



MD Anderson  
~~Cancer Center~~



# Allogeneic CAR-T: Is there a strategy moving forward?

**Sattva S. Neelapu, MD**

Professor and Deputy Chair

Department of Lymphoma and Myeloma

The University of Texas MD Anderson Cancer Center

Houston, Texas, USA

**9th Postgraduate Lymphoma Conference**

**Florence, Hotel Brunelleschi, March 20-21, 2025**

# Disclosures

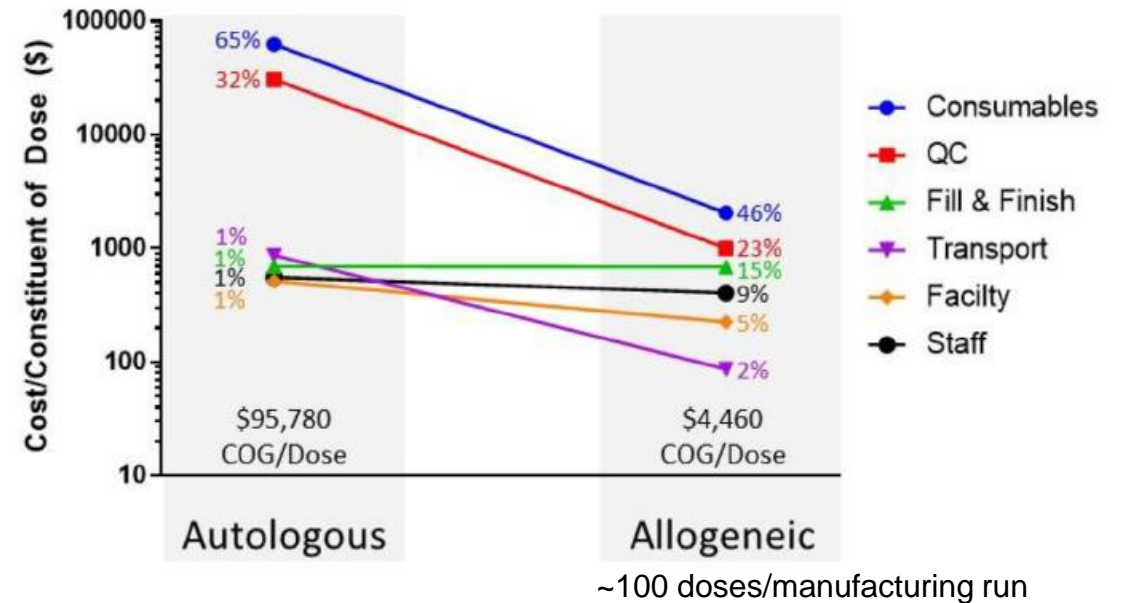
Disclosure	Company name
Research Support	Kite/Gilead, Allogene, Precision Biosciences, Adicet Bio, Sana Biotechnology, Cargo Therapeutics
Advisory Board / Consultant	Kite/Gilead, Sellas Life Sciences, Allogene, Adicet Bio, BMS, Fosun Kite, Caribou, Astellas Pharma, Morphosys, Janssen, Chimagen, ImmunoACT, Takeda, Synthekine, Carsgen, Appia Bio, GlaxoSmithKline, Galapagos, ModeX Therapeutics, Jazz Pharmaceuticals, ADC Therapeutics, BioOra Limited, Arovella Therapeutics, Merck, Pfizer, Poseida
Honoraria	MJH Life Sciences, PeerView, MD Education
Speaker's Bureau	None
Employment	None
Royalties	None
Stocks / Stock Options	None
Patents	Related to cell therapy

- I will discuss investigational use of CAR T-cell therapy

# Advantages of allogeneic CAR cell therapy

- Potential for improved **efficacy** due to improved T-cell fitness
- **Consistent** product quality
- **No wait period** as they are off-the-shelf
- Improve **access** at non-transplant centers
- Potential to **lower the cost** of CAR T-cell therapy

## Cost of goods/dose: Auto vs. Allo



# Clinical trial publications of allogeneic CAR T/NK cell therapy

SCIENCE TRANSLATIONAL MEDICINE | REPORT

## CANCER

### Molecular remission of infant B-ALL after infusion of universal TALEN gene-edited CAR T cells

Waseem Qasim,<sup>1,2\*</sup> Hong Zhan,<sup>1</sup> Sujith Samarasinghe,<sup>2</sup> Stuart Adams,<sup>2</sup> Persis Amrolia,<sup>1,2</sup> Sian Stafford,<sup>1</sup> Katie Butler,<sup>1</sup> Christine Rivat,<sup>1</sup> Gary Wright,<sup>2</sup> Kathy Somana,<sup>2</sup> Sara Ghorashian,<sup>1</sup> Danielle Pinner,<sup>2</sup> Gul Ahsan,<sup>2</sup> Kimberly Gilmour,<sup>2</sup> Giovanna Lucchini,<sup>2</sup> Sarah Inglott,<sup>2</sup> William Mifsud,<sup>2</sup> Robert Chiesa,<sup>2</sup> Karl S. Peggs,<sup>3</sup> Lucas Chan,<sup>4</sup> Farzin Farzaneh,<sup>4</sup> Adrian J. Thrasher,<sup>1</sup> Ajay Vora,<sup>5</sup> Martin Pule,<sup>3</sup> Paul Veys<sup>1</sup>

*Sci Transl Med* 2017

2017 © The Authors, some rights reserved; exclusive licensee American Association for the Advancement of Science.

### Genome-edited, donor-derived allogeneic anti-CD19 chimeric antigen receptor T cells in paediatric and adult B-cell acute lymphoblastic leukaemia: results of two phase 1 studies

Reuben Benjamin, Charlotte Graham, Deborah Yallop, Agnieszka Jozwik, Oana C Mirci-Danica, Giovanna Lucchini, Danielle Pinner, Nitin Jain, Hagop Kantarjian, Nicolas Boissel, Marcela V Maus, Matthew J Frigault, André Baruchel, Mohamad Mohty, Athos Gianella-Borradori, Florence Binlich, Svetlana Balandraud, Fabien Vitry, Elisabeth Thomas, Anne Philippe, Sylvain Fouliard, Sandra Dupouy, Ibtissam Marchiq, Maria Almena-Carrasco, Nicolas Ferry, Sylvain Arnould, Cyril Konto, Paul Veys, Waseem Qasim, for the UCART19 Group\*

*Lancet* 2020

### Allogeneic CAR T Cell Products Cemacabtagene Ansegedleucel/ALLO-501 in Relapsed/Refractory Large B-Cell Lymphoma: Phase 1 Experience From the ALPHA2/ALPHA Clinical Studies

Authors: Frederick L. Locke, Javier L. Munoz, Michael T. Tees, Lazaros J. Lekakis, Sven de Vos, Rajneesh Nath, Don A. Stevens, Shahbaz A. Malik, Geoffrey P. Shouse, Mehdi Hamadani, Olalekan O. Oluwole, Miguel-Angel Perales, David B. Miklos, Paul W. Fisher, Amy Feng, Lynn Navale, John B. Le Gall, and Sattva S. Neelapu. SHOW FEWER AUTHORS INFO & AFFILIATIONS

Publication: Journal of Clinical Oncology • Just Accepted • <https://doi.org/10.1200/JCO-24-01933>

*J Clin Oncol* 2025

### Use of CAR-Transduced Natural Killer Cells in CD19-Positive Lymphoid Tumors

Enli Liu, M.D., David Marin, M.D., Pinaki Banerjee, Ph.D., Homer A. Macapinlac, M.D., Philip Thompson, M.B., B.S., Rafet Basar, M.D., Lucila Nassif Kerbauy, M.D., Bethany Overman, B.S.N., Peter Thall, Ph.D., Mecit Kaplan, M.S., Vandana Nandivada, M.S., Indresh Kaur, Ph.D., Ana Nunez Cortes, M.D., Kai Cao, M.D., May Daher, M.D., Chitra Hosing, M.D., Evan N. Cohen, Ph.D., Partow Kebriaei, M.D., Rohtesh Mehta, M.D., Sattva Neelapu, M.D., Yago Nieto, M.D., Ph.D., Michael Wang, M.D., William Wierda, M.D., Ph.D., Michael Keating, M.D., Richard Champlin, M.D., Elizabeth J. Shpall, M.D., and Katayoun Rezvani, M.D., Ph.D.

*N Eng J Med* 2020

### Induced pluripotent stem-cell-derived CD19-directed chimeric antigen receptor natural killer cells in B-cell lymphoma: a phase 1, first-in-human trial

Armin Ghobadi, Veronika Bachanova, Krish Patel, Jae H Park, Ian Flinn, Peter A Riedell, Carlos Bachier, Catherine S Diefenbach, Carol Wong, Cara Bickers, Lilly Wong, Deepa Patel, Jode Goodridge, Matthew Denholt, Bahram Valamehr, Rebecca L Elstrom, Paolo Strati

*Lancet* 2025

### Safety and activity of CTX130, a CD70-targeted allogeneic CRISPR-Cas9-engineered CAR T-cell therapy, in patients with relapsed or refractory T-cell malignancies (COBALT-LYM): a single-arm, open-label, phase 1, dose-escalation study

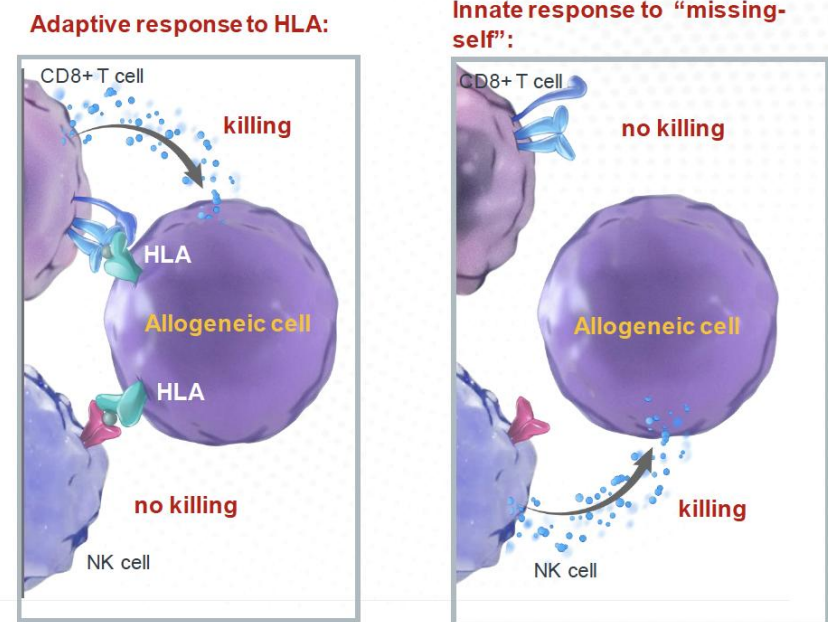
Swaminathan P Iyer\*, R Alejandro Sica\*, P Joy Ho, Anca Prisca, Jasmine Zain, Francine M Foss, Boyu Hu, Amer Beitinjaneh, Wen-Kai Weng, Youn H Kim, Michael S Khodadoust, Auris O Huen, Leah M Williams, Anna Ma, Elaine Huang, Avanti Ganpule, Shashwat Deepali Nagar, Parin Sripakdeevong, Erika L Cullingford, Sushant Karnik, Mary-Lee Dequeant, Janki N Patel, Xinyi Shirley He, Ziliang Li, Qiuling Ally He, Joy H Mendonza, Alissa Keegan, Steven M Horwitz

*Lancet Oncol* 2025

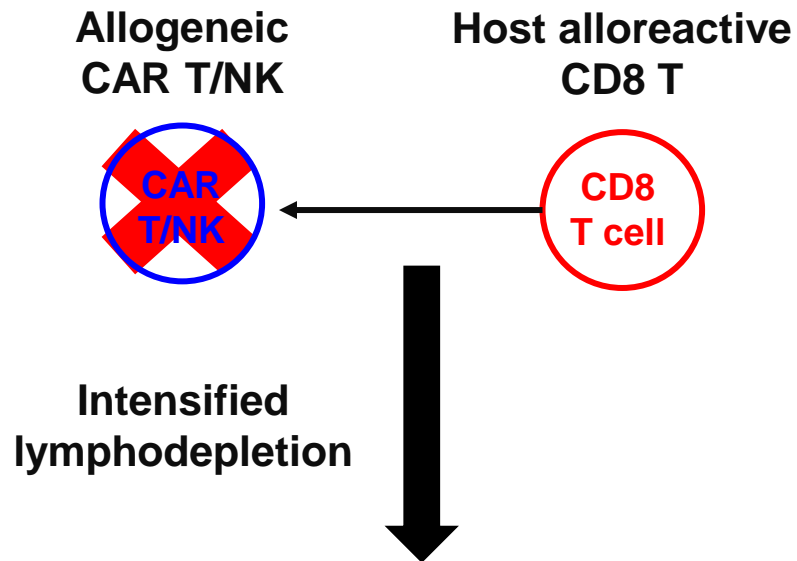
# Challenges for allogeneic CAR T-cell therapy

- GVHD
  - Mediated by  $\alpha\beta$  T cells
  - May be overcome by TCR knock-out or by using alternative cell types such as NK cells, NKT,  $\gamma\delta$  T cells
- Graft rejection
  - Mediated by  $\alpha\beta$  T cells and NK cells

## Graft rejection by T and NK cells



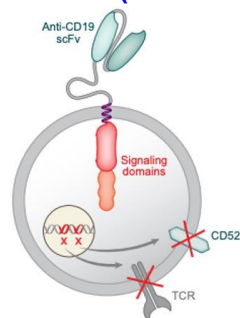
# Overcoming immune rejection by intensified lymphodepletion



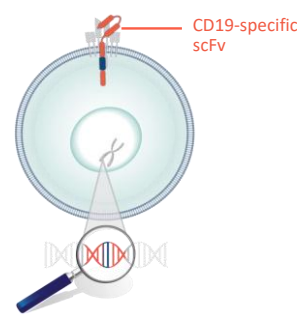
Eliminate host T and NK cells for few weeks to allow allo CAR T cells to expand and mediate antitumor effects

Product / Sponsor	Cell type	CAR Target	Allorejection strategy	Comments
ALLO-501/A Allogene	$\alpha\beta$ T cells	CD19	Anti-CD52 Ab + Standard Cy/Flu	TCR KO CD52 KO
PBCAR0191 Precision Bio	$\alpha\beta$ T cells	CD19	Enhanced Cy/Flu	TCR KO
CB-010 Caribou Biosciences	$\alpha\beta$ T cells	CD19	High-dose Cy/Flu	TCR KO PD1 KO
ADI-001 Adicet Bio	$\gamma\delta$ T cells	CD20	Enhanced Cy/Flu	

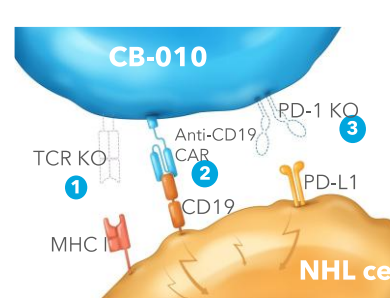
ALLO-501A (Cema-cel)



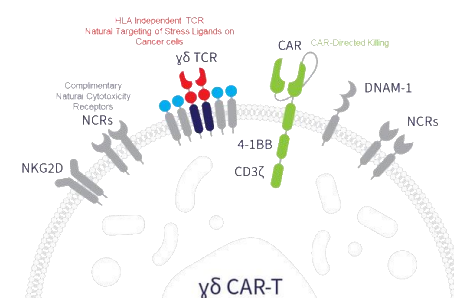
PBCAR0191



CB-010

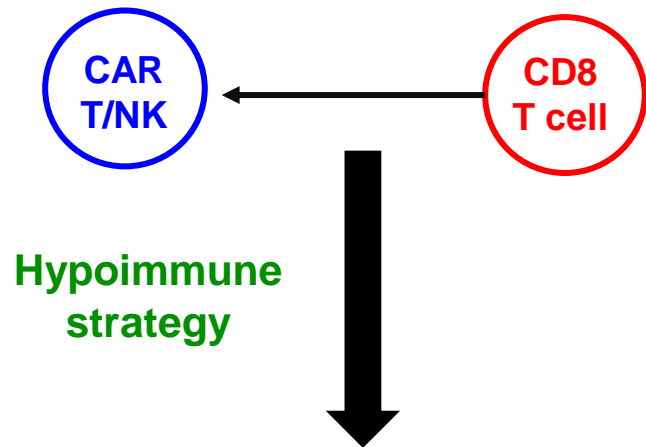


ADI-001



# Overcoming immune rejection by hypoimmune strategy

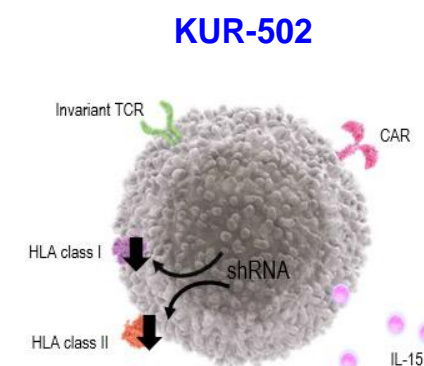
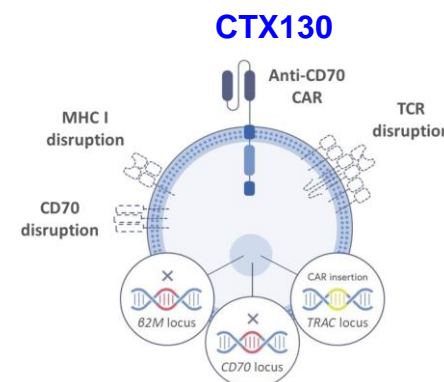
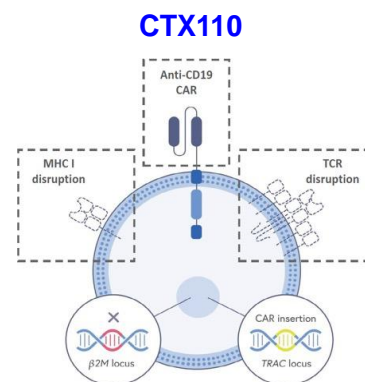
Allogeneic CAR T/NK with MHC I<sup>KO</sup>      Host alloreactive CD8 T



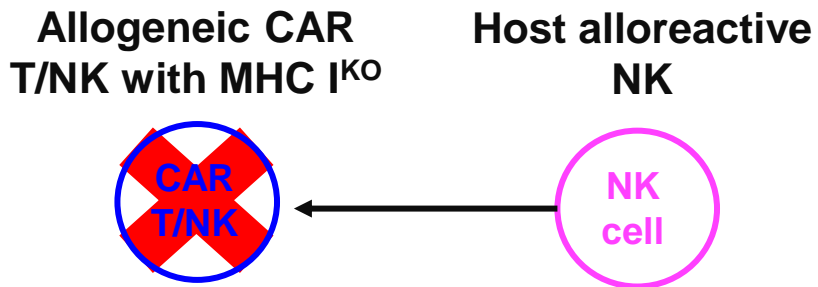
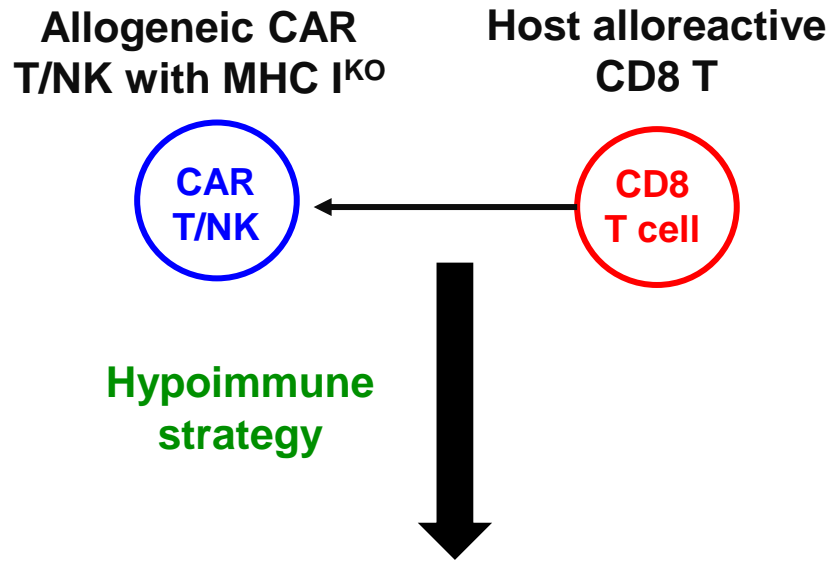
Hypoimmune strategy

Make donor CAR T/NK cells invisible / hyporeactive to the host immune system

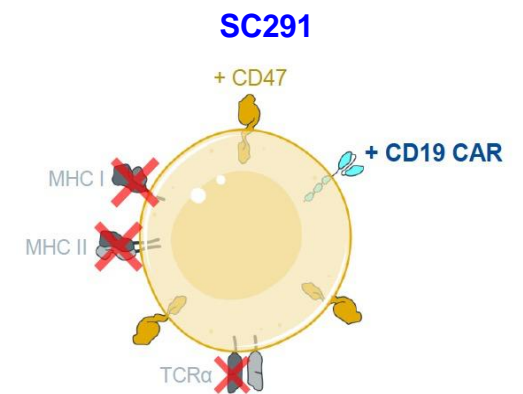
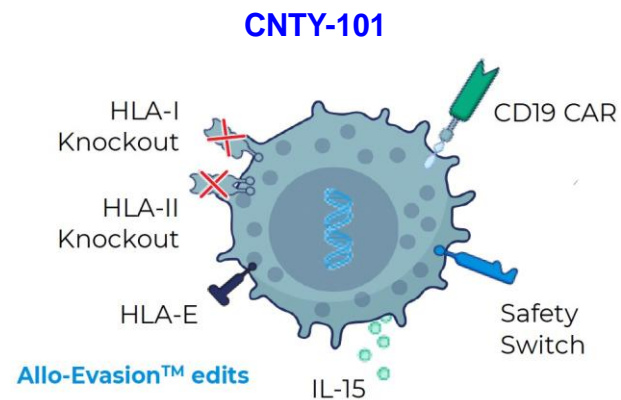
Product / Sponsor	Cell type	CAR Target	Allorejection strategy	Additional comments
CTX110 CRISPR Therapeutics	ab T cells	CD19	B2M KO	Standard Cy/Flu
CTX130 CRISPR Therapeutics	ab T cells	CD70	B2M KO CD70 KO	Standard Cy/Flu CD70 KO
KUR-502 Athenex	iNKT cells	CD19	B2M & CD74 down regulation	Standard Cy/Flu IL-15 transgene



# Overcoming immune rejection by hypoimmune strategy



Product / Sponsor	Cell type	CAR Target	Allorejection strategy	Additional comments
<b>CTX110</b> CRISPR Therapeutics	ab T cells	CD19	B2M KO	Standard Cy/Flu
<b>CTX130</b> CRISPR Therapeutics	ab T cells	CD70	B2M KO	Standard Cy/Flu CD70 KO
<b>KUR-502</b> Athenex	iNKT cells	CD19	B2M & CD74 down regulation	Standard Cy/Flu IL-15 transgene
<b>CNTY-101</b> Century Therapeutics	iPSC CAR NK	CD19	B2M KO, CIITA KO, & HLA-E overexpression	Standard Cy/Flu IL-15 transgene
<b>SC291</b> Sana Biotechnology	ab T cells	CD19	B2M KO, CIITA KO, & CD47 overexpression	Standard Cy/Flu





# Auto vs Allo CD19 CAR-T: Safety in r/r $\geq 3^{\text{rd}}$ line LBCL

	Product	Study	CRS All / Gr $\geq 3$	ICANS All / Gr $\geq 3$	Gr $\geq 3$ cytopenia >30d
Autologous	Axi-cel	ZUMA-1	93 / 11	64 / 30	38
	Tisa-cel	JULIET	57 / 23	20 / 11	34
	Liso-cel	TRANSCEND	42 / 2	30 / 10	37
	Rapa-cel	Phase 1	35 / 6	25 / 6	NA
Allogeneic	ALLO-501A	Phase 1	24 / 0	0 / 0	29
	PBCAR0191	Phase 1	65 / 0	30 / 6	NA
	CB-010	Phase 1 (2 <sup>nd</sup> line)	57 / 0	22 / 7	20
	CTX110	Phase 1	18 / 0	9 / 6	NA

Neelapu SS et al. *N Engl J Med.* 2017;377:2531-2544. Locke FL et al. *Lancet Oncol.* 2019;20(1):31-42; Schuster SJ et al. *N Engl J Med.* 2019;380:45-56. Schuster SJ et al. *Lancet Oncol.* 2021;22(10):1403-1415; Abramson JS et al. *Lancet.* 2020;396(10254):839-852; Locke et al. Neelapu, ASH 2023 Abstract 2095; Shah et al. ASH 2021, Abstract 302; Hu B et al. ASCO 2024 Abstract 2025; McGuirk et al. EBMT 2023

# Auto vs Allo CD19 CAR-T: Safety in r/r $\geq 3^{\text{rd}}$ line LBCL

	Product	Study	CRS All / Gr $\geq 3$	ICANS All / Gr $\geq 3$	Gr $\geq 3$ cytopenia >30d	Infections Gr $\geq 3$
Autologous	Axi-cel	ZUMA-1	93 / 11	64 / 30	38	NA / 10
	Tisa-cel	JULIET	57 / 23	20 / 11	34	37 / 19
	Liso-cel	TRANSCEND	42 / 2	30 / 10	37	NA / 12
	Rapa-cel	Phase 1	35 / 6	25 / 6	NA	19 / 6
Allogeneic	ALLO-501A	Phase 1	24 / 0	0 / 0	29	58 / 15
	PBCAR0191	Phase 1	65 / 0	30 / 6	NA	59 / 41
	CB-010	Phase 1 (2 <sup>nd</sup> line)	57 / 0	22 / 7	20	48 / 22
	CTX110	Phase 1	18 / 0	9 / 6	NA	25 / 13

Neelapu SS et al. *N Engl J Med.* 2017;377:2531-2544. Locke FL et al. *Lancet Oncol.* 2019;20(1):31-42. Schuster SJ et al. *N Engl J Med.* 2019;380:45-56. Schuster SJ et al. *Lancet Oncol.* 2021;22(10):1403-1415; Abramson JS et al. *Lancet.* 2020;396(10254):839-852; Locke et al. Neelapu, ASH 2023 Abstract 2095; Shah et al. ASH 2021, Abstract 302; Hu B et al. ASCO 2024 Abstract 2025; McGuirk et al. EBMT 2023

# Auto vs Allo CD19 CAR-T: Efficacy in r/r $\geq 3^{\text{rd}}$ line LBCL

	Product	Study	ORR	CR rate
Autologous	Axi-cel	ZUMA-1	83%	58%
	Tisa-cel	JULIET	53%	39%
	Liso-cel	TRANSCEND	73%	53%
	Rapa-cel	Phase 1	80%	73%
Allogeneic	ALLO-501A	Phase 1	67%	58%
	PBCAR0191	Phase 1	69%	56%
	CB-010	Phase 1 (2 <sup>nd</sup> line)	75%	50%
	CTX110	Phase 1	67%	41%

Neelapu SS et al. *N Engl J Med.* 2017;377:2531-2544. Locke FL et al. *Lancet Oncol.* 2019;20(1):31-42. Schuster SJ et al. *N Engl J Med.* 2019;380:45-56. Schuster SJ et al. *Lancet Oncol.* 2021;22(10):1403-1415; Abramson JS et al. *Lancet.* 2020;396(10254):839-852; Locke et al. Neelapu, ASH 2023 Abstract 2095; Shah et al. ASH 2021, Abstract 302; Hu B et al. ASCO 2024 Abstract 2025; McGuirk et al. EBMT 2023

# Auto vs Allo CD19 CAR-T: Efficacy in r/r $\geq 3^{\text{rd}}$ line LBCL

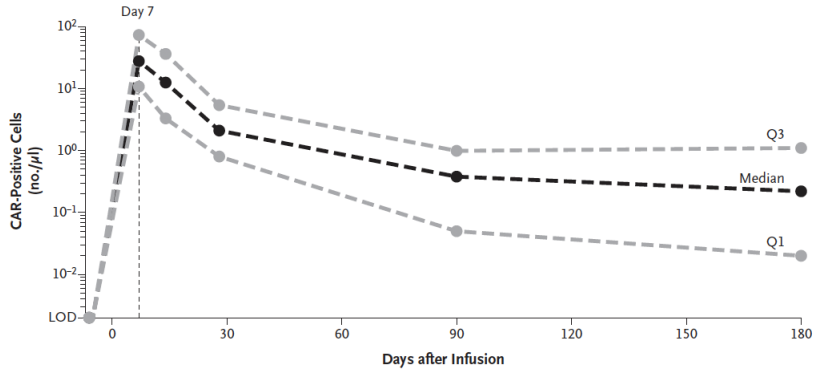
	Product	Study	ORR	CR rate	6-mo PFS rate
Autologous	Axi-cel	ZUMA-1	83%	58%	49%
	Tisa-cel	JULIET	53%	39%	39%
	Liso-cel	TRANSCEND	73%	53%	50%
	Rapa-cel	Phase 1	80%	73%	83%
Allogeneic	ALLO-501A	Phase 1	67%	58%	42%
	PBCAR0191	Phase 1	69%	56%	17%
	CB-010	Phase 1 (2 <sup>nd</sup> line)	75%	50%	52% ( $\geq 4$ HLA match)
	CTX110	Phase 1	67%	41%	15%

Neelapu SS et al. *N Engl J Med.* 2017;377:2531-2544. Locke FL et al. *Lancet Oncol.* 2019;20(1):31-42. Schuster SJ et al. *N Engl J Med.* 2019;380:45-56. Schuster SJ et al. *Lancet Oncol.* 2021;22(10):1403-1415; Abramson JS et al. *Lancet.* 2020;396(10254):839-852; Locke et al. Neelapu, ASH 2023 Abstract 2095; Shah et al. ASH 2021, Abstract 302; Hu B et al. ASCO 2024 Abstract 2025; McGuirk et al. EBMT 2023

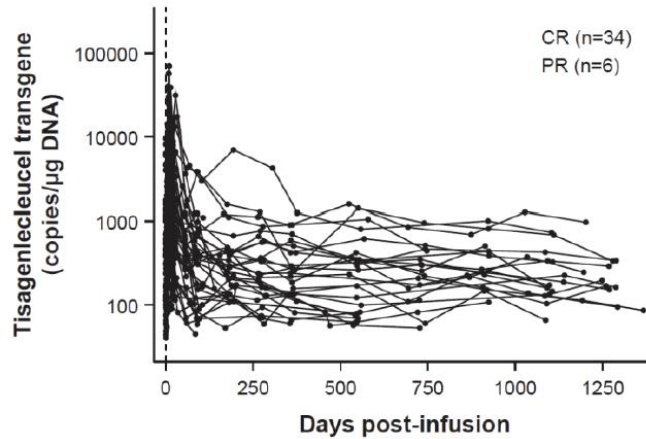
# Auto vs. Allo CAR-T expansion

Auto CAR-T

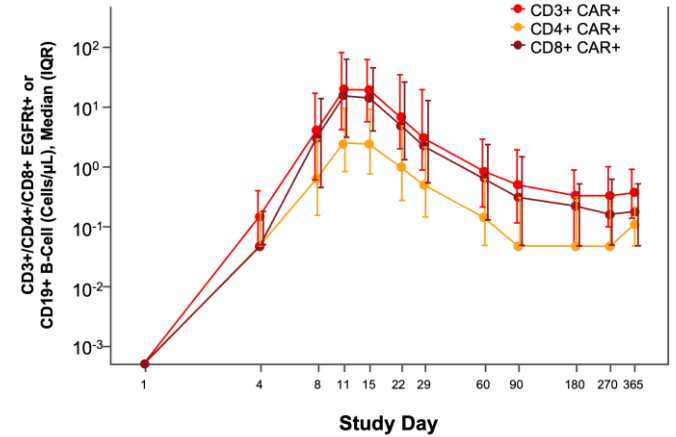
ZUMA-1 / Axi-cel



JULIET / Tisa-cel



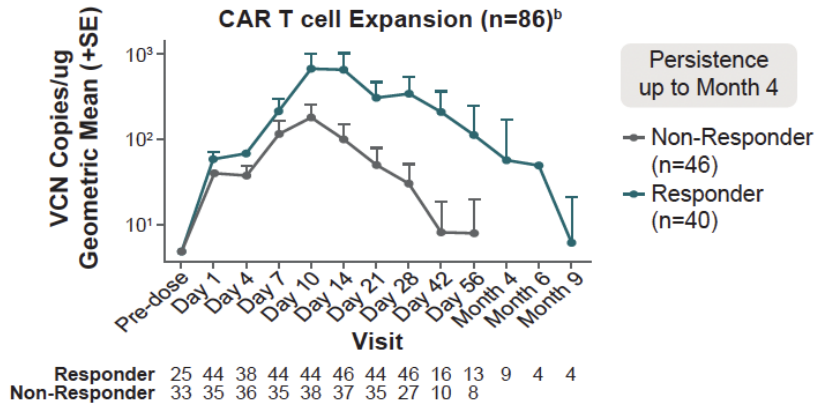
TRANSCEND / Liso-cel



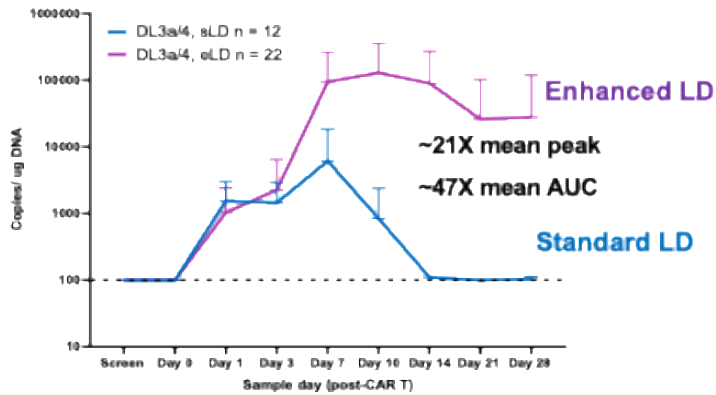
Neelapu et al. *N Eng J Med*, 2017; Schuster et al, *Lancet Oncol*, 2021; Abramson et al, *ASH 2019*, Abstract 241

Allo CAR-T

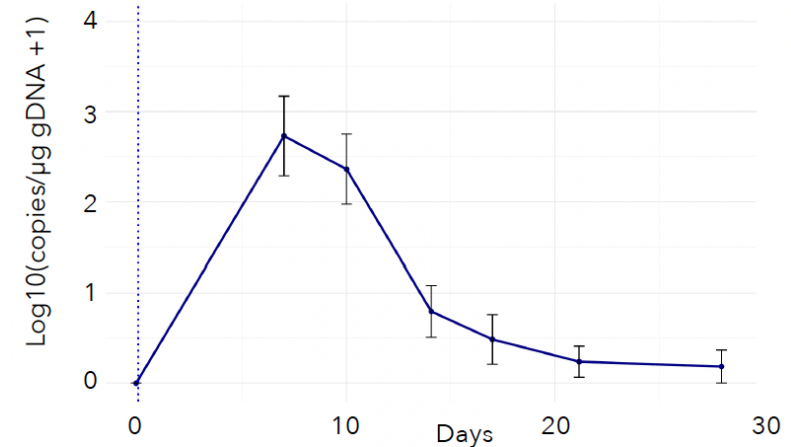
ALPHA / Cema-cel (ALLO-501)



PBCAR0191



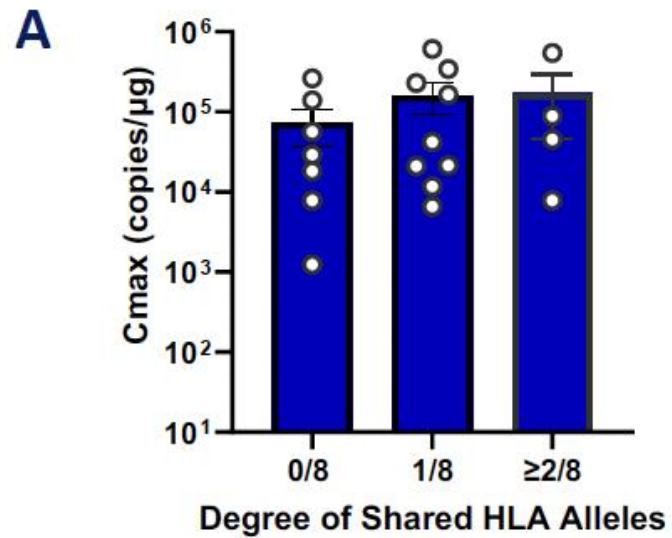
CB-010



Locke et al. Neelapu, *ASH 2023 Abstract 2095*; Shah et al. *ASH 2021*, Abstract 302; Hu B et al. *ASCO 2024 Abstract 2025*

# Cellular kinetics and response were not associated with degree of shared HLA alleles

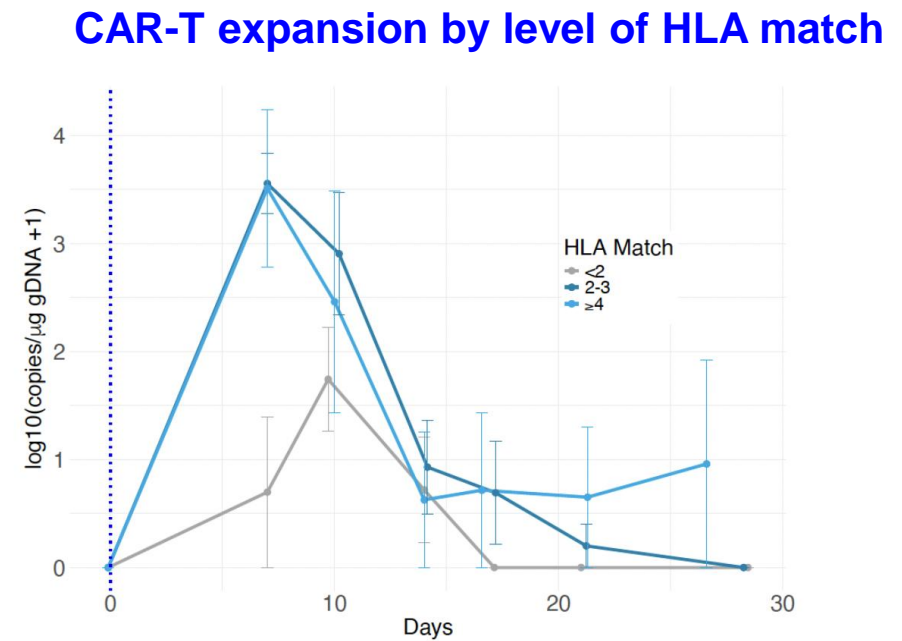
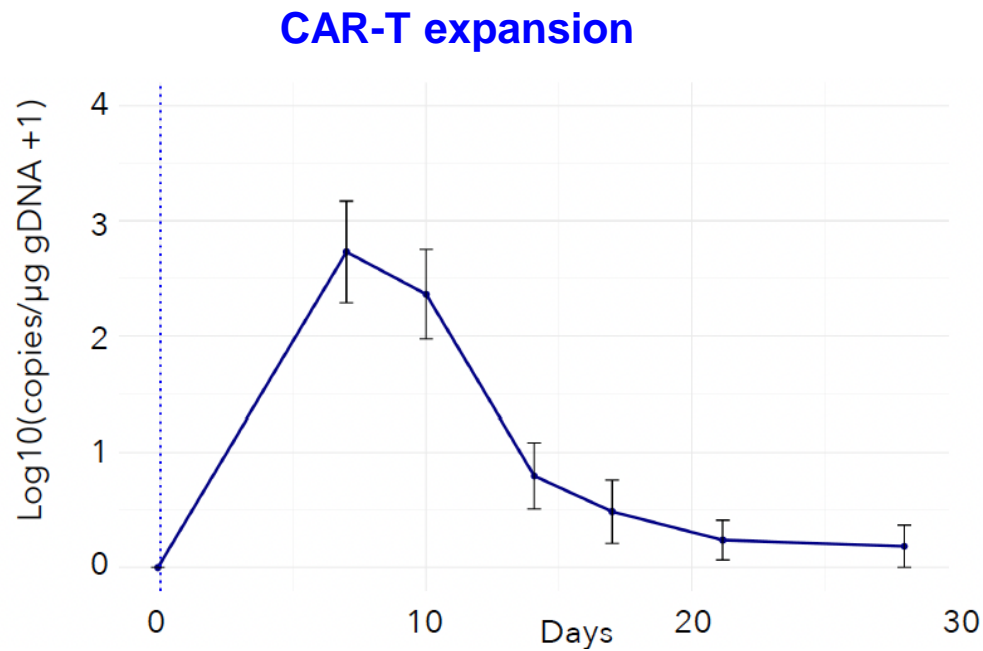
ADI-001 Study  
( $\gamma\delta$  CD20 CART)



**B**

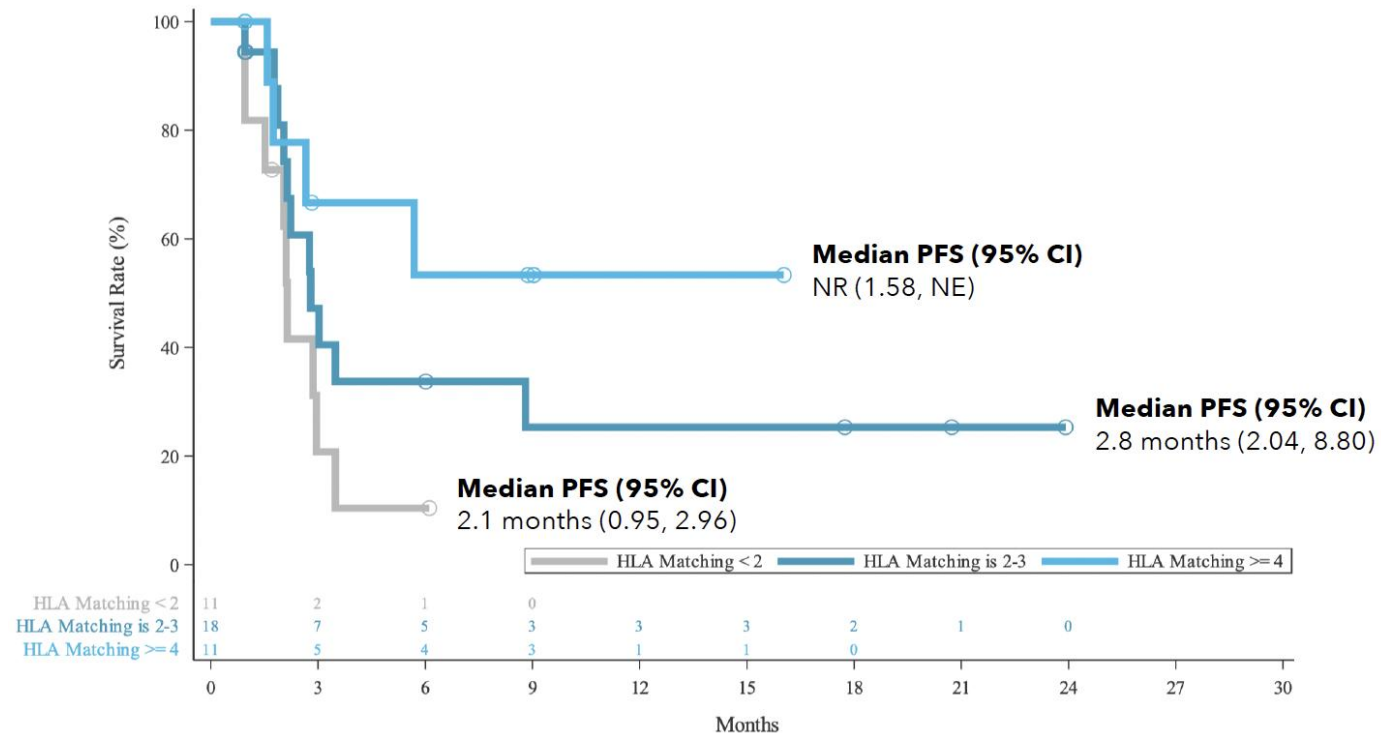
Shared HLA Alleles	CR/PR Rate n/N (%)
0/8	7/8 (87.5)
1/8	7/11 (63.6)
$\geq 2/8$	3/5 (60.0)

# CB-010 Antler Phase 1 Study: CAR-T expansion



# CB-010 Antler Phase 1 Study: PFS

## PFS by level of HLA match: LBCL patients (N=40)



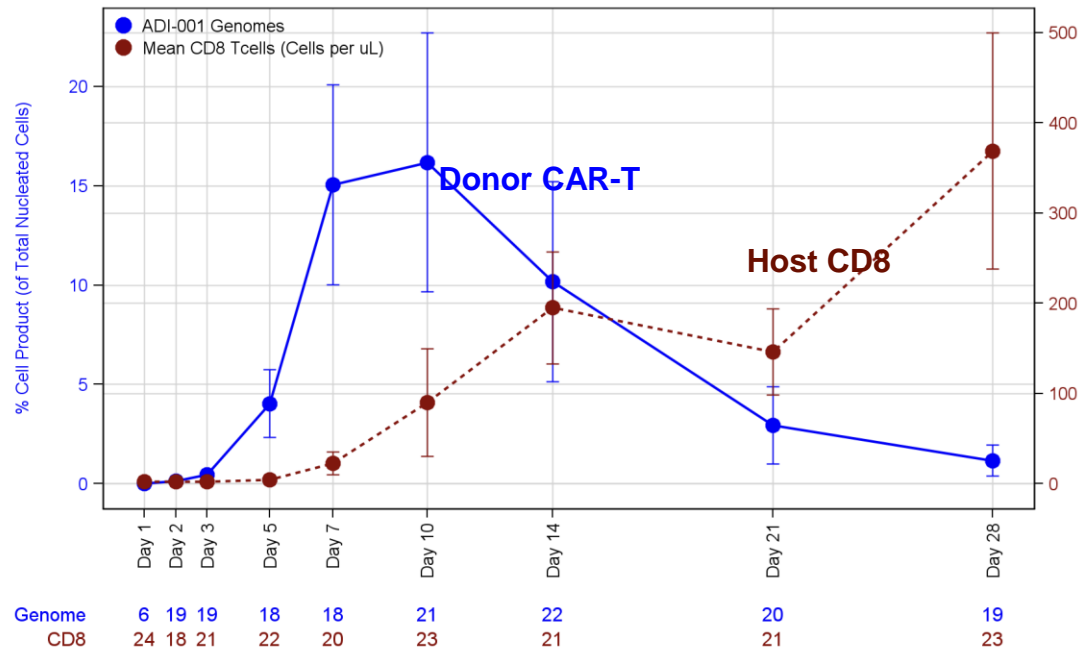
- RP2D:  $80 \times 10^6$  CAR T cells
- Higher HLA matching was associated with improved PFS
- 20 additional 2L LBCL patients with partial HLA matching ( $\geq 4$  alleles) planned to be enrolled at RP2D



# Loss of CAR-T persistence associated with host lymphocyte recovery

## ADI-001 Study ( $\gamma\delta$ CD20 CART)

### CAR-T persistence vs. CD8 T cell recovery



Moreno et al, ASH 2023, Abstract 3478

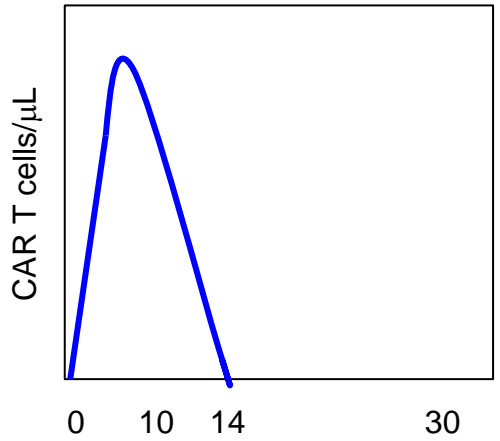
**Is there a strategy moving forward?**

# Can short-term persistence lead to durable CR with allogeneic CAR-T?

70 yo F  
 BR for FL  
 Obin-Len → tFL/DHL  
 R-CHOP + Ibrutinib  
 CD19 CART  
 Rit+Len

Flu: 30 mg/m<sup>2</sup>/d  
 Cy: 500 mg/m<sup>2</sup>/d

Allogeneic αβ  
 CD20 CAR T  
 1x10<sup>6</sup>  
 CAR+ cells/kg



Grade 2 CRS  
 Grade 3 ICANS

Days -5 to -3

Day 0

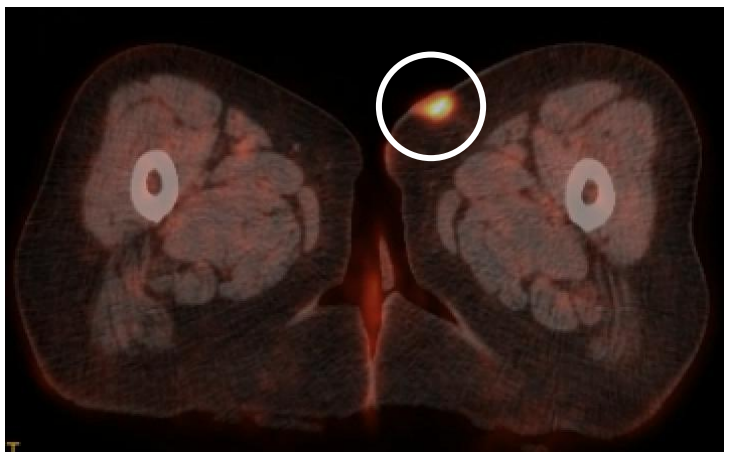
Day 10-14

CR

Day 30

CR

5 yrs



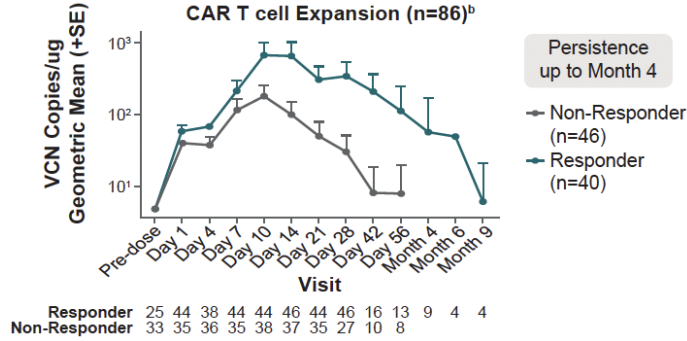
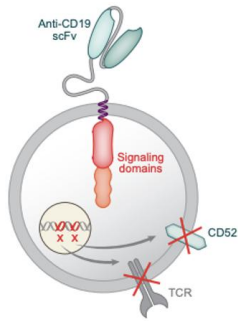
Low tumor burden  
 Peak CAR-T : Tumor  
 ratio was likely optimal  
 to eradicate lymphoma

1 of 20 patients responded  
 on a phase 1 trial

Product development  
 terminated

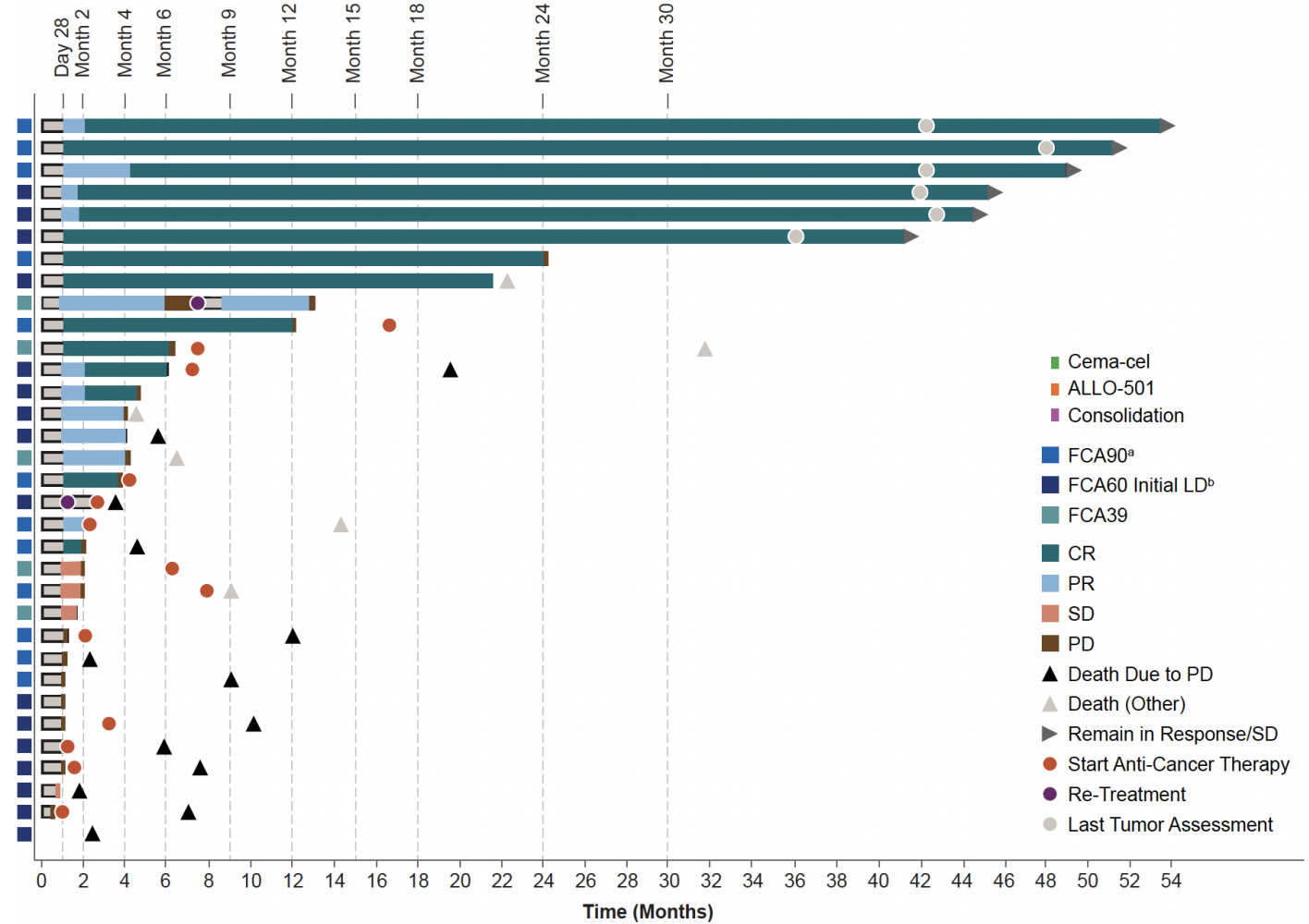
# ALPHA 1&2 studies: Efficacy in CAR naïve R/R LBCL

## Cema-cel

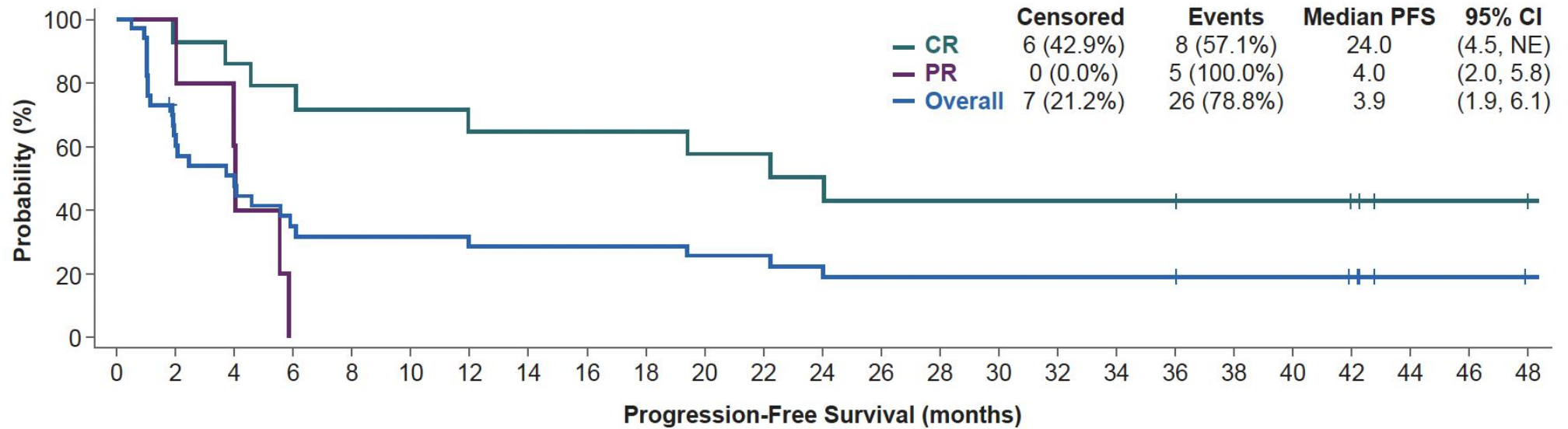


## Cy + Flu + Anti-CD52 Ab

	All (N=33)	Phase 2 dose (N=12)
ORR, n (%)	19 (58)	8 (67)
CRR, n (%)	14 (42)	7 (58)
6 mo CRR, n (%)	10 (30)	5 (42)
12 mo CRR, n (%)	8 (24)	4 (33)



# ALPHA 1&2 studies: PFS in CAR naïve R/R LBCL

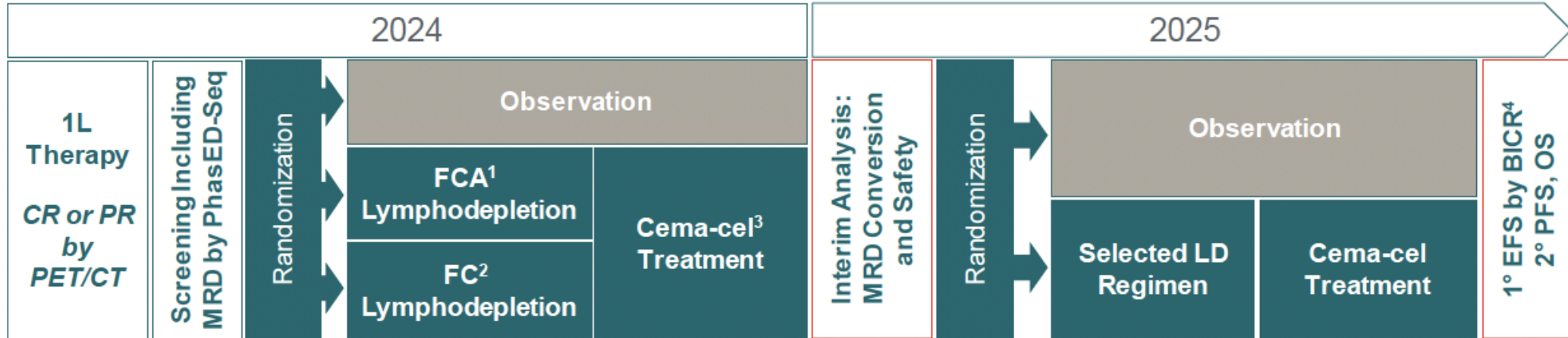


**Patients At Risk**

CR	14	14	13	13	12	11	11	10	10	10	10	10	9	9	9	9	9	9	9	9	8	8	8	7	7	6	6	6	6	6	6	6	6	6	6	6	6	5	5	5	5	5	5	4	1	1	1	1	1	0						
PR	5	5	5	4	3	2	0																																																	
Overall	33	25	19	17	15	13	11	10	10	10	10	10	9	9	9	9	9	9	9	9	9	8	8	8	7	7	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	5	5	5	5	5	5	4	1	1	1	1	1	0

Median follow-up: 10.1 mo (0.4 - 62.7 mo)

# ALPHA 3: Phase 3 study in first line LBCL



## ALPHA3 Startup Underway, Enrollment Projected to Commence Mid-2024

- All LBCL potentially eligible: no upfront risk assessment (e.g., IPI score, double-hit, HGBCL)
- Approximately 110 patients in observation and treatment arms
  - All patients treated with “Selected LD Regimen” during LD selection will count toward pivotal sample
  - Continuous enrollment planned, no pause in enrollment for LD regimen selection
- Expected median time to EFS in observation arm ~8 months

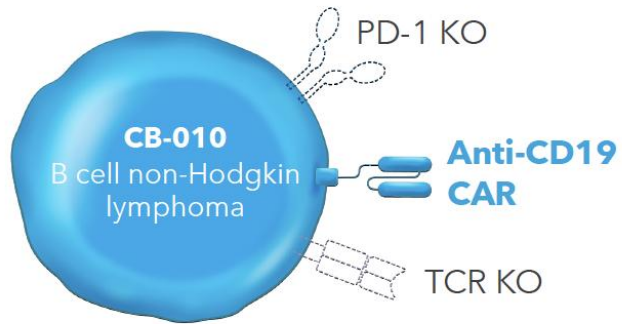
Allogene Corporate Presentation, Jan 2024

**Strategy for current allogeneic CAR-T products: Evaluate in MRD setting**

**But can we do better?**

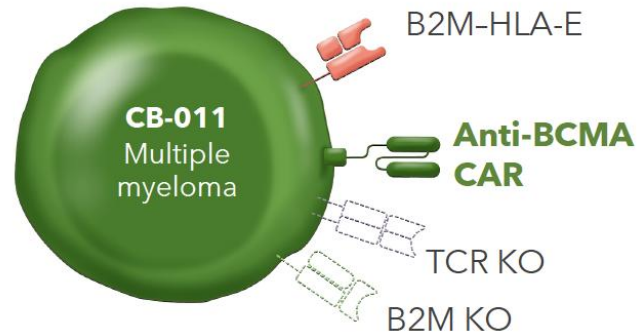
# Next generation allogeneic CAR T

## 3 Edits



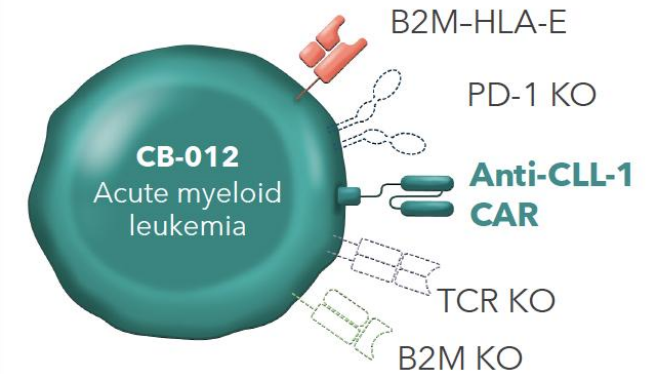
1<sup>st</sup> allogeneic anti-CD19 CAR-T cell therapy in the clinic with **checkpoint disruption** via PD-1 knockout (KO)<sup>1</sup> to reduce CAR-T cell exhaustion

## 4 Edits



1<sup>st</sup> allogeneic anti-BCMA CAR-T cell therapy with **immune cloaking** via B2M KO and insertion of B2M-HLA-E fusion protein<sup>1</sup>

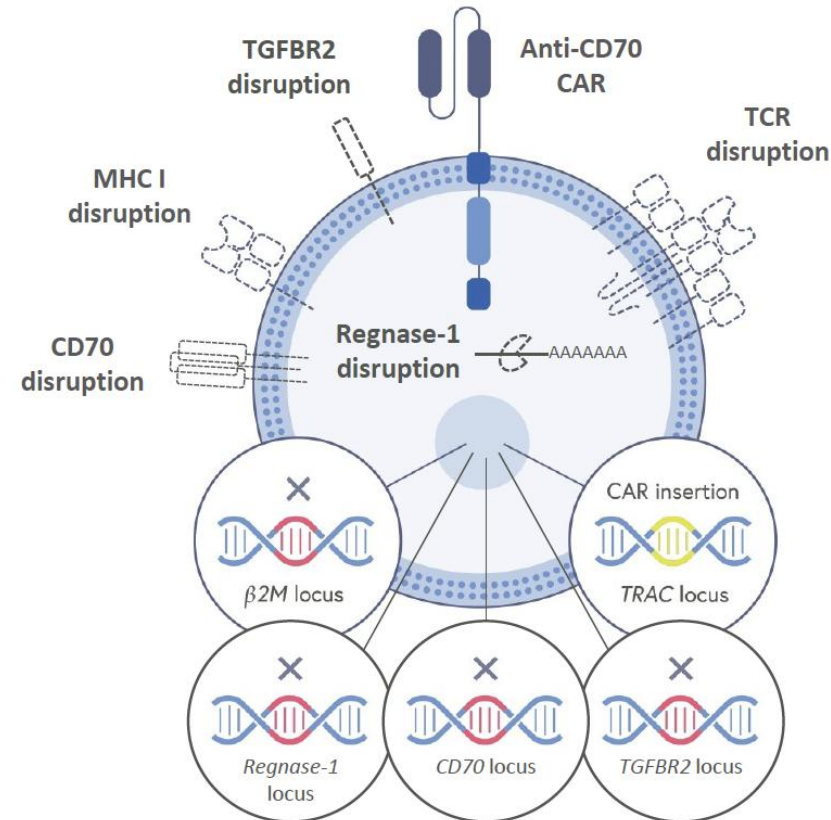
## 5 Edits



1<sup>st</sup> allogeneic CAR-T cell therapy with both **checkpoint disruption** and **immune cloaking**<sup>1</sup>

# Next generation CD70 allogeneic CAR T

## CTX131 (6 edits)

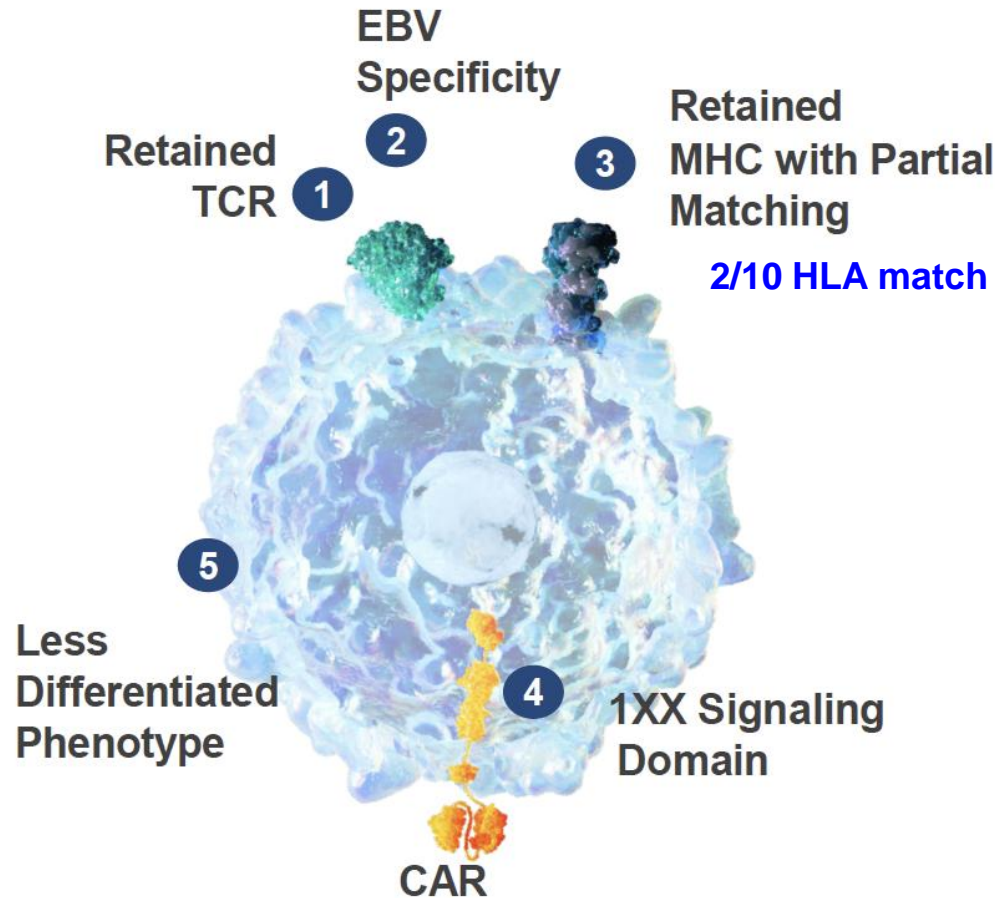


- **Regnase-1:** Removes intrinsic “brake” on T cell function
- **Increases functional persistence, cytokine secretion and sensitivity, effector function on tumors**

- **TGFBR2 KO:** Removes key extrinsic “brake” on T cell anti-tumor activity
- **Reduces TME inhibition of multiple CAR-T cell functions**

# CAR insertion in allogeneic EBV-specific T cells

## Atara's Allogeneic CAR T Platform



## Addressing Key Challenges

**Challenge:** *Graft vs Host Disease (GvHD) and Allojection*

### Atara Approach:

- 1 Retained TCR:** Unedited TCR serves as a key T cell survival signal<sup>1,2,3</sup> contributing to functional persistence<sup>3</sup>
- 2 EBV Specificity:** Low GvHD risk due to TCR recognition of viral antigens
- 3 Retained MHC with Partial Matching:** Enables allogeneic approach that avoids host versus graft rejection<sup>4,5</sup>

**Challenge:** *Exhaustion, Diminished Persistence, and Inflammatory Response*

### Atara Approach:

- 4 1XX Signaling Domain:** Novel CD3 $\zeta$  signaling domain<sup>6</sup> optimizes potency, expansion and mitigates T-cell exhaustion while modulating activation
- 5 Less Differentiated Phenotype:**  $\alpha\beta$  T-cell manufactured with less differentiated phenotype contributes to potency and moderates *in vivo* expansion of CAR-T cells, translating to potentially less severe inflammatory reactions

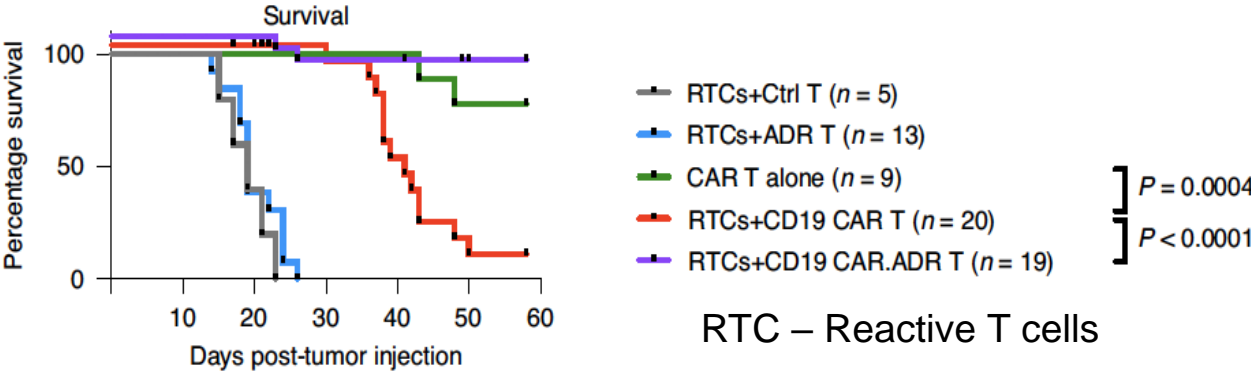
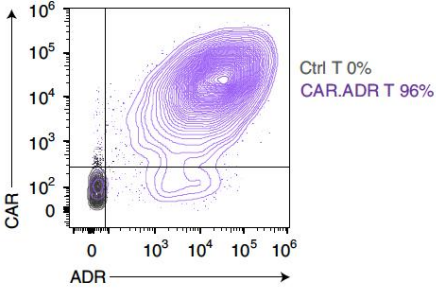
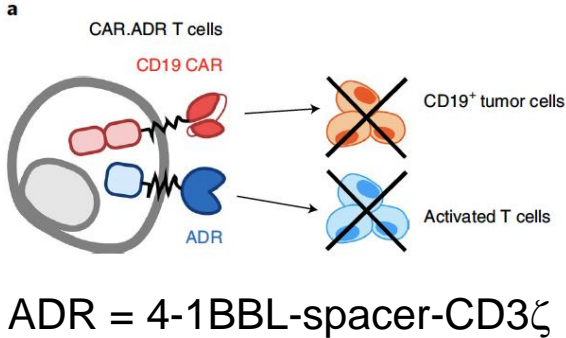
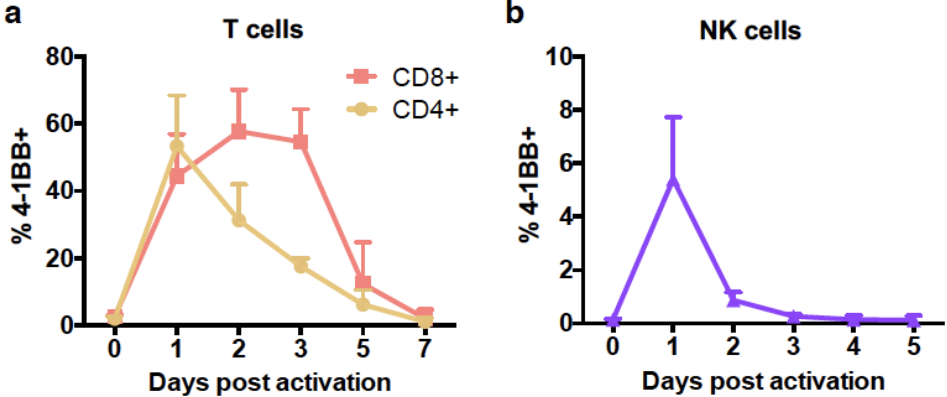


# Alloimmune defense receptor to resist host immune rejection

## Engineered off-the-shelf therapeutic T cells resist host immune rejection

Feiyan Mo<sup>1,2</sup>, Norihiro Watanabe<sup>1</sup>, Mary K. McKenna<sup>1</sup>, M. John Hicks<sup>3</sup>, Madhuwanti Srinivasan<sup>1</sup>, Diogo Gomes-Silva<sup>1</sup>, Erden Atilla<sup>1</sup>, Tyler Smith<sup>1</sup>, Pinar Ataca Atilla<sup>1</sup>, Royce Ma<sup>1,4</sup>, David Quach<sup>1</sup>, Helen E. Heslop<sup>1,2</sup>, Malcolm K. Brenner<sup>1,2</sup> and Maksim Mamonkin<sup>1,2,3,4</sup> ✉

### 4-1BB is temporarily upregulated by activated lymphocytes



- ADR-expressing T cells resist cellular rejection by targeting alloreactive lymphocytes *in vitro* and *in vivo*, while sparing resting lymphocytes

# Disrupting the immune synapse to reduce rejection



Cell Stem Cell

Sep 2024

Short article

## Genetic ablation of adhesion ligands mitigates rejection of allogeneic cellular immunotherapies

Quirin Hammer,<sup>1,9,\*</sup> Karlo Perica,<sup>2,3,4,9</sup> Rina M. Mbofung,<sup>5</sup> Hanna van Ooijen,<sup>6</sup> Karen E. Martin,<sup>7,8</sup> Pouria Momayyezi,<sup>1</sup> Erika Varady,<sup>5</sup> Yijia Pan,<sup>5</sup> Mark Jelcic,<sup>5</sup> Brian Groff,<sup>5</sup> Ramzey Abujarour,<sup>5</sup> Silje Z. Krokeide,<sup>7,8</sup> Tom Lee,<sup>5</sup> Alan Williams,<sup>5</sup> Jode P. Goodridge,<sup>5</sup> Bahram Valamehr,<sup>5</sup> Björn Önfelt,<sup>1,6</sup> Michel Sadelain,<sup>3</sup> and Karl-Johan Malmberg<sup>1,7,8,10,\*</sup>

## Alloimmune Defense Receptor Combined with Genetic Ablation of Adhesion Ligand CD58 Is a Comprehensive Approach to Promote Functional Persistence of Allogeneic Cell Therapies without Conditioning Chemotherapy

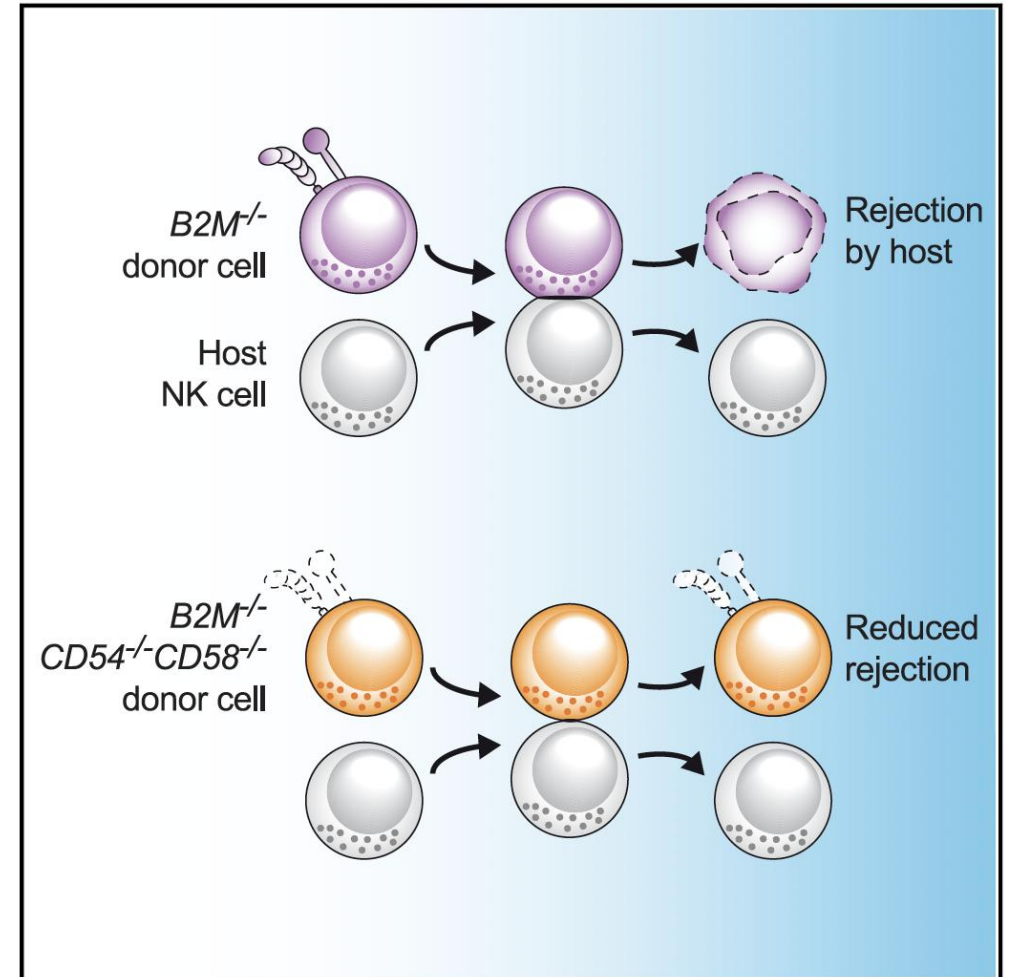
Alan Williams, Rina Mbofung, Daniel Morales-Mantilla, Brian Groff, Alison O'Connor, Binzhong Li, Ramesh Janani, Betsy Rezner, Mark Jelcic, Yijia Pan, Tom Lee, Karl-Johan Malmberg, Maksim Mamonkin, John Goulding, Jode Goodridge, Bahram Valamehr



Blood (2024) 144 (Supplement 1): 503.

<https://doi.org/10.1182/blood-2024-210846>

ASH 2024



# Selective deletion of HLA-A/B (but not HLA-C/E/G) to prevent rejection

CellPress

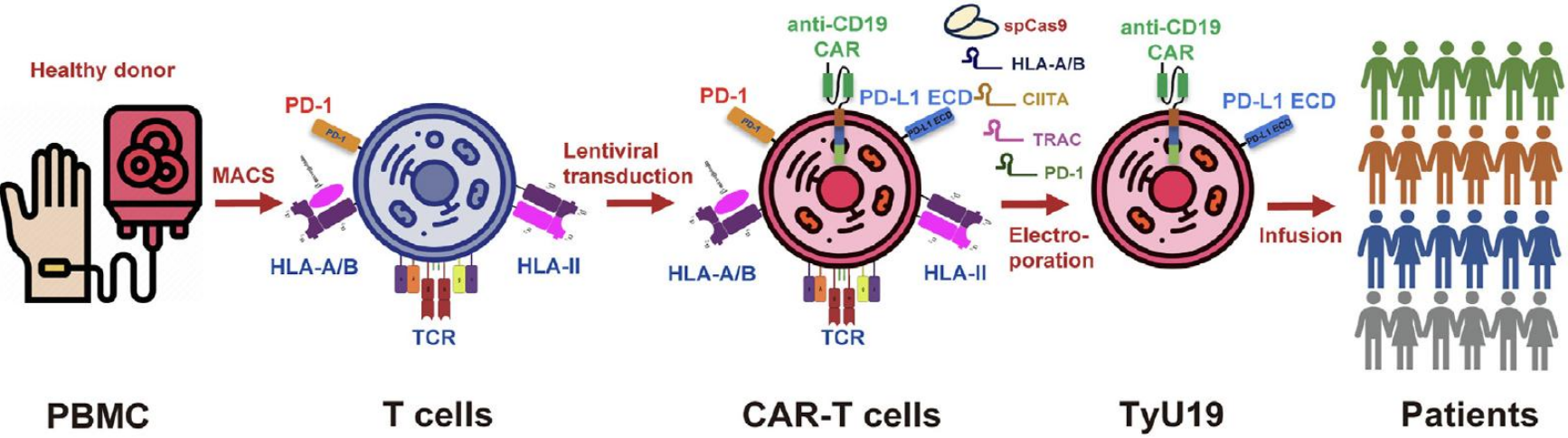
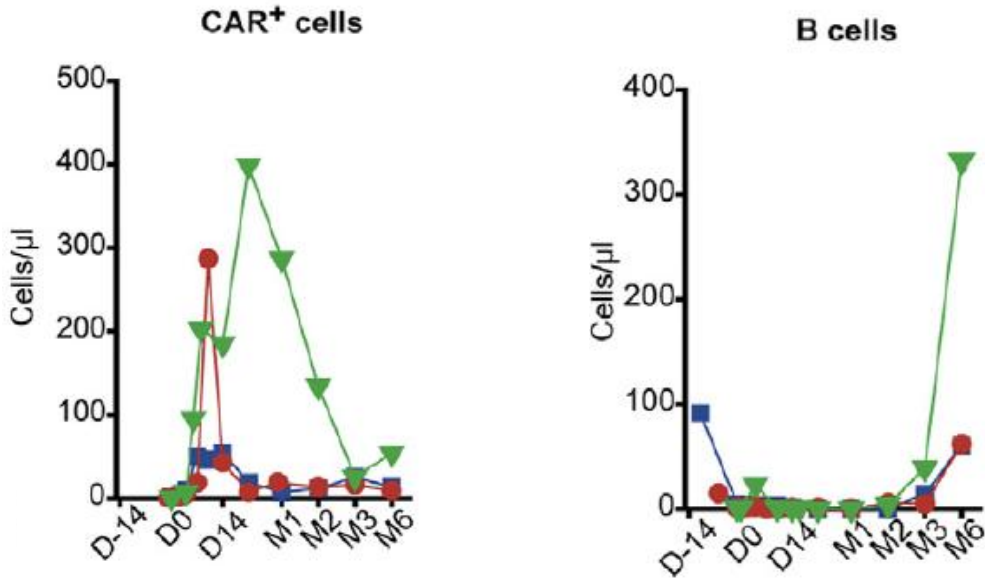
Cell

Sep 2024

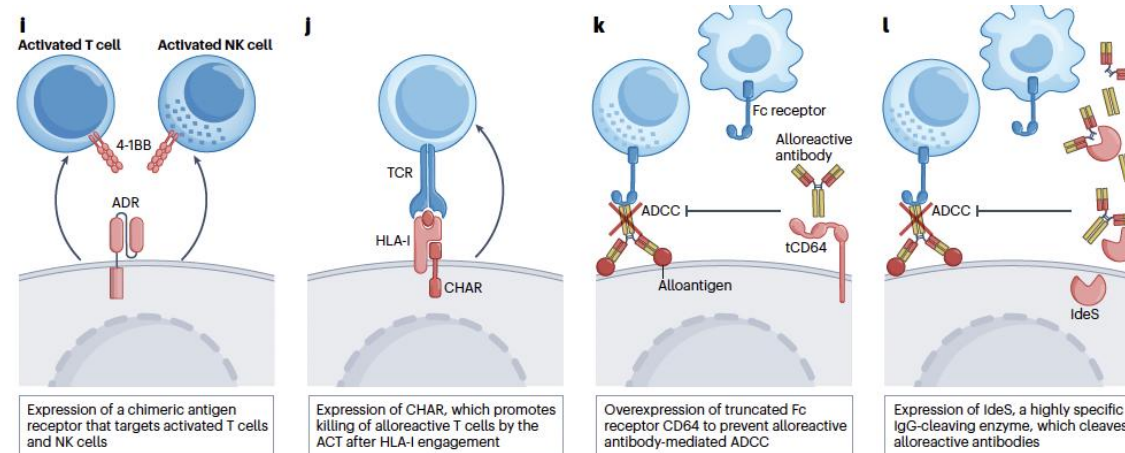
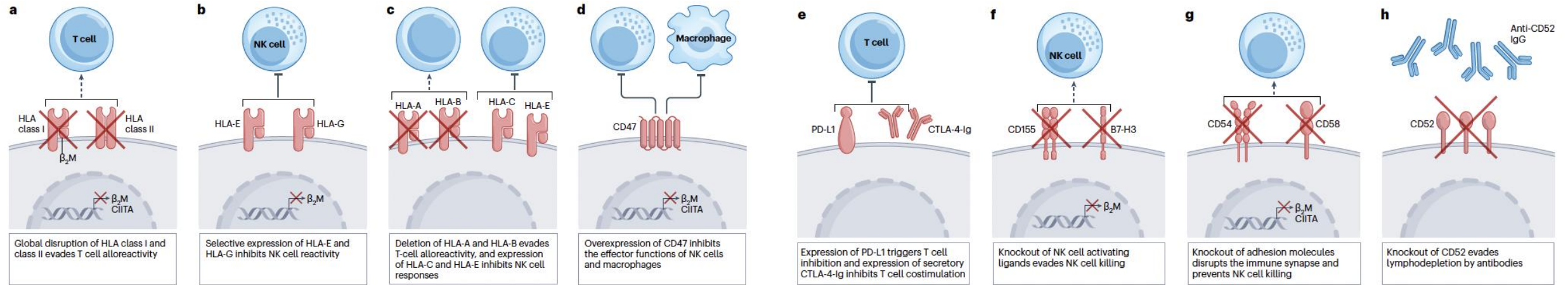
Article  
**Allogeneic CD19-targeted CAR-T therapy in patients with severe myositis and systemic sclerosis**

Xiaobing Wang,<sup>1,2,22</sup> Xin Wu,<sup>1,2,22</sup> Binghe Tan,<sup>3,4,22</sup> Liang Zhu,<sup>5,22</sup> Yi Zhang,<sup>1</sup> Li Lin,<sup>1,2</sup> Yi Xiao,<sup>6</sup> An Sun,<sup>6</sup> Xinyi Wan,<sup>6</sup> Shiyuan Liu,<sup>6</sup> Yanfang Liu,<sup>2,7</sup> Na Ta,<sup>7</sup> Hang Zhang,<sup>8</sup> Jialin Song,<sup>8</sup> Ting Li,<sup>1</sup> Ling Zhou,<sup>1</sup> Jian Yin,<sup>1</sup> Lingying Ye,<sup>1</sup> Hongjuan Lu,<sup>1</sup> Jinwei Hong,<sup>9</sup> Hui Cheng,<sup>9</sup> Ping Wang,<sup>9</sup> Weiqing Li,<sup>10</sup> Jianfeng Chen,<sup>3</sup> Jin Zhang,<sup>11</sup> Jing Luo,<sup>12</sup> Miaozen Huang,<sup>12</sup> Lehong Guo,<sup>13</sup> Xiaoming Pan,<sup>14</sup> Yi Jin,<sup>15</sup> Wenjing Ye,<sup>16</sup> Lie Dai,<sup>17</sup> Jian Zhu,<sup>18</sup> Lingyun Sun,<sup>19</sup> Biao Zheng,<sup>4</sup> Dali Li,<sup>3,4</sup> Yanran He,<sup>20</sup> Mingyao Liu,<sup>3,4,\*</sup> Huaxiang Wu,<sup>5,\*</sup> Bing Du,<sup>3,4,\*</sup> and Huji Xu<sup>1,2,12,21,23,\*</sup>

N = 3 patients



# Strategies for immune evasion by allogeneic CAR T cells



***Thank you for your attention!***

***Email: [sneelapu@mdanderson.org](mailto:sneelapu@mdanderson.org)***