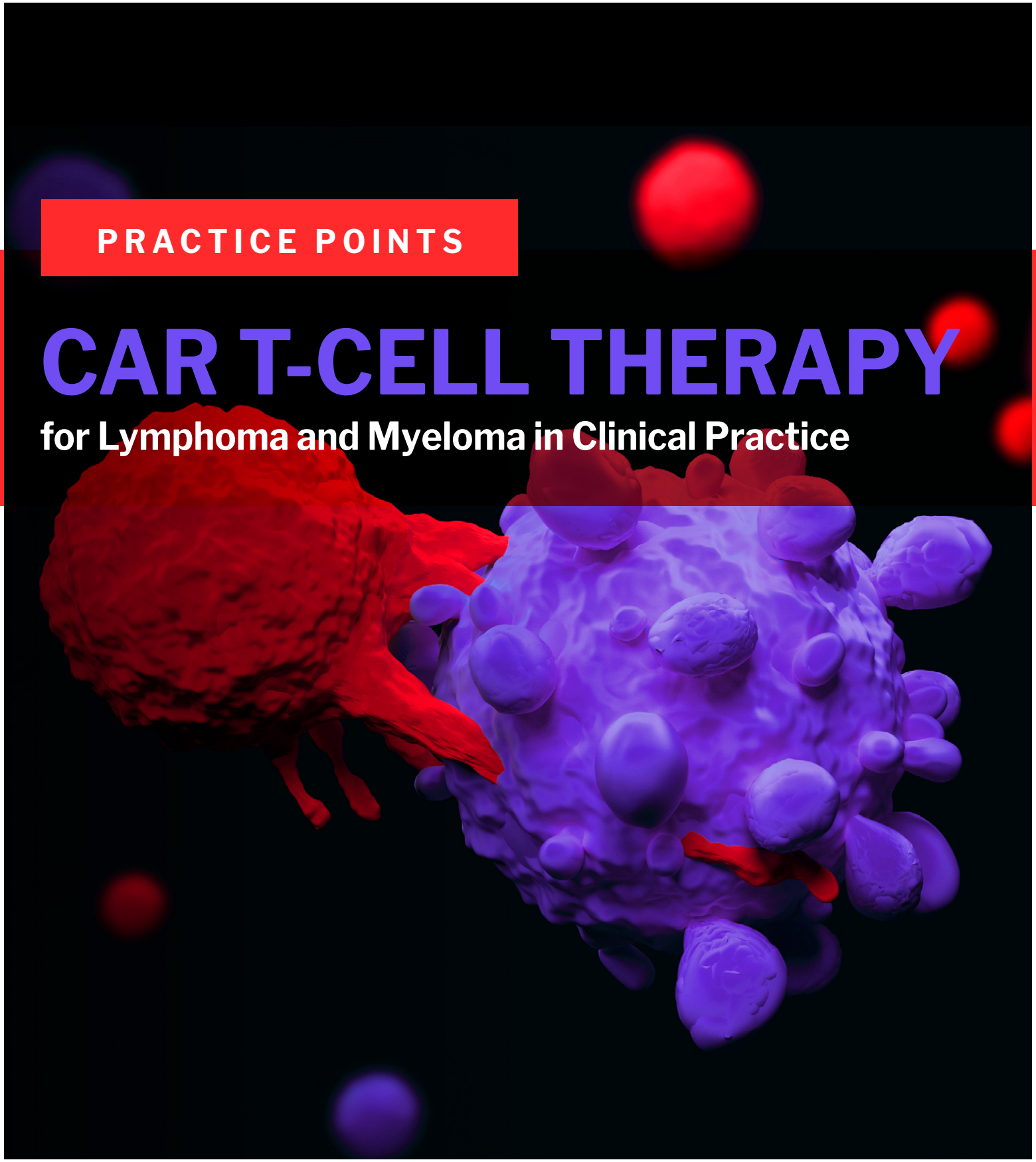
PRACTICE POINTS

CAR T-CELL THERAPY

for Lymphoma and Myeloma in Clinical Practice



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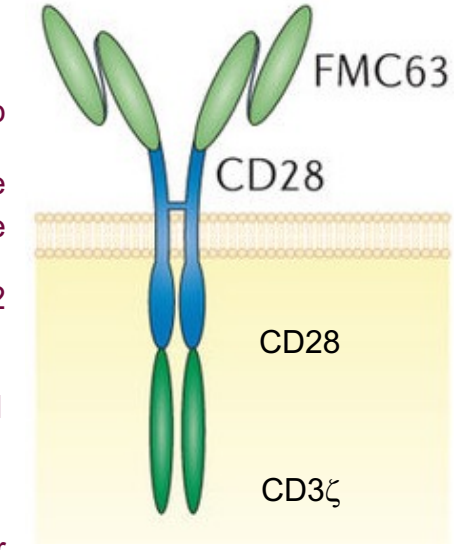
Axicabtagene Ciloleucel



FDA Approved

- R/R large B-cell lymphoma after 2 or more lines of systemic therapy including (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high-grade B-cell lymphoma, and DLBCL arising from follicular lymphoma (FL)
- R/R follicular lymphoma after 2 or more lines of systemic therapy
- Not indicated for the treatment of patients with primary central nervous system lymphoma

Study	ZUMA 1
CAR T-cell dose	2×10^6/kg
Conditioning therapy	Cy/Flu
Lymphoma subtypes	DLBCL /PMBCL/TFL
Treated/enrolled	101/111 (91%)
Relapsed/refractory	Refractory
Relapse post-ASCT	21%
Bridging therapy	None
Manufacturing success	99%
ORR/CR (%)	82/54

SAFETY

CRS All Grades	CRS Grade ≥3	NT All Grades	NT Grade ≥3
93%	13%	64%	28%

R/R: relapsed/refractory; DLBCL: diffuse large B-cell lymphoma; CAR T-cell dose: chimeric antigen receptor; CR: complete response; NT: neurotoxicity; CRS: cytokine release syndrome

YESCARTA. Prescribing information. Kite Pharma, Inc.; 2021. Neelapu SS, Locke FL, Bartlett NL, et al. Axicabtagene Ciloleucel CAR T-Cell Therapy in Refractory Large B-Cell Lymphoma. *N Engl J Med* 2017;377(26):2531-2544. van der Stegen S, Hamieh M, Sadelain M. The Pharmacology of Second-Generation Chimeric Antigen Receptors. *Nat Rev Drug Discov*. 2015;14(7):499-509.

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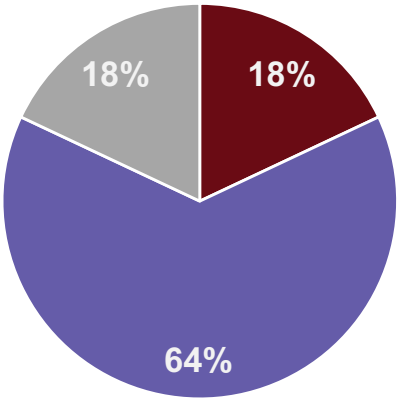
Axi-Cel in Clinical Practice

Response to SOC Axi-Cel Treatment



82% ORR

PR
CR
SD/PD

- Median time to response was 30 days, and no patients achieved a first response beyond day 90
- The majority of patients who achieved a CR (n = 121) at day 30 remained in CR at day 90 (78%)
- Among the 93 patients with a partial response (PR) at day 30, 32% improved to a CR at day 90, and even 1 (7%) of 14 patients with stable disease at day 30 improved to a CR at day 90

SAFETY

	SOC axi-cel N=275	ZUMA 1 N=108
All grade CRS	91%	93%
Grade ≥3	7%	13%
Median time to onset	3 days	2 days
All grade neurotoxicity	69%	65%
Grade ≥3	31%	31%
Median time to onset	6 days	5 days
Median hospital stay	14 days	NA
ICU stay	33%	NA
Tocilizumab use	62%	45%
Corticosteroid use	54%	29%

SD/PD: stable disease/progressive disease

Nastoupil L, Jain M, Feng L, et al. Standard-of-Care Axicabtagene Ciloleucel for Relapsed or Refractory Large B-Cell Lymphoma: Results From the US Lymphoma CAR T Consortium. *J Clin Oncol.* 2020;38(27):3119-3128.

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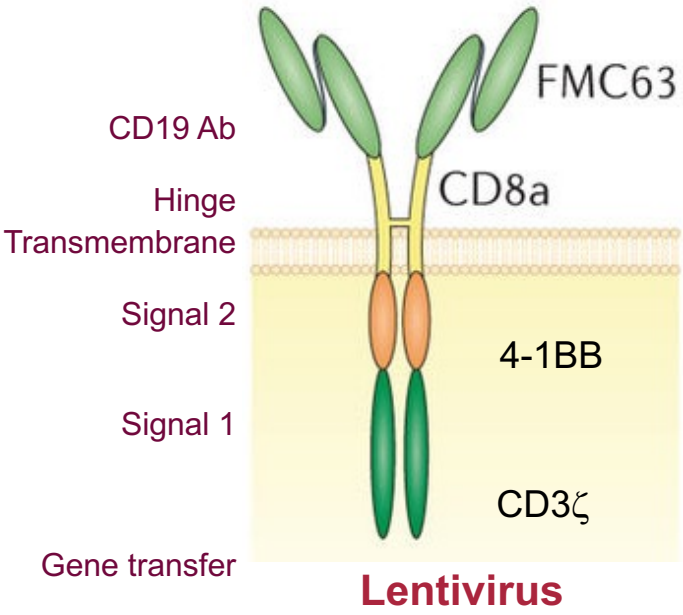
Tisagenlecleucel



FDA Approved

- Patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse
- R/R large B-cell lymphoma after 2 or more lines of systemic therapy including DLBCL not otherwise specified, high-grade B-cell lymphoma and DLBCL arising from FL
- Not indicated for treatment of patients with primary central nervous system lymphoma

Study	JULIET
CAR T-cell dose	0.6-6×10^8
Conditioning therapy	Cy/Flu or Bendamustine
Lymphoma subtypes	DLBCL/TFL
Treated/enrolled	111/165 (67%)
Relapsed/refractory	Relapsed or refractory
Relapse post-ASCT	49%
Bridging therapy	Allowed
Manufacturing success	93%
ORR/CR (%)	52/40

SAFETY

N	CRS All Grades	CRS Grade ≥3	NT All Grades	NT Grade ≥3
111	58%	22%	21%	12%

KYMRIAH. Prescribing information. Novartis Pharmaceuticals Corporation; 2021. Schuster SJ, Bishop MR, Tam CS, et al. Tisagenlecleucel in Adult Relapsed or Refractory Diffuse Large B-Cell Lymphoma. *N Engl J Med.* 2018;380(1):45-56. van der Stegen S, Hamieh M, Sadelain M. The pharmacology of second-generation chimeric antigen receptors. *Nat Rev Drug Discov*. 2015;14(7):499-509.

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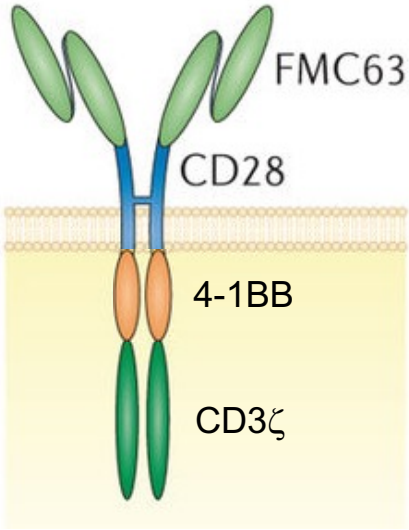
Lisocabtagene Maraleucel



FDA Approved

- Adult patients with relapsed or refractory large B-cell lymphoma after 2 or more lines of systemic therapy, including DLBCL not otherwise specified (including DLBCL arising from indolent lymphoma), high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and FL grade 3B
- Not indicated for the treatment of patients with primary central nervous system lymphoma

Study	TRANSCEND
CAR T-cell dose	$0.5\text{-}1.5\times10^6$
Conditioning therapy	Cy/Flu
Lymphoma subtypes	DLBCL/PMBCL/TFL/FL Grade 3B
Treated/enrolled	269/344 (78%)
Relapsed/refractory	Relapsed or refractory
Relapse post-ASCT	33%
Bridging therapy	Allowed
Manufacturing success	99%
ORR/CR (%)	73/53

SAFETY

N	CRS All Grades	CRS Grade ≥3	NT All Grades	NT Grade ≥3
268	42%	2%	30%	10%

BREYANZI. Prescribing information. Juno Therapeutics Inc; 2021. Abramson JS, Palomba ML, Gordon LI, et al. *Lisocabtagene maraleucel for patients with relapsed or refractory large B-cell lymphomas* (TRANSCEND NHL 001): a multicentre seamless design study. *The Lancet*. 2020;396(10254):839-852. van der Stegen S, Hamieh M, Sadelain M. The pharmacology of second-generation chimeric antigen receptors. *Nat Rev Drug Discov*. 2015;14(7):499-509.

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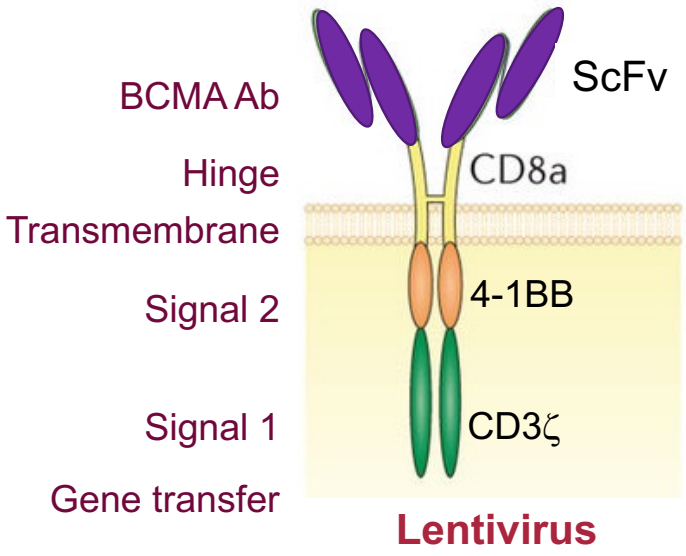
Idecabtagene Vicleucel



FDA Approved

- Adult patients with relapsed or refractory multiple myeloma after 4 or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody

Study	KarMMA
CAR T-cell dose	150-450×10^6
Treated/enrolled	128
Relapsed/refractory	Relapsed or Refractory
Previous auto-SCT	94%
Bridging therapy	88%
Manufacturing success	99%
ORR/CR (%)	73/33

SAFETY

N	CRS All Grades	CRS Grade ≥3	NT All Grades	NT Grade ≥3
128	**84%**	**5%**	**18%**	**3%**

Munshi NC, Larry D. Anderson Jr, Shah N, et al. Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma. *N Engl J Med.* 2021;384(8):705-716. doi:10.1056/NEJMOA2024850 ABECMA. Prescribing information. Cengene Corporation; 2021.

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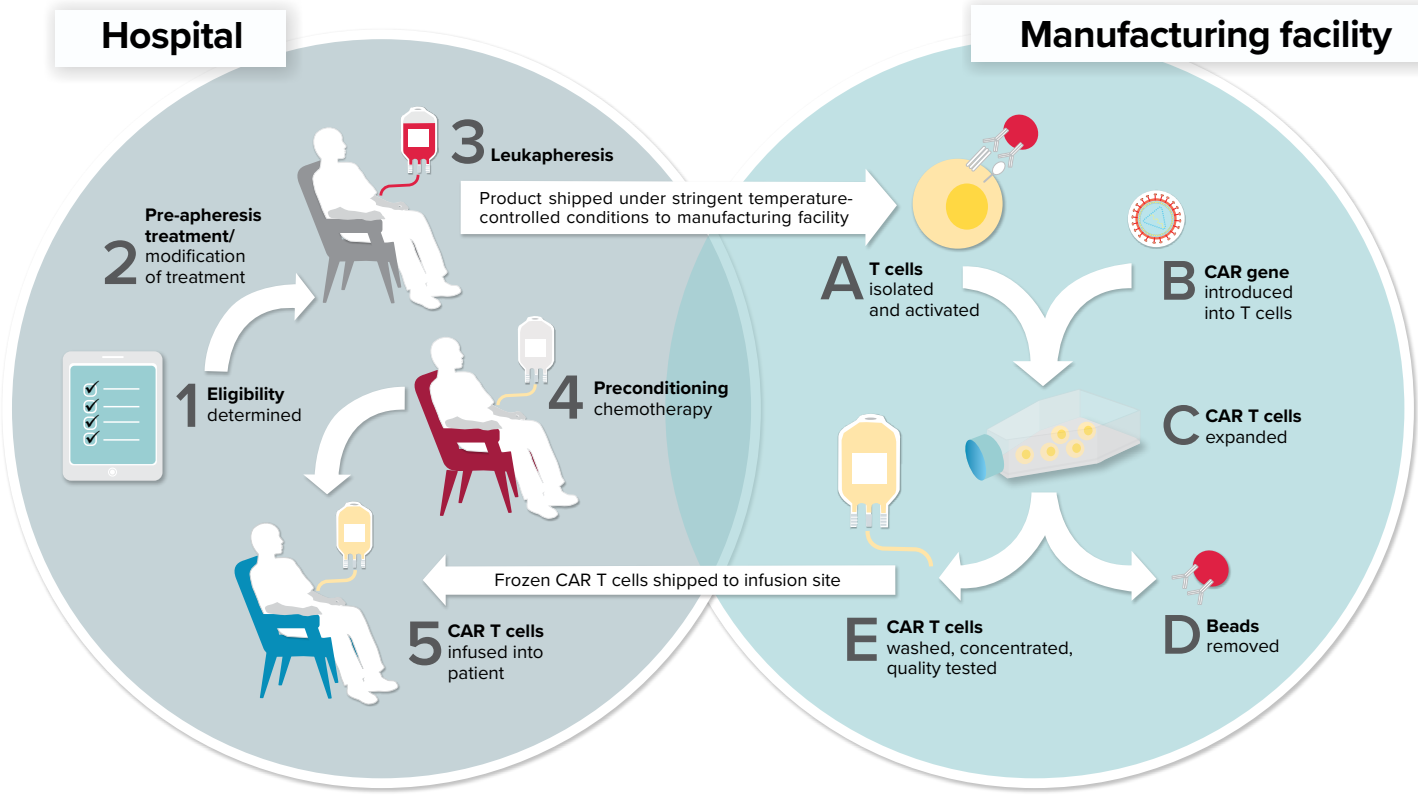
How Are CAR T Cells Manufactured/Engineered?



- On average, the production of CAR T cells takes approximately 10 to 14 days
- The time from endogenous T-cell collection to CAR T-cell infusion varies, but typically ranges from 1 to 4 weeks

Leukemia & Lymphoma Society. Facts about chimeric antigen receptor (CAR) T-cell therapy. Accessed October 20, 2021. https://www.lls.org/sites/default/files/2021-05/FSHP1_CART_Factsheet_Sept2020_Rev.pdf

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