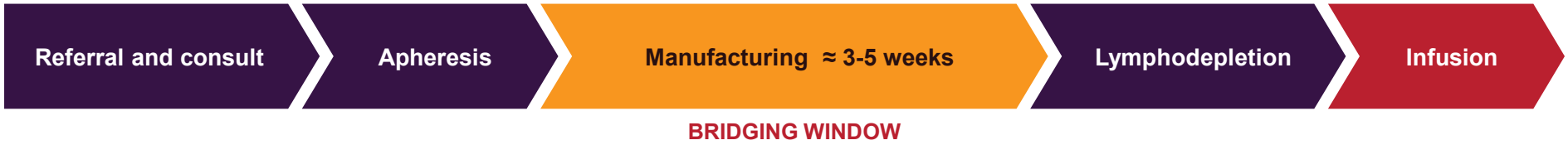
| 74 | 80% | 54% |
|---|---|---|
| median age years | overall response | complete response |

**Same signal elsewhere:** ALYCANTE (axi-cel) and real-world registries in older adults

CrCl = creatinine clearance; LVEF = left ventricular ejection fraction; PS = performance status; DLCO = diffusing capacity of the lungs for carbon monoxide; AST = aspartate transaminase; ALT = alanine transaminase; ULN = upper limit of normal.

Sehgal A, et al. *Lancet Oncol*. 2022;23(8):1066-1077. Sehgal A, et al. *Blood Adv*. 2025;9(15):3694-3705. Houot R, et al. *Nat Med*. 2023;29(10):2593-2601. Chihara D, et al. *Blood*. 2023;142(12):1047-1055.

# Bridging: Hold the Disease, Protect the T Cells




## Collect first

Apheresis before T cell-toxic therapy such as bendamustine

## Control, not cure

The goal is a stable, fit patient on infusion day

## Tailor the bridge

Steroids, chemoimmunotherapy, radiation, targeted agents

Locke FL, et al. *N Engl J Med*. 2022;386(7):640-654. Kamdar M, et al. *Lancet*. 2022;399(10343):2294-2308. Iacoboni G, et al. *J Clin Oncol*. 2024;42(2):205-217.

# Logistical Requirements for CAR T Have Eased

**June 2025:** FDA removed REMS for all approved CD19- and BCMA-directed autologous CAR T-cell therapies

**Stay near the treatment center**

4 → **2** weeks

**24-hour caregiver**

4 → **2** weeks

**No driving**

8 → **2** weeks

**REMS certification and tocilizumab stocking**

~~Required~~

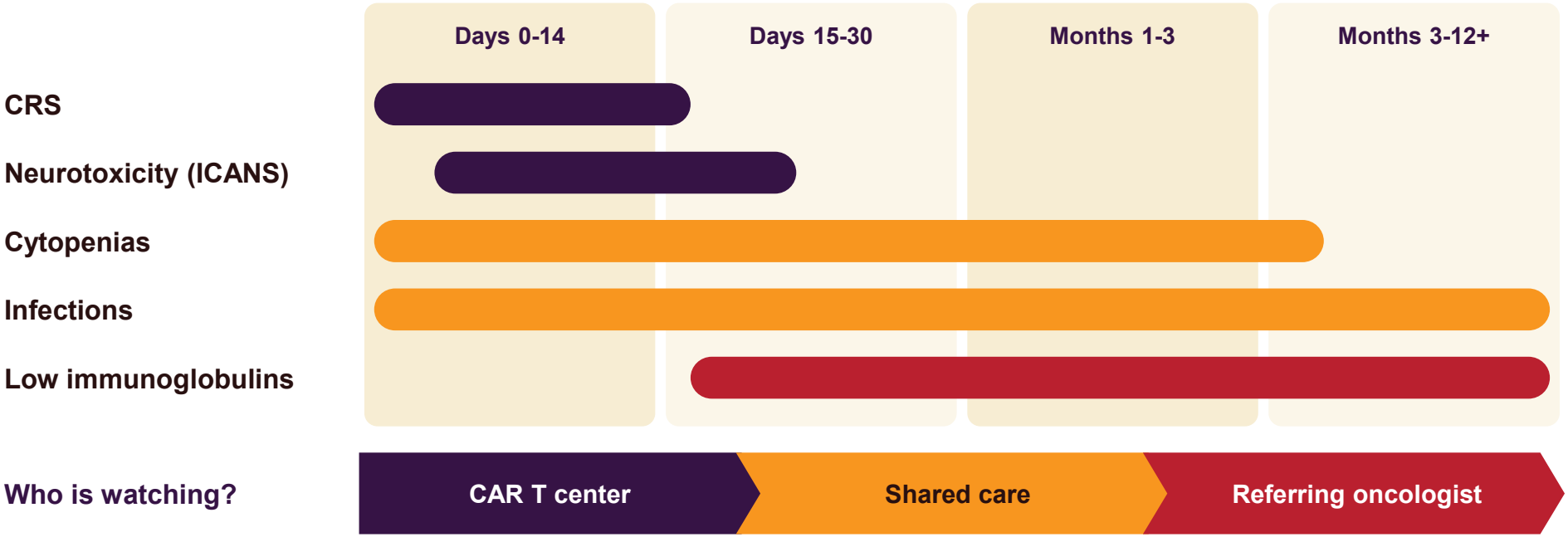
**Removed**

**REMS is gone. The toxicities, and the need for a trained team, are not.**

REMS = Risk Evaluation and Mitigation Strategies.

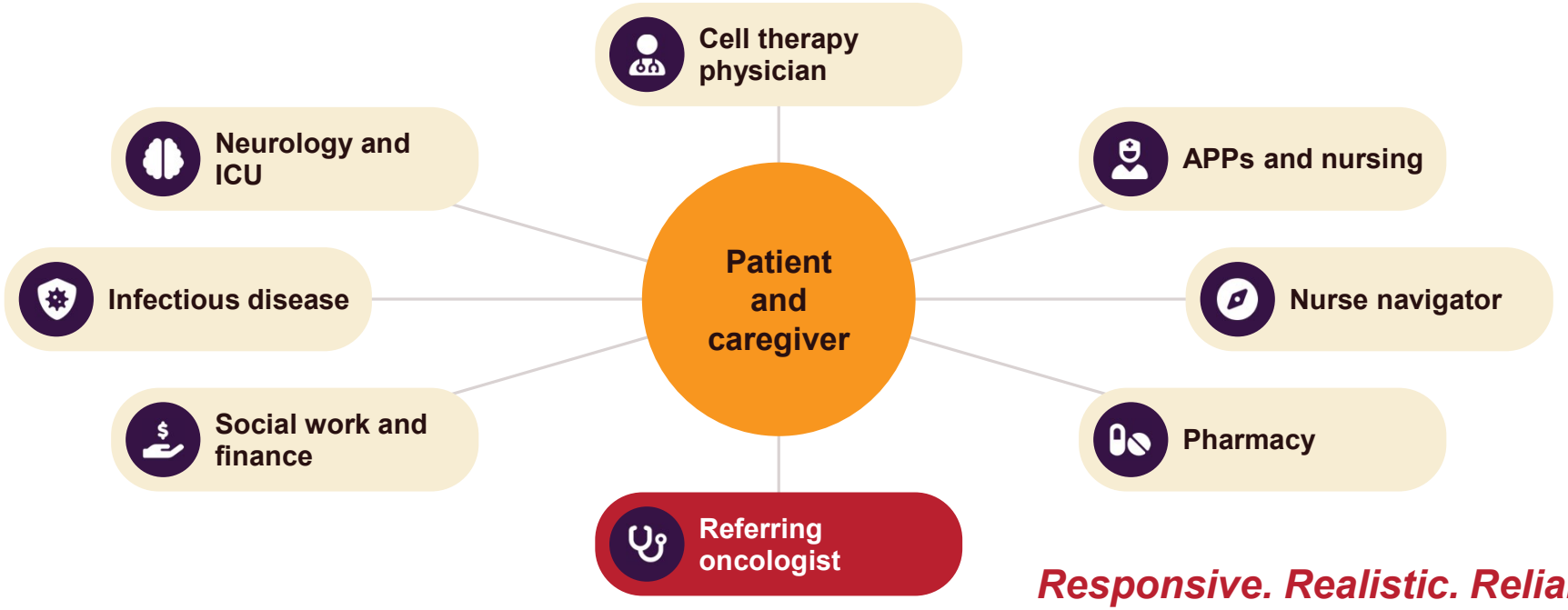
US Food and Drug Administration (FDA) [www.fda.gov]. Last updated June 27, 2025. https://www.fda.gov/news-events/press-announcements/fda-eliminates-risk-evaluation-and-mitigation-strategies-rems-autologous-chimeric-antigen-receptor

# CAR T Is a Team Sport




Adapted from Hill JA, Seo SK. *Blood*. 2020;136(8):925-935. Jain T, et al. *Blood*. 2023;141(20):2460-2469.

# CAR T Is a Team Sport




***Responsive. Realistic. Reliable.***

ICU = intensive care unit; APP = advanced practice provider.

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PATIENT-CENTERED CARE

# What Matters to ***the Patient in Front of You***?

- **Is cure the goal?**
- **Who can stay with me?**
- **How far is the center?**
- **One treatment, or ongoing?**

## CAR T

one-time infusion

- Longest track record for cure
- Intense first month: CRS, ICANS
- Needs a treatment center and a caregiver

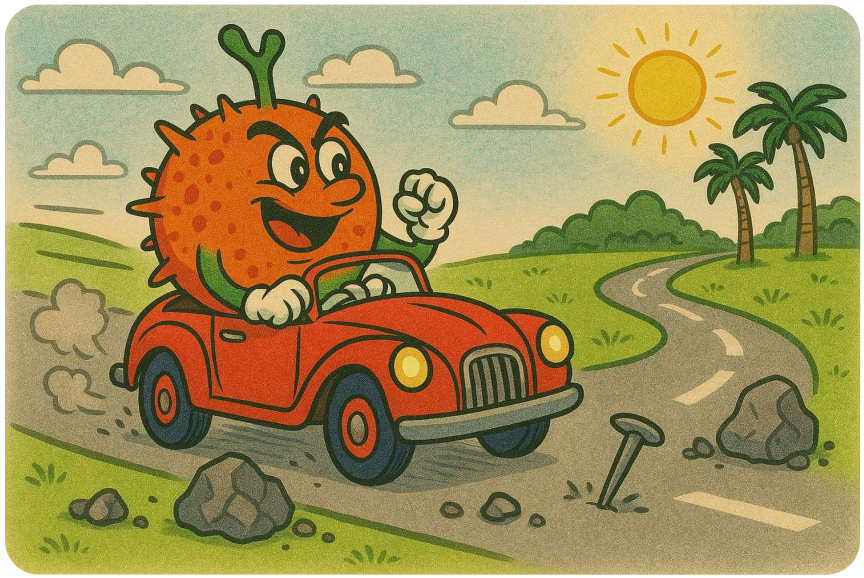
## Bispecific antibody

off the shelf, repeated dosing

- Durability still maturing
- Gentler start, many more visits
- Closer to home, ongoing infection risk

**Both are good options. The right one depends on the person in front of you.**

# The Journey Does Not End with Remission



## What should travel home with the patient

- Infection prophylaxis plan
- Thresholds for IVIG, growth factor, transfusion
- Revaccination schedule
- Scan and visit calendar

IVIG = intravenous immunoglobulin.

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# Key Learning Points



1. **Refer at first relapse**
   A referral is a conversation, not a commitment.

2. **Assume eligible until the CAR T center says otherwise**
   Age and comorbidity rarely rule it out on their own.

3. **Plan the bridge and the handoff up front**
   After REMS, more of the journey happens close to home.

4. **Let the patient's priorities steer the choice**
   Caregiver, distance, and goals are clinical data.

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# Discussion and Q&A