Penn Medicine

CAR-T FOR T-CELL LYMPHOMA – Are we catching up?

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Disclosures

- **Consultancy:** Acrotech; Citius; Daiichi Sankyo; Kyowa Kirin; ONO Pharmaceuticals
- **DSMC:** Janssen
- **Research support:** Vittoria Biotherapeutics

Overview

The Roadblocks in Developing CAR-T in T-cell lymphomas

Targeting CD30

Targeting CD7

Targeting CD5

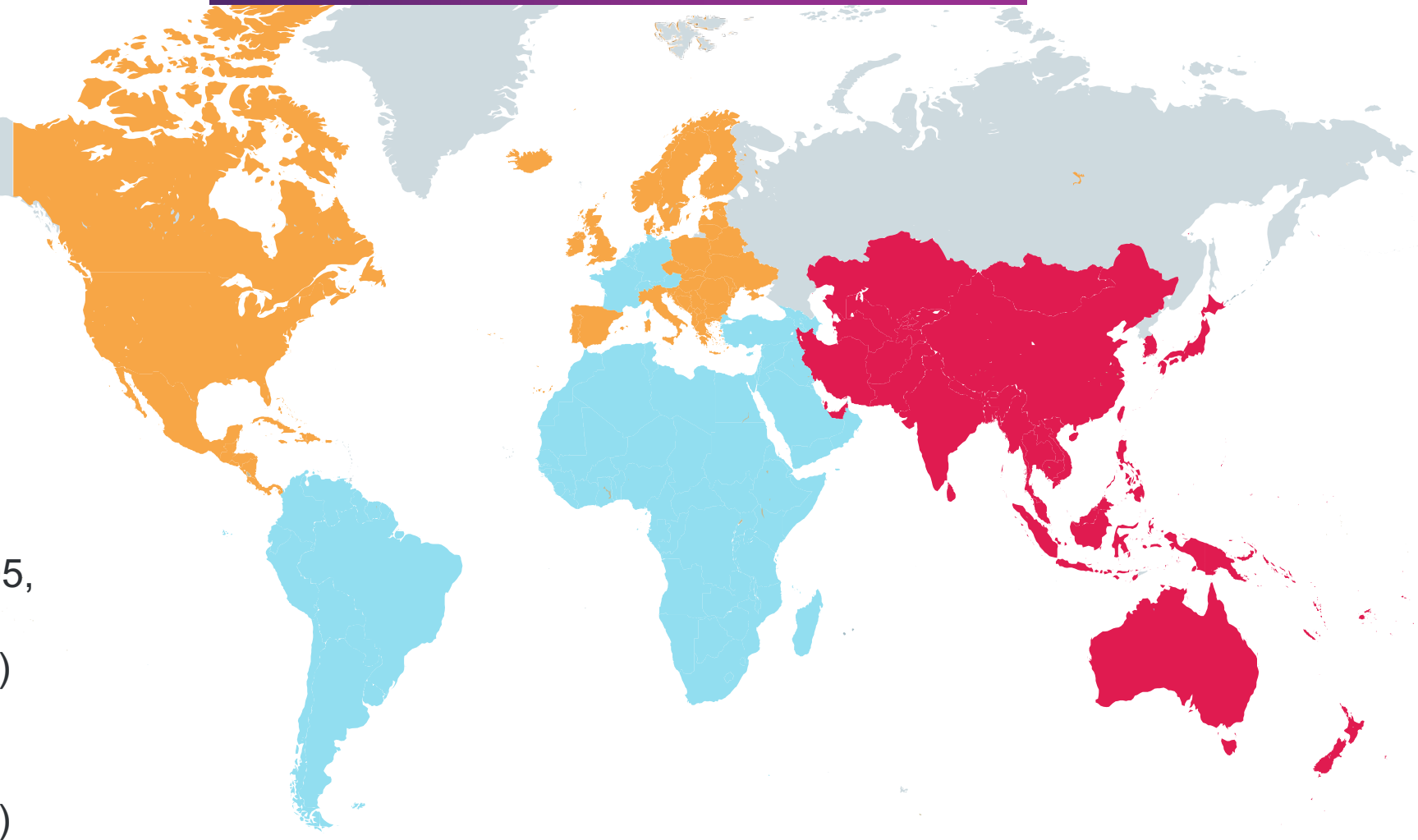
Other Notable Targets in TCL

T-cell Lymphomas

In the US, 10-15% of NHLs are T-cell lymphomas 10,000+ cases/year → Orphan designation eligible

From 1992 to 2005, peripheral T-cell lymphoma (PTCL) incidence **increased by 280%** (SEER)

T-CELL LYMPHOMA – GROWTH RATE BY REGION



Source: Adapted from Mordor Intelligence

Data from UK Haematology Malignancy Research Network Smith et al. Br J Cancer (2015) 112, 1575-1584

The WHO Classification of Haematolymphoid Tumours 5th edition

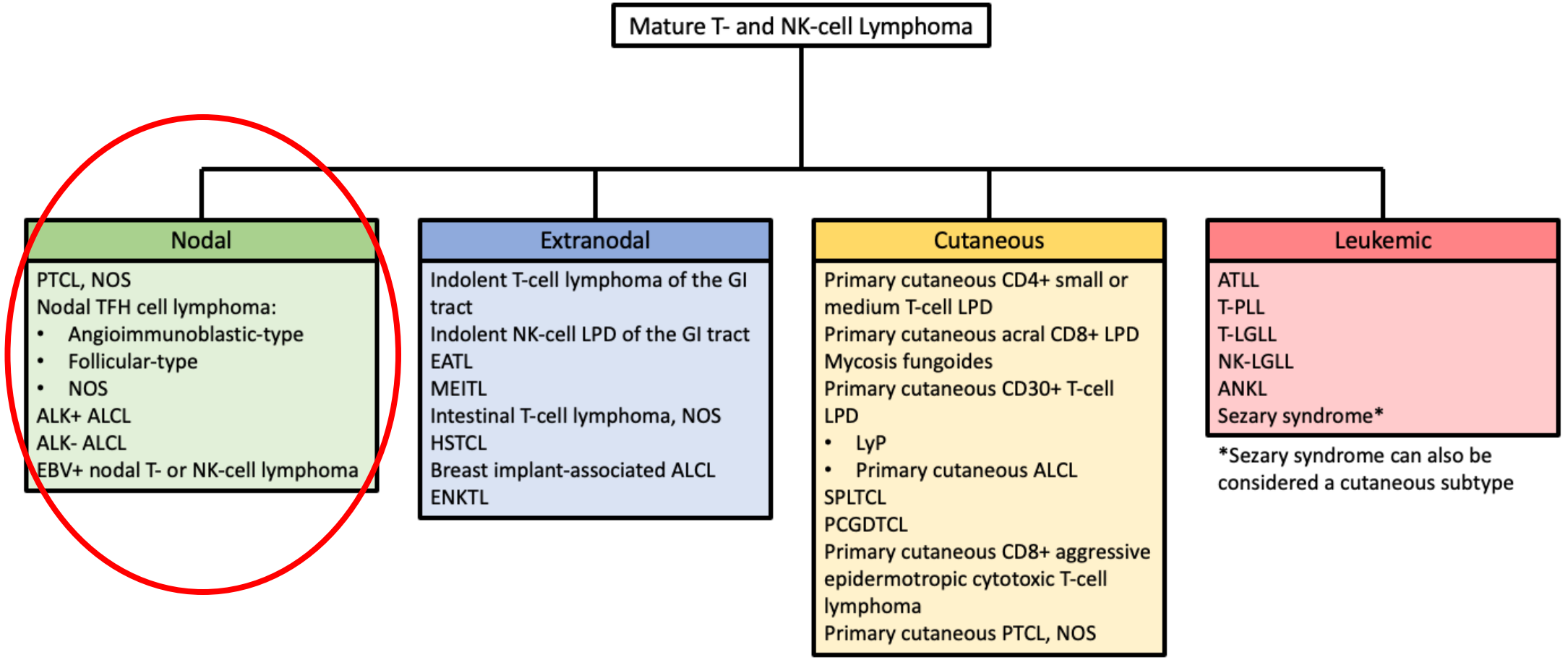
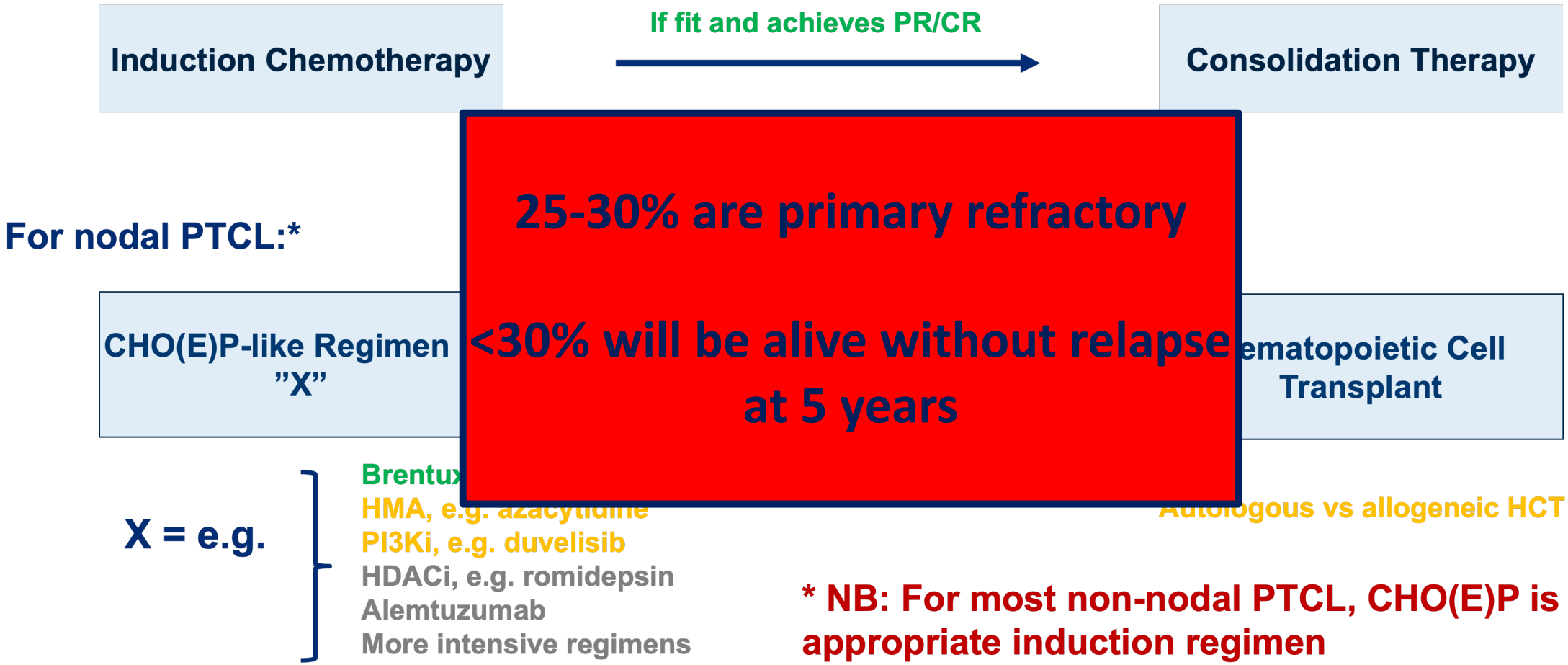


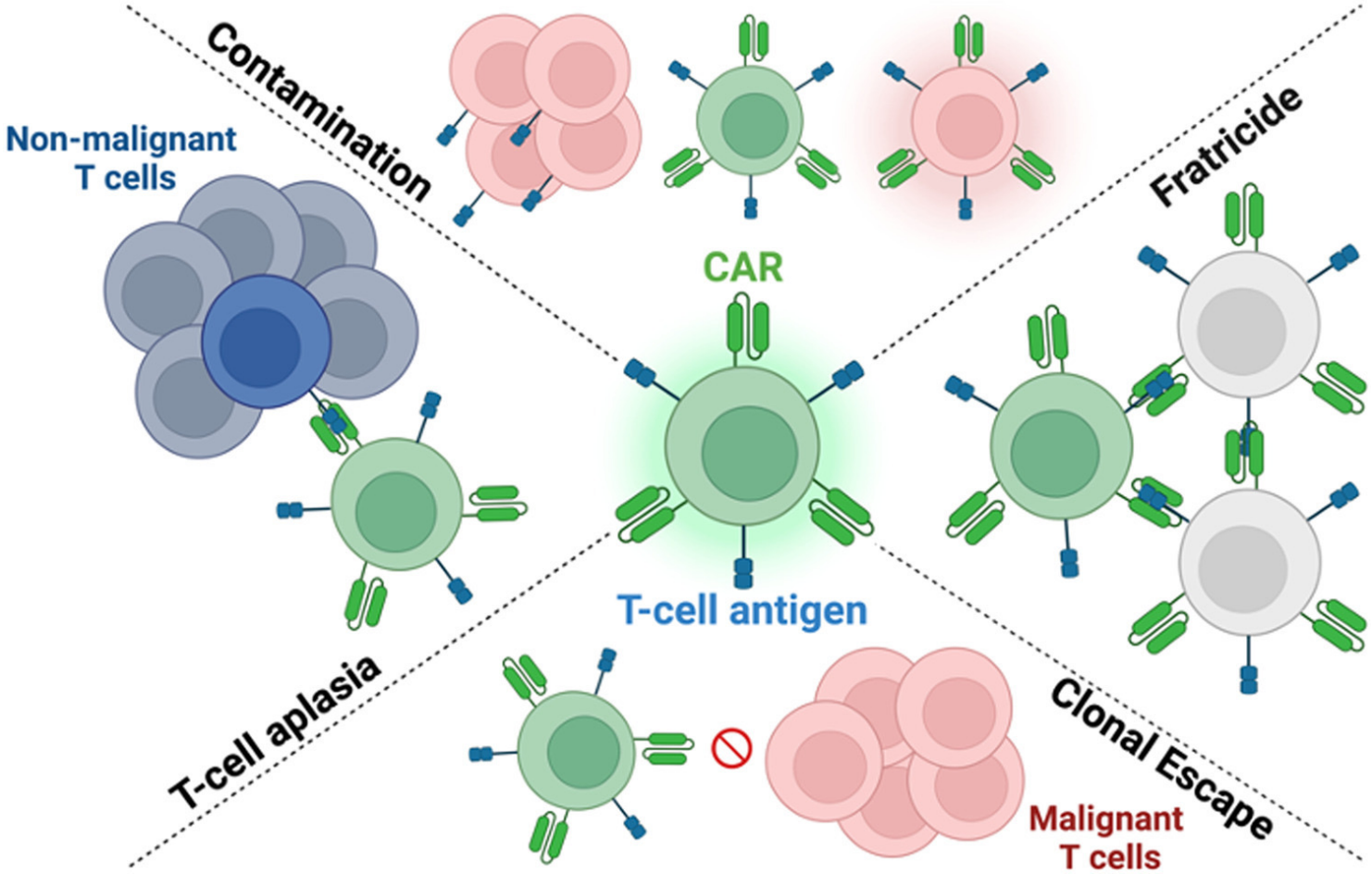
Figure from Bhansali RS and Barta SK et al, unpublished
Cree, I.A. The WHO Classification of Haematolymphoid Tumours. *Leukemia 2022, 36, 1701-1702*

Current Treatment Approach for Newly Diagnosed T-Cell Lymphomas



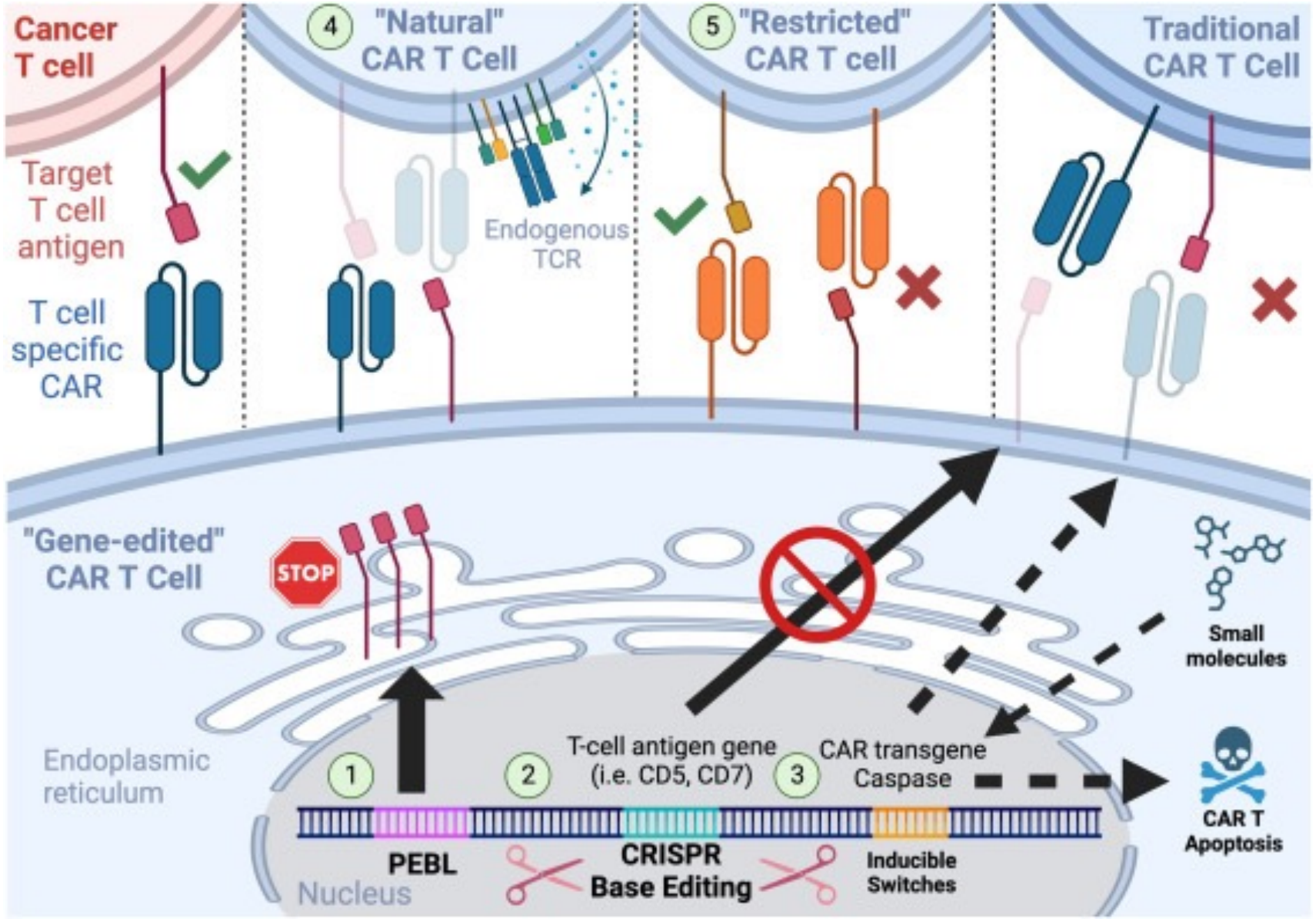
*** NB: For most non-nodal PTCL, CHO(E)P is not the appropriate induction regimen**

Challenges for CART cell therapy in T-cell malignancies



PROBLEM:
Shared antigens between **tumor** and **normal** T cells

Angelos MG, Patel RP, Ruella M, and Barta SK. Transplantation and Cellular Therapy 2024: 30(2): 171-186



Strategies to overcome those challenges

Angelos MG, Patel RP, Ruella M, and Barta SK. Transplantation and Cellular Therapy 2024: 30(2): 171-186

CT.GOV List of CAR T-cell Therapy Trials for T-Cell Malignancies as of March 21, 2025

NCT Number	Study Title	Study Status	Conditions
NCT03081910	Autologous T-Cells Expressing a Second Generation CAR for Treatment of T-Cell Malignancies Expressing CD5 Antigen	RECRUITING	T-cell Acute Lymphoblastic Lymphoma|T-non-Hodgkin Lymphoma|T-cell Acute Lymphoblastic Leukemia
NCT05110742	Phase I/II Study of CD5 CAR Engineered IL15-Transduced Cord Blood-Derived NK Cells in Conjunction With Lymphodepleting C	RECRUITING	Hematological Malignancy
NCT06316856	CD5 Chimeric Antigen Receptor (CAR) T Cells in Subjects with Relapsed or Refractory T-cell Malignancies	RECRUITING	T-Cell Acute Lymphocytic Leukemia|Acute Lymphoblastic Leukemia, in Relapse|Refractory Acute Lymphoblastic Leukemia|T-cell Malignancies
NCT06420076	Sequential CAR-T Cells Therapy for CD5/CD7 Positive T-cell Acute Lymphoblastic Leukemia and Lymphoblastic Lymphoma Usin	RECRUITING	T Cell Lymphoma|T Cell Leukemia|T-cell Acute Lymphoblastic Leukemia|T-Cell Lymphoma of CNS|T Cell Prolymphocytic Leukemia|T Cell Childhood ALL
NCT06420089	CD5-deleted Chimeric Antigen Receptor Cells (Senza5 CART5) for T Cell Non-Hodgkin Lymphoma (NHL)	RECRUITING	T Cell Non-Hodgkin Lymphoma
NCT06534060	MB-105 in Patients With CD5 Positive T-cell Lymphoma	RECRUITING	Lymphoma, T-Cell
NCT06633341	Targeting CD5 CAR-T Cells in the Treatment of r/r CD5+ T-lymphoma	RECRUITING	T-lymphoblastic Lymphoma
NCT05138458	A Study of MT-101 in Subjects With CD5+ Relapsed/Refractory TCL	SUSPENDED	Lymphoma, T-Cell, Peripheral|Lymphoma, T-Cell, Cutaneous|Mycosis Fungoides|Adoptive Cellular Immunotherapy|Cell Therapy
NCT04594135	Anti-CD5 CAR T Cells for Relapsed/Refractory T Cell Malignancies	UNKNOWN	T-cell Acute Lymphoblastic Leukemia|T-cell Non-Hodgkin Lymphoma
NCT04767308	Safety and Efficacy of CT125A Cells for Treatment of Relapsed/Refractory CD5+ Hematopoietic Malignancies	UNKNOWN	CD5+ Relapsed/Refractory Hematopoietic Malignancies|Chronic Lymphocytic Leukemia (CLL)|Mantle Cell Lymphoma (MCL)|Diffuse Large B-cell Lymphom
NCT05596266	CD5 CAR-T Therapy for Refractory/Relapsed CD5+ T-cell Acute Lymphoblastic Leukemia	RECRUITING	T-cell Acute Lymphoblastic Leukemia
NCT06874946	Nanobody-Based Anti-CD5 CAR-T for Relapsed/Refractory T-ALL/LBL	RECRUITING	Precursor T-Cell Lymphoblastic Leukemia-Lymphoma
NCT05032599	Donor-Derived CD5 CAR T Cells in Subjects with Relapsed or Refractory T-Cell Acute Lymphoblastic Leukemia	TERMINATED	T-Cell Acute Lymphoblastic Leukemia
NCT05487495	Donor-Derived CD5 CAR T (CT125B) Cells for Relapsed or Refractory T- Cell Acute Lymphoblastic Leukemia/Lymphoma	WITHDRAWN	T-Cell Acute Lymphoblastic Leukemia/Lymphoma
NCT01192464	EBV CTLs Expressing CD30 Chimeric Receptors For CD 30+ Lymphoma	ACTIVE_NOT_RECRUITING	Hodgkin's Lymphoma|Non-Hodgkin's Lymphoma
NCT02663297	Administration of T Lymphocytes for Prevention of Relapse of Lymphomas	ACTIVE_NOT_RECRUITING	Hodgkin Disease|Lymphoma|Lymphoma, Non-Hodgkin|Immune System Diseases|Immunoproliferative Disorders|Lymphatic Diseases|Lymphoproliferati
NCT04526834	Phase 1 Study of Autologous CD30.CAR-T in Relapsed or Refractory CD30 Positive Non-Hodgkin Lymphoma	ACTIVE_NOT_RECRUITING	Anaplastic Large Cell Lymphoma|Peripheral T Cell Lymphoma|Extranodal NK/T-cell Lymphoma|Diffuse Large B Cell Lymphoma|Primary Mediastinal Large B
NCT03049449	T Cells Expressing a Fully-Human Anti-CD30 Chimeric Antigen Receptor for Treating CD30-Expressing Lymphomas	COMPLETED	Lymphoma, Large-Cell, Anaplastic|Enteropathy-Associated T-Cell Lymphoma|Lymphoma, Large B-Cell, Diffuse|Lymphoma, Extranodal NK-T-Cell|Lymphor
NCT06176690	Constitutive IL7R (C7R) Modified Banked Allogeneic CD30.CAR EBVSTS for CD30-Positive Lymphomas	NOT_YET_RECRUITING	CD30-Positive Diffuse Large B-Cell Lymphoma|Anaplastic Large Cell Lymphoma, T Cell and Null Cell Type|Anaplastic Large Cell Lymphoma, ALK-Positive|P
NCT02690545	Study of CD30 CAR for Relapsed/Refractory CD30+ HL and CD30+ NHL	RECRUITING	Lymphoma|Lymphoma, Non-Hodgkin|Immune System Diseases|Immunoproliferative Disorders|Lymphatic Diseases|Lymphoproliferative Disorders|Neop
NCT02917083	CD30 CAR T Cells, Relapsed CD30 Expressing Lymphoma (RELY-30)	RECRUITING	Hodgkin's Lymphoma|Non-Hodgkin Lymphoma
NCT03383965	CD30 Targeted CAR-T in Treating CD30-Expressing Lymphomas	RECRUITING	Hodgkin Lymphoma|Anaplastic Large Cell Lymphoma
NCT03602157	Study of CAR-T Cells Expressing CD30 and CCR4 for r/r CD30+ HL and CTCL	RECRUITING	Lymphoma|Immune System Diseases|Immunoproliferative Disorders|Lymphatic Diseases|Lymphoproliferative Disorders|Neoplasms|Cutaneous Lympho
NCT04083495	CD30 CAR for Relapsed/Refractory CD30+ T Cell Lymphoma	RECRUITING	Peripheral T Cell Lymphoma
NCT04288726	Allogeneic CD30.CAR-EBVSTs in Patients with Relapsed or Refractory CD30-Positive Lymphomas	RECRUITING	Extranodal Natural Killer/T-Cell Lymphoma, Nasal Type|Classical Hodgkin Lymphoma
NCT06494371	A Study of LCAR-HL30 in Subjects With Relapsed/Refractory Hodgkin's Lymphoma and Anaplastic Large Cell Lymphoma	RECRUITING	Hodgkin's Lymphoma|Anaplastic Large Cell Lymphoma
NCT06532643	Safety and Efficacy of Anti-CD20/CD30 CAR-T Cells in Subjects with Relapsed/Refractory Lymphoma	RECRUITING	Relapsed/Refractory Lymphoma
NCT01645293	Multicentre Phase I Trial of Engineered T Cells for Patients With Relapsed or Refractory Primary Cutaneous CD30+ Large T Cell Ly	UNKNOWN	CD30 Positive Cutaneous T Cell Lymphoma|CD30 Positive Transformed Mycosis Fungoides
NCT02274584	CAR T Cells Targeting CD30 Positive Lymphomas (4SCAR30273)	UNKNOWN	Lymphomas
NCT04008394	Anti-CD30 CAR-T Therapy in Patients With Refractory/Relapsed Lymphocyte Malignancies	UNKNOWN	Adult T-Cell Lymphoma/Leukaemia|Anaplastic Large Cell Lymphoma|Angioimmunoblastic T-cell Lymphoma|NK/T-cell Lymphoma|Peripheral T Cell Lympho
NCT04653649	CAR T-cells Against CD30 (HSP-CAR30) for Relapsed/ Refractory Hodgkin and T-cell Lymphoma.	UNKNOWN	Hodgkin Lymphoma, Adult|T Cell Lymphoma
NCT05208853	An Exploratory Clinical Study Evaluating the Safety and Efficacy of Anti CD30 CAR T Cells in Patients With CD30+ Relapsed/Refr	UNKNOWN	Hodgkin Lymphoma|NK/T Cell Lymphoma|Peripheral T Cell Lymphoma, Unspecified|Angioimmunoblastic T-cell Lymphoma|Anaplastic Large Cell Lymphor
NCT01316146	Administration of T Lymphocytes for Hodgkin's Lymphoma and Non-Hodgkin's Lymphoma (CART CD30)	WITHDRAWN	Non-Hodgkin's Lymphoma|Hodgkin's Lymphoma
NCT04952584	Allogeneic CD30 Chimeric Antigen Receptor Epstein-Barr Virus-Specific T Lymphocytes in Relapsed or Refractory CD30-Positive	WITHDRAWN	Extranodal Natural Killer/T-Cell Lymphoma, Nasal Type|Classical Hodgkin Lymphoma
NCT04702841	CAR - Î³ Î´ T Cells in the Treatment of Relapsed and Refractory CD7 Positive T Cell-derived Malignant Tumors	UNKNOWN	CAR|Malignant Tumors
NCT05909527	A Clinical Study of CAR-T Treating Relapsed or Refractory T Cell Lymphoblastic Acute Leukemia/ Lymphoma	ACTIVE_NOT_RECRUITING	T-Cell Acute Lymphocytic Leukemia
NCT04572308	Cell Therapy for CD7 Positive T-cell Acute Lymphoblastic Leukemia and Lymphoblastic Lymphoma Using CD7-Specific CAR-T Ce	COMPLETED	T-cell Acute Lymphoblastic Leukemia|Lymphoma
NCT04840875	Phase I Clinical Trial of Autologous CD7-CAR T Cell Therapy for High-risk Acute T-cell Leukemia/lymphoma	COMPLETED	T Cell Lymphoma|T-cell Leukemia
NCT04984356	A Phase 1/2 Study of the Safety and Efficacy of Anti-CD7 Allogeneic CAR-T Cells (WU-CART-007) in Patients With Relapsed or R	COMPLETED	T-cell Acute Lymphoblastic Leukemia|Lymphoblastic Lymphoma
NCT05716113	CD7 CAR-T for Patients With r/r CD7+ T-ALL/T-LBL	COMPLETED	Neoplasms|Hematologic Neoplasms|Neoplasms by Site|Hematologic Diseases
NCT05902845	RD13-02 CAR-T Cell Injection for Patients With r/r CD7+ T-ALL/T-LBL	COMPLETED	Neoplasms|Hematologic Neoplasms|Hematologic Diseases
NCT05907603	Research Developmentï¼ˆRDï¼‰13-02 Chimeric Antigen Receptor(CAR) -T Cell Injection for Patients With r/r Cluster Of Differe	COMPLETED	Neoplasms|Hematologic Neoplasms|Hematologic Diseases
NCT05885464	A Study Evaluating the Safety and Efficacy of BEAM-201 in Relapsed/Refractory T-Cell Acute Lymphoblastic Leukemia (T-ALL) or	ACTIVE_NOT_RECRUITING	Lymphoblastic Lymphoma|T-Cell Lymphoblastic Leukemia|Lymphoma|Lymphoblastic Leukemia
NCT04599556	Clinical Trial for the Safety and Efficacy of Anti-CD7 CAR-T Cell Therapy for Patients With Relapsed or Refractory CD7 Positive H	RECRUITING	CD7+ Acute Leukemia|CD7+ Lymphoma
NCT05043571	CARTALL: Chimeric-Antigen Receptor (CAR) T-Cell Therapy for Relapsed/ Refractory T-Lineage Acute Lymphoblastic Leukaemia	RECRUITING	Lymphoblastic Leukemia, Acute, Childhood|Lymphoblastic Leukemia|Lymphoblastic Leukemia, Acute Adult|Lymphoblastic Leukemia in Children|CAR
NCT05626400	Clinical Study of Senl-T7 CAR T Cells in the Treatment of Relapsed and Refractory CD7+ Acute T-ALL/T-LBL	RECRUITING	T-cell Acute Lymphoblastic Leukemia|Lymphoma
NCT06064903	CD7-CAR-T Cells in Pediatric Relapsed/Refractory CD7+ T-ALL/LL	RECRUITING	T-cell Acute Lymphoblastic Leukemia|Lymphoblastic Lymphoma
NCT06514794	A Phase 2 Study of WU-CART-007, an Anti-CD7 Allogeneic CAR-T Cell Therapy inT-Cell Acute Lymphoblastic Leukemia and Lymp	RECRUITING	T-cell Acute Lymphoblastic Leukemia|Lymphoblastic Lymphoma
NCT04762485	Humanized CD7 CAR T-cell Therapy for r/r CD7+ Acute Leukemia	UNKNOWN	T Lymphoblastic Leukemia|Myeloid/Mixed Phenotype Acute Leukemia|Acute Myeloid Leukemia
NCT04785833	CD7 CAR-T in the Treatment of CD7 Positive Refractory Relapsed Acute Leukemia	UNKNOWN	T-ALL
NCT04916860	Clinical Study of SenL-T7 CAR T Cells in the Treatment of Relapsed and Refractory CD7+ T-cell Lymphoblastic Leukemia or T-cell	UNKNOWN	SenL-T7 CAR T Cells for CD7+ T-cell Lymphoblastic Leukemia or T-cell Lymphoblastic Lymphoma
NCT05170568	PA3-17 Injection Treatment of Adult Patients With CD7-positive Relapsed/Refractory Lymphoid Hematologic Malignancies	UNKNOWN	CD7-positive Relapsed/Refractory Lymphoid Hematologic Malignancies
NCT05212584	CD7 CAR-T Cell Treatment of Relapsed/Refractory CD7+ T -Acute Lymphoblastic Leukemia/ Lymphoma	UNKNOWN	Relapsed/Refractory, High Risk Hematologic Malignancies|T-ALL Lymphoma
NCT05554575	Chimeric Antigen Receptor T-Cell (CAR-T) Cells in Patients With R/R T-LBL	UNKNOWN	T Cell Lymphoblastic Lymphoma
NCT04860817	A Study of Anti-CD7 CAR-T Cells in Pediatric and Young Adult Patients With Relapse and Refractory T-ALL/ T-LBL	WITHDRAWN	T-cell Acute Lymphoblastic Leukemia|T Lymphoblastic Lymphoma
NCT05454241	CD7 CAR-T for Patients With r/r CD7+ Hematologic Malignancies	COMPLETED	Hematological Malignancies
NCT05923541	RD13-02 for Patients With r/r CD7+ T Cell Hematologic Malignancies	COMPLETED	Hematologic Malignancies
NCT05979792	Clinical Study of CD7 CAR-T Cell Injection in the Treatment of Patients With Relapsed or Refractory CD7-positive Peripheral T Ce	NOT_YET_RECRUITING	Peripheral T Cell Lymphoma
NCT05290155	Anti-CD7 CAR-T Cell Therapy for Relapse and Refractory CD7 Positive T Cell Malignancies	RECRUITING	T Lymphoblastic Leukemia/Lymphoma|T-cell Acute Lymphoblastic Leukemia|Peripheral T Cell Lymphoma|Angioimmunoblastic T-cell Lymphoma|Anaplasti
NCT05377827	Dose-Escalation and Dose-Expansion Study to Evaluate the Safety and Tolerability of Anti-CD7 Allogeneic CAR T-Cells (WU-CAR	RECRUITING	T-Cell Non-Hodgkin Lymphoma|Acute Myeloid Leukemia|Angioimmunoblastic T-cell Lymphoma|Enteropathy-Associated T-Cell Lymphoma|Monomorphic
NCT05827835	CD7 CAR-T Bridging to alloHSCT for R/R CD7+Malignant Hematologic Diseases	RECRUITING	Hematologic Diseases|Neoplasms
NCT05895994	Research Development13(RD13)-02 Cell Injection in Patients With Relapsed or Refractory Cluster Of Differentiation 7(CD7)-Po	RECRUITING	Neoplasms|Hematologic Neoplasms|Neoplasms by Site|Hematologic Diseases
NCT05995028	Universal 4SCAR7U Targeting CD7-positive Malignancies	RECRUITING	T-cell Acute Lymphoblastic Leukemia|T-cell Acute Lymphoblastic Lymphoma|Acute Myeloid Leukemia|NK Cell Lymphoma
NCT06720324	CD7-specific CAR-T Cell in the Treatment of CD7-positive Relapsed/Refractory Hematologic Tumors	RECRUITING	Hematologic Malignancy
NCT04934774	Non-gene Edited Anti-CD7 CAR T Cells for Relapsed/Refractory T Cell Malignances	UNKNOWN	T-cell Acute Lymphoblastic Leukemia|T-cell Acute Lymphoblastic Lymphoma|T-cell Non-Hodgkin Lymphoma
NCT02742727	CAR-pNK Cell Immunotherapy in CD7 Positive Leukemia and Lymphoma	UNKNOWN	Acute Myeloid Leukemia|Precursor T-Cell Lymphoblastic Leukemia-Lymphoma|T-cell Prolymphocytic Leukemia|T-cell Large Granular Lymphocytic Leukemia
NCT04264078	Anti-CD7 U-CAR-T Cell Therapy for T/NK Cell Hematologic Malignancies	UNKNOWN	T-cell Leukemia|T-cell Lymphoma
NCT04480788	CD7-CART in the Treatment of r / r CD7 Positive Hemolymph System Malignancies on Increasing Dose and Open Label Study	UNKNOWN	T Lymphoblastic Leukemia/Lymphoma|Extramedullary NK-T-cell Lymphoma, Nasal Type|Peripheral T-cell Lymphoma, Nonspecific|Angioimmunoblastic T-c
NCT04689659	Multi-centers, Open-Label, Phase 2 Study to Evaluate the Efficacy and Safety of Donor-Derived CD7 CAR T Cells in Subjects Wit	UNKNOWN	T-cell Leukemia/Lymphoma|Refractory T Lymphoblastic Leukemia/Lymphoma|Relapse/Recurrence
NCT04823091	Anti-CD7 CAR-Engineered T Cells for T Lymphoid Malignancies Malignancies	UNKNOWN	T-Cell Lymphocytic Leukemia|T-Cell Chronic Lymphocytic Leukemia|T Cell Non-Hodgkin Lymphoma
NCT04928105	Senl-T7 CAR-T Cells for Treatment of Relapsed or Refractory CD7+ Lymphoma	UNKNOWN	Lymphoma, T-Cell
NCT05059912	CD7 CAR T-cell for R/R CD7+ T Cell Lymphoma	UNKNOWN	Refractory and Relapsed T Cell Lymphoma
NCT05127135	Safety and Efficacy of ThisCART7 in Patients With Refractory or Relapsed T Cell Malignancies	UNKNOWN	T-Acute Lymphoblastic Leukemia|T-cell Non-Hodgkin Lymphoma|T-cell Acute Lymphoblastic Lymphoma
NCT05398614	SENL101 Autologous T Cell Injection in Adults With Relapsed or Refractory CD7+ Hematolymphoid Malignancies	UNKNOWN	T-ALL|Lymphoma, T-Cell
NCT03590574	Phase I/II Study Evaluating AUTO4 in Patients with TRBC1 Positive T Cell Lymphoma	ACTIVE_NOT_RECRUITING	T Cell Non-Hodgkin Lymphoma|Peripheral T-Cell Lymphoma, Not Otherwise Specified|Angioimmunoblastic T-cell Lymphoma|Anaplastic Large Cell Lymph
NCT04712864	Study of CD4-Targeted Chimeric Antigen Receptor T-Cells (CD4- CAR-T) in Subjects With Relapsed or Refractory T-Cell Lymphor	ACTIVE_NOT_RECRUITING	T-Cell Lymphoma|Peripheral T-Cell Lymphoma Refractory|Cutaneous T-Cell Lymphoma Refractory|Cutaneous T-Cell Lymphoma Recurrent|Peripheral T-C
NCT06345027	Chimeric Antigen Receptor Treatment Targeting CD70 (SEVENTY)	NOT_YET_RECRUITING	Leukemia, Myeloid, Acute|Leukemia, B-cell|Leukemia, T-Cell|Lymphoma
NCT03829540	CD4CAR for CD4+ Leukemia and Lymphoma	RECRUITING	T-cell Lymphoma|T-cell Leukemia
NCT05679895	Safety and Efficacy of OC-1 Therapy in Patients With R/R T-ALL/LL	RECRUITING	T-cell Acute Lymphoblastic Leukemia|Lymphoblastic T-Cell Lymphoma
NCT04828174	Anti-TRBC1 CAR-T Cell Therapy in Patients With TRBC1 Positive T Cell Malignancies	SUSPENDED	Peripheral T Cell Lymphoma|Angioimmunoblastic T-cell Lymphoma|Anaplastic Lymphoma|Acute T Cell Leukemia|T-lymphoblastic Lymphoma
NCT05013372	CD147-CAR T Cells for Relapsed/Refractory T Cell Non-Hodgkin's Lymphoma	UNKNOWN	T-cell Non-Hodgkin's Lymphoma
NCT04136275	CAR-37 T Cells in Hematologic Malignancies	COMPLETED	Hematologic Malignancy|Leukemia|Lymphoma|Lymphoma, B-Cell|Lymphoma, T-Cell|Lymphoma, Non-Hodgkin

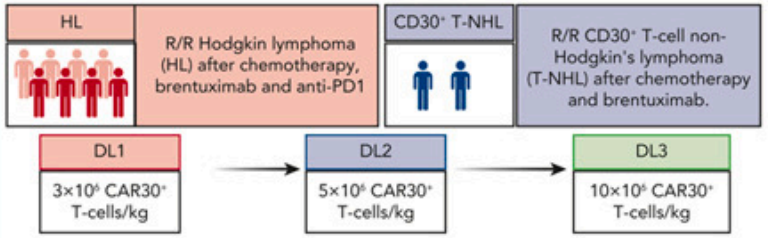
CD30 as target in T-NHL

Context of Research

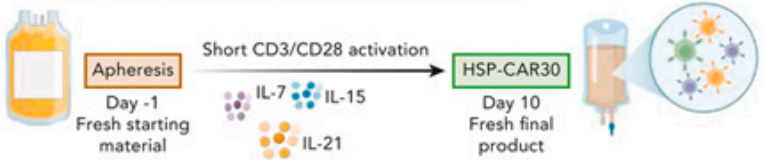
- Current CD30-directed CART therapy (CART30) has limited efficacy in patients with refractory or relapsed (R/R) CD30$^+$ lymphoma.
- Less-differentiated memory T cells have long-term persistence and enhanced antitumor efficacy.
- We have developed an autologous CART30 product (HSP-CAR30) with a significant increase in the proportion of less-differentiated CAR30$^+$ memory T cells.

Patients and Methods

- Phase 1 dose escalation clinical trial: 10 patients

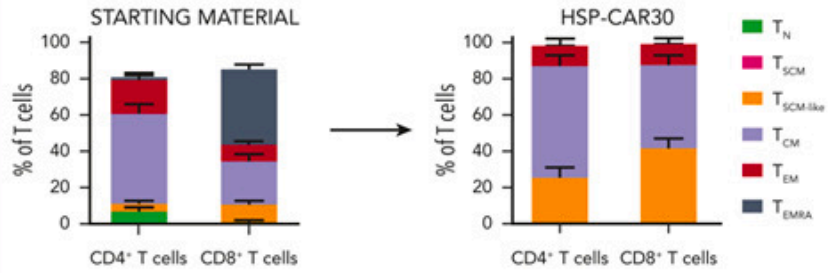


- Manufacturing procedure of HSP-CAR30

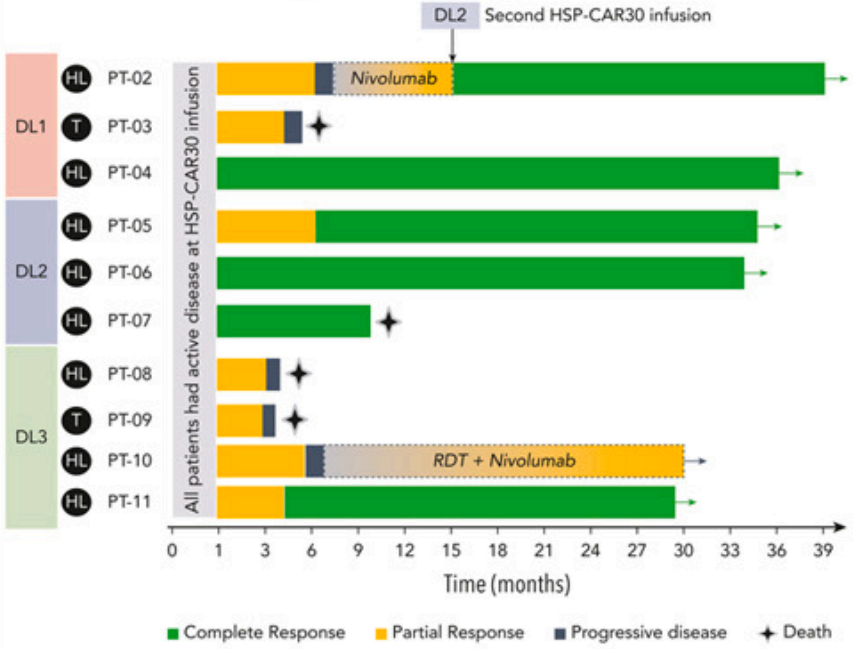


Findings

- HSP-CAR30: CART30 cell product with a high proportion of memory T cells



- HSP-CAR30 efficacy of treated patients



- ORR 72% w/ 60% CR rate
- Median FU of 34 months
- 1-year PFS 41%
- 60% of pts in CR remained in CR
- N=2 T-NHL -> PR @1 months, but died <1y of CART.
- Skin rash in 40% - resolved in 3/4 w/o intervention

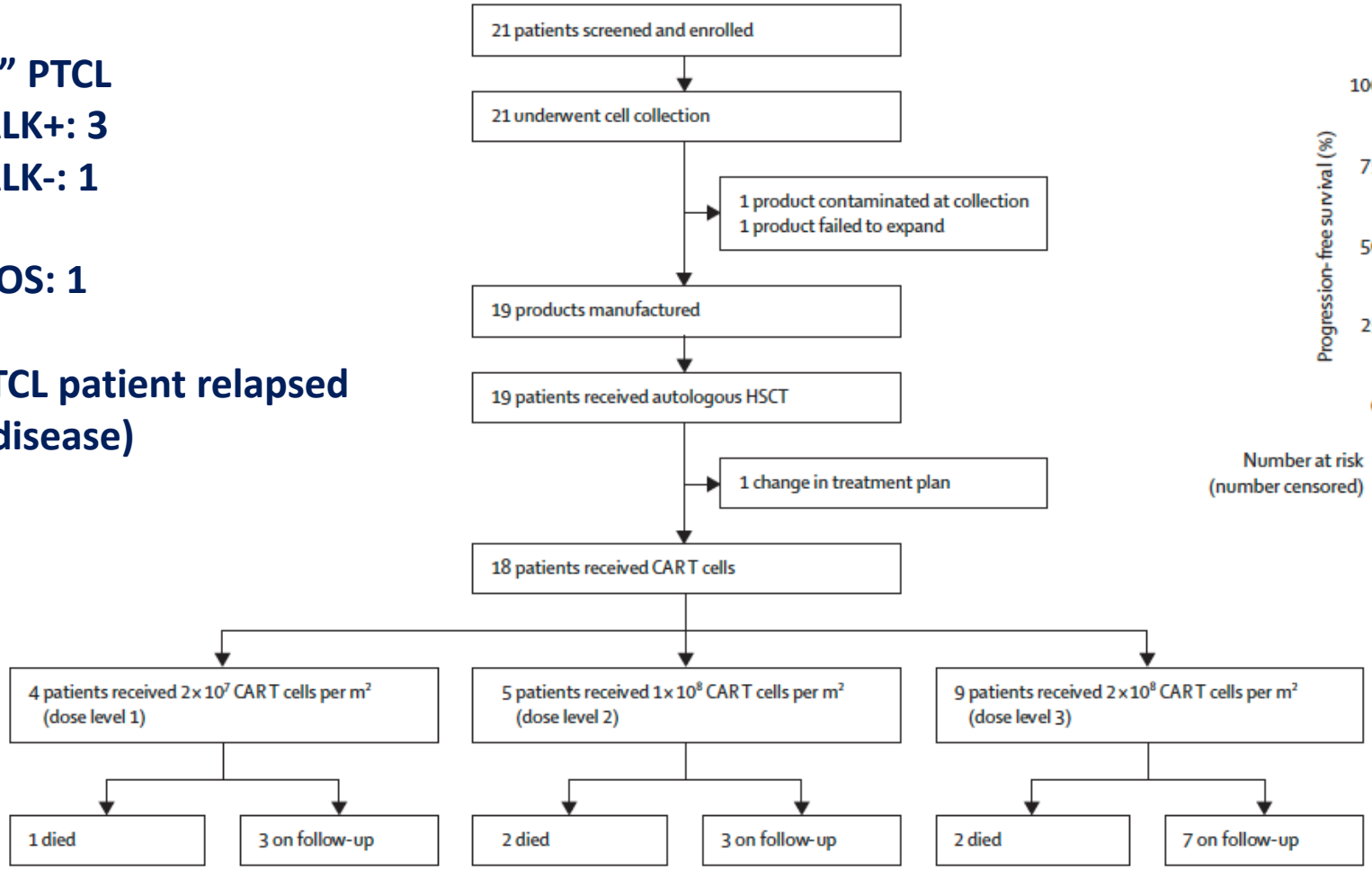
Caballero, et al. *Blood* 2025; 145 (16): 1788–1801.

Anti-CD30 CAR T cells as consolidation after autologous haematopoietic stem-cell transplantation in patients with high-risk CD30⁺ lymphoma: a phase 1 study

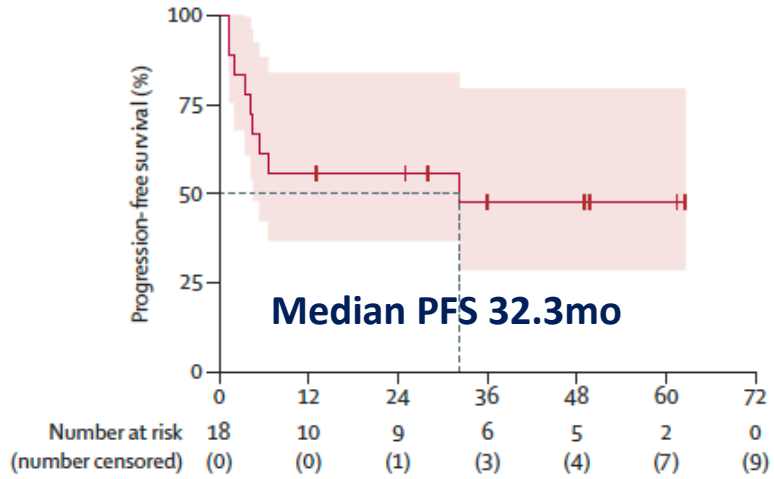
Natalie S Grover, George Hucks, Marcie L Riches, Anastasia Ivanova, Dominic T Moore, Thomas C Shea, Mary Beth Seegars, Paul M Armistead, Kimberly A Kasow, Anne W Beaven, Christopher Dittus, James M Coghill, Katarzyna J Jamieson, Benjamin G Vincent, William A Wood, Catherine Cheng, Julia Kaitlin Morrison, John West, Tammy Cavallo, Gianpietro Dotti, Jonathan S Serody, Barbara Savoldo

N=6 "CD30+" PTCL
- **ALCL, ALK+: 3**
- **ALCL, ALK-: 1**
- **AITL: 1**
- **PTCL-NOS: 1**

5 out of 6 PTCL patient relapsed (n=1 CD30- disease)



PFS for all infused patients



Grover NS, et al. Lancet Haematology 2024

CD30 CART in T-cell NHL

Publication	Target	Diagnosis	Pts w/ T-cell malignancy	Age	Type of CART	Lympho-depletion	Cell dose	Response	Survival	Toxicities	Infection/ CMV & EBV
Ramos, et al. J Clin Invest 2017	CD30	CD30+ LPD	N=2 (pcALCL; Alk+ ALCL)	35 (20-65)	Auto T cell	No LD	$2x10^7$-$2x10^8$ cells/m^2	N=1 PD; n=1 CR for 9 months	Both alive with disease	No CRS or ICANS	No viral infections
Vorhees, et al. Blood Adv 2020	CD30	EATL	N=1	69	Auto T cell	Benda 70mg/m^2 Flu 30mg/m^2 x3d	$2x10^8$ cells/m^2	CR	In remission >30 months	CRS: n=1 (G1); No ICANS	None reported
Brudno, et al. Blood Adv 2023	CD30	CD30+ LPD	N=1 (ALCL)		Auto T cell	Flu/Cy	0.3 - 9 × 10^6 CAR^+ T cells/kg	No response (HL 43% - n=1 CR)	Median EFS 13 weeks; mDOR 9 weeks	CRS 54% - mostly <3; ICANS 24% - all G2; rash & prolonged cytopenias	EBV reactivation in the context of prolonged steroids for rash
Caballero, et al. Blood 2025	CD30	CD30+ LPD	N=2 (PTCL-NOS; ALCL); n=11	65 x2 (21-65)	Auto T cell + IL			CR) . hs	2y PFS 40% and 2y OS 60%	No ICANS, CRS 60% - all G1; rash (40%).	Infection 50%; G3 30%

Summary:
While CD30 is an ideal target for CART therapy, as it has limited expression on normal tissue, current outcomes are challenged by the limited durability of responses.

Phase 1/2 Trial of Anti-CD7 Allogeneic WU-CART-007 in Patients with Relapsed/Refractory T-Cell Malignancies

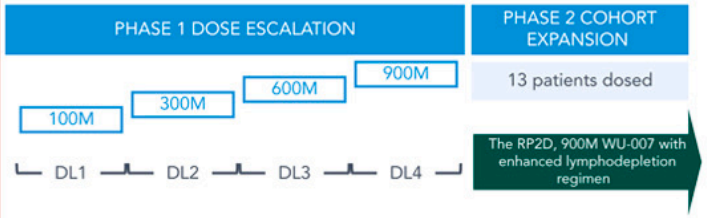
Context of Research

- Relapsed/refractory T-cell acute lymphoblastic leukemia (ALL) and lymphoma (LBL) remain challenging diseases and represent a critical unmet medical need
- WU-CART-007 is an allogeneic, CD7-targeted chimeric antigen receptor (CAR) T cell therapy, engineered from healthy donor T cells to resist fratricide

Patients and Methods

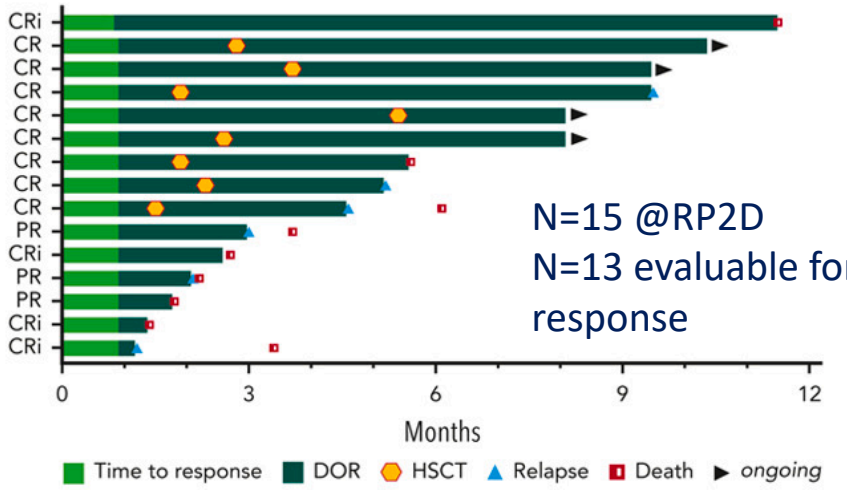
ClinicalTrials.gov ID NCT04984356

- Global phase 1-2 study
- RR T ALL/LBL
- ≥ 12 years



Findings

- Response at the recommended phase 2 dose (RP2D) of 900 million cells with enhanced lymphodepleting chemotherapy:
  - Overall response rate: 90.9%
  - Composite complete remission rate: 72.7%
- Duration of response:

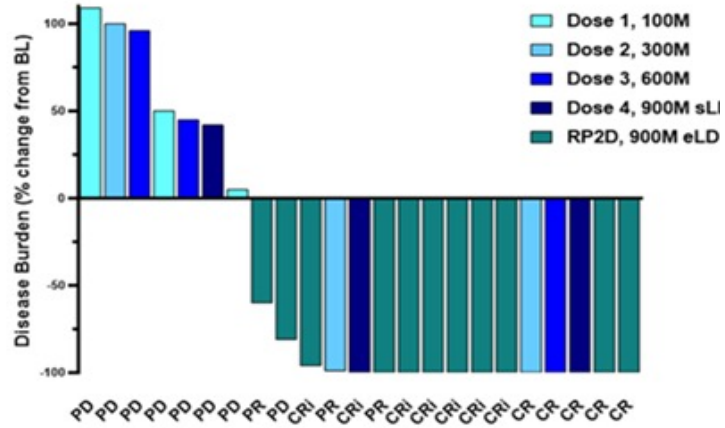


N=15 @RP2D
N=13 evaluable for response

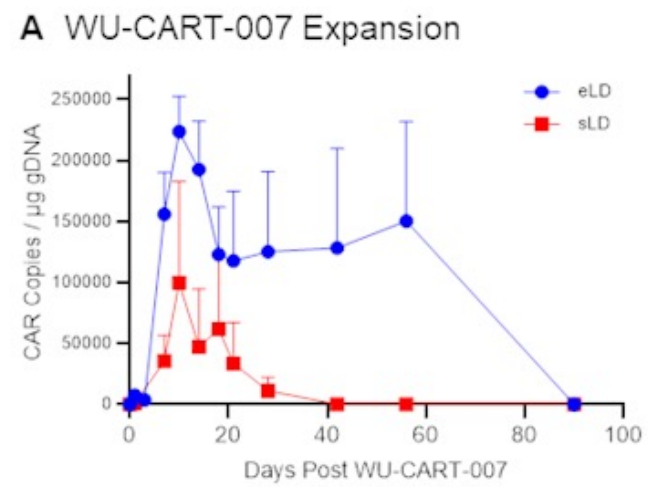
Most common TRAE: CRS in 88.5%; (19.2% grade 3–4). Others: G2 HLH n=1; n=1 G1 ICANS; n=1 aGVHD. N=3 G5 events: fungal infection n=2 and multi-organ failure (w/ PD)

Ghobadi A, et al. Blood 2025
Ghobadi A, et al. Res Sq [Preprint]. 2024 Aug 5:rs.3.rs-4676375

WU-CART-007: donor derived CRISPR-Cas9 edited to delete CD7 & T-cell receptor alpha constant gene (TRAC), transduced with a 2nd gen CAR targeting CD7



A Change from baseline in % blasts by WU-CART-007 dose, response-evaluable population

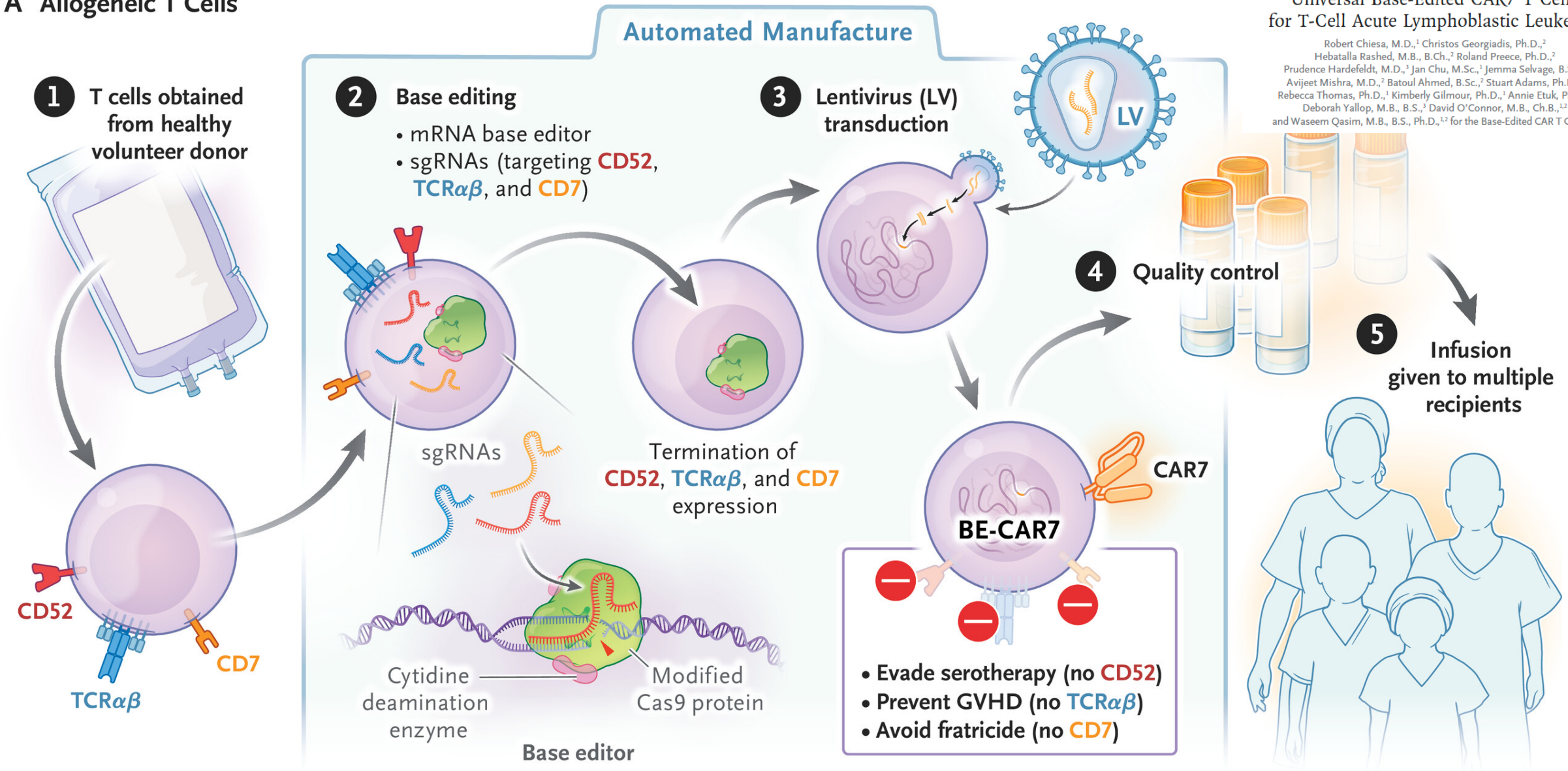


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

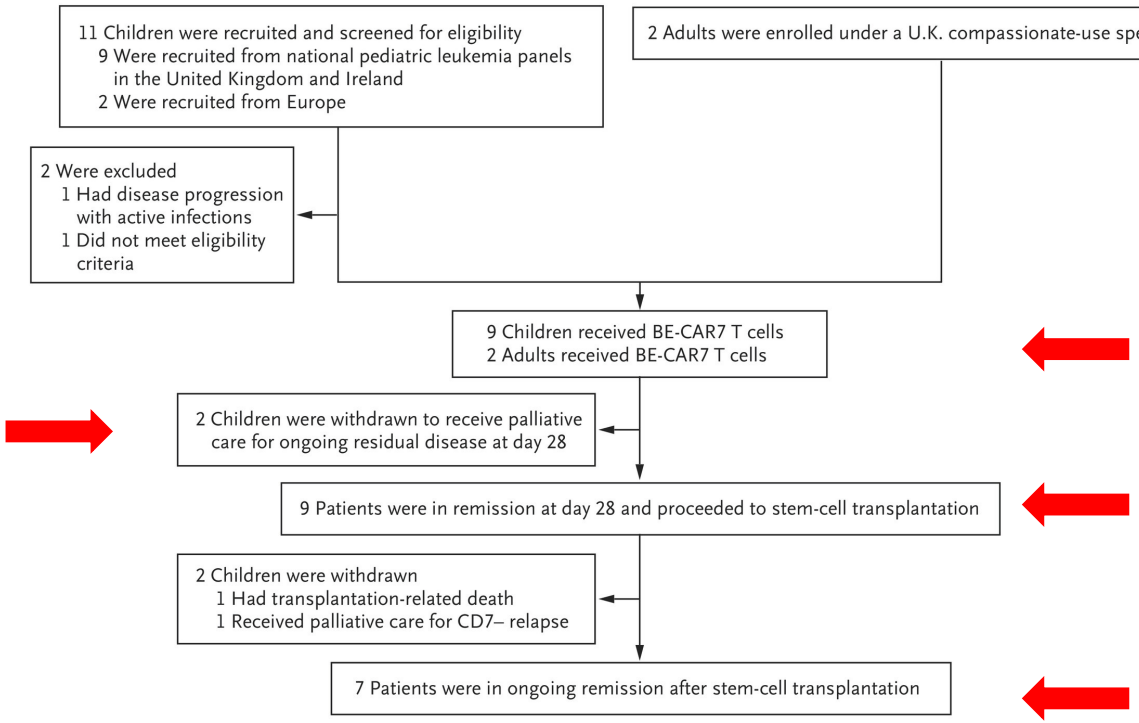
Universal Base-Edited CAR7 T Cells for T-Cell Acute Lymphoblastic Leukemia

Robert Chiesa, M.D.,[1] Christos Georgiadis, Ph.D.,[2] Hebatalla Rashed, M.B., B.Ch.,[2] Roland Preece, Ph.D.,[2] Prudence Hardefeldt, M.D.,[3] Jan Chu, M.Sc.,[1] Jemma Selvage, B.Sc.,[1] Avijeet Mishra, M.D.,[2] Batoul Ahmed, B.Sc.,[2] Stuart Adams, Ph.D.,[1] Rebecca Thomas, Ph.D.,[1] Kimberly Gilmour, Ph.D.,[1] Annie Etuk, Ph.D.,[1] Deborah Yallop, M.B., B.S.,[3] David O'Connor, M.B., Ch.B.,[1,2] and Waseem Qasim, M.B., B.S., Ph.D.,[1,2] for the Base-Edited CAR T Group*

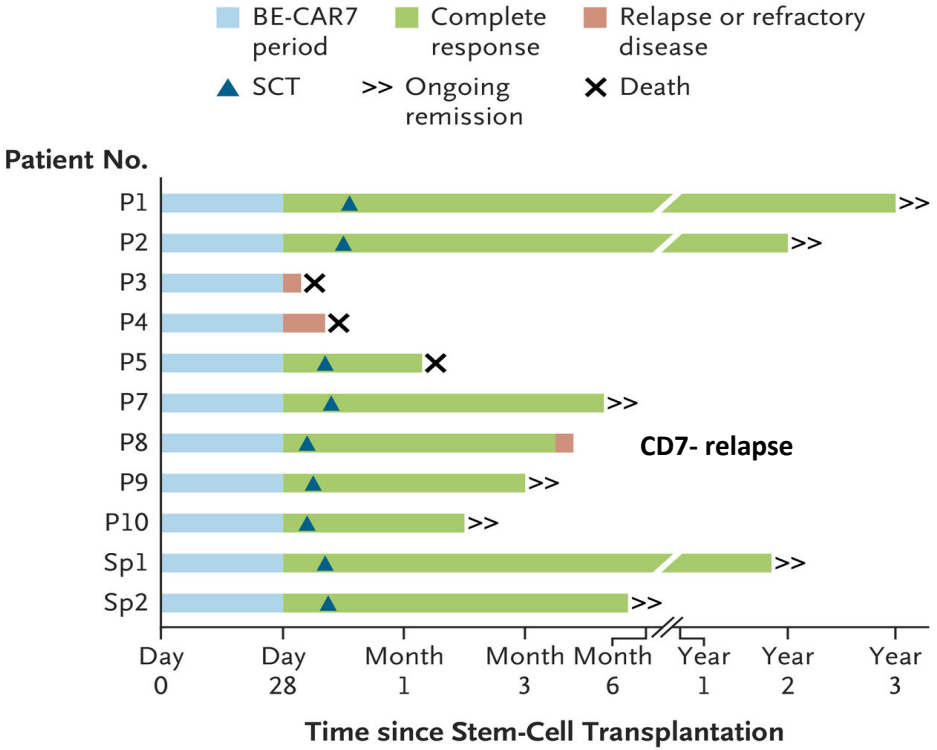


Chiesa R, et al. Universal Base-Edited CAR7 T Cells for T-Cell Acute Lymphoblastic Leukemia. N Engl J Med 2026;394:152-165

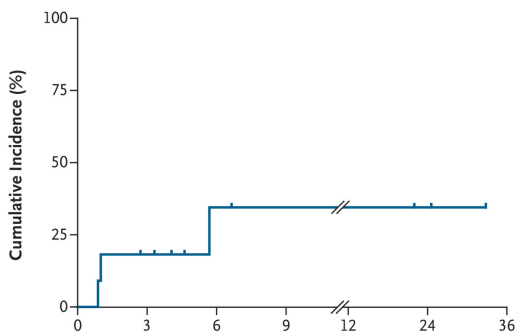
Enrollment and Screening of Patients and Administration of BE-CAR7 T Cells



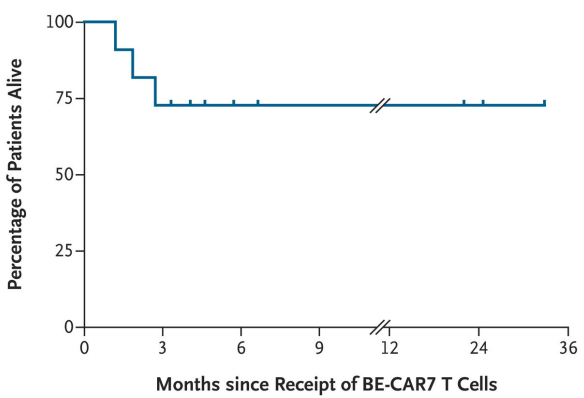
F Swimmer Plot after Receipt of BE-CAR7 T Cells



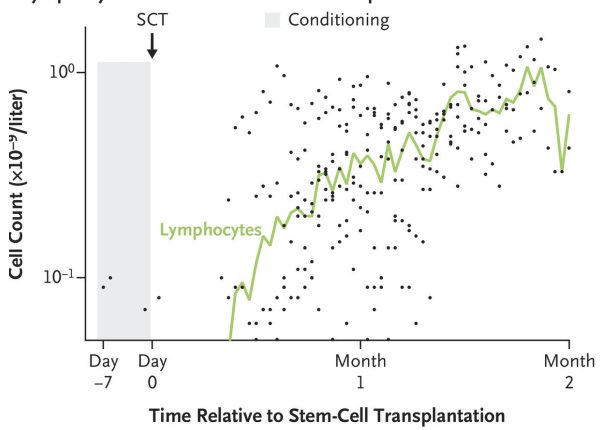
Incidence of Relapse or Refractory T-Cell ALL



D Overall Survival after Receipt of BE-CAR7 T Cells

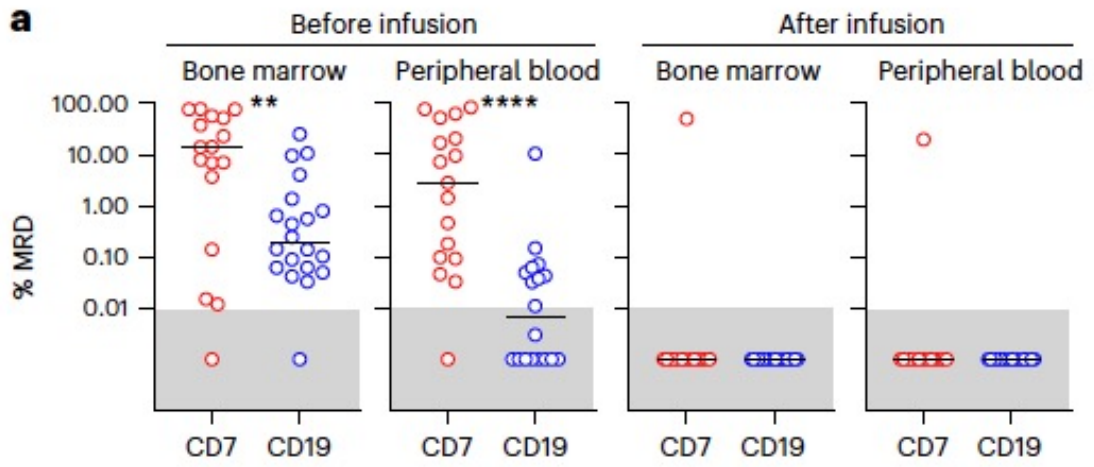


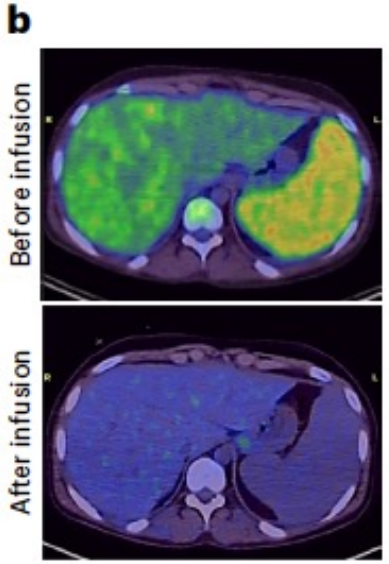
Lymphocyte Counts after Stem-Cell Transplantation

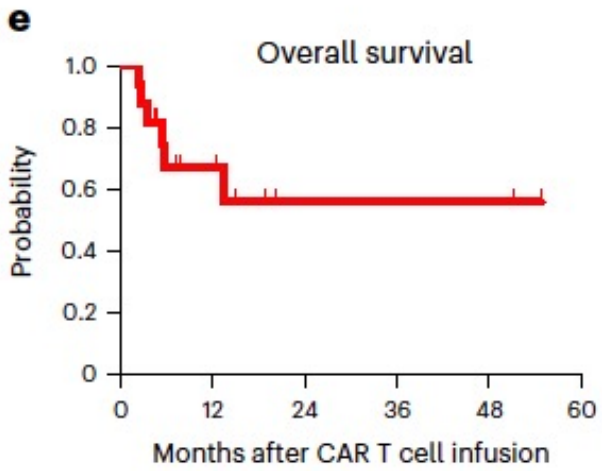


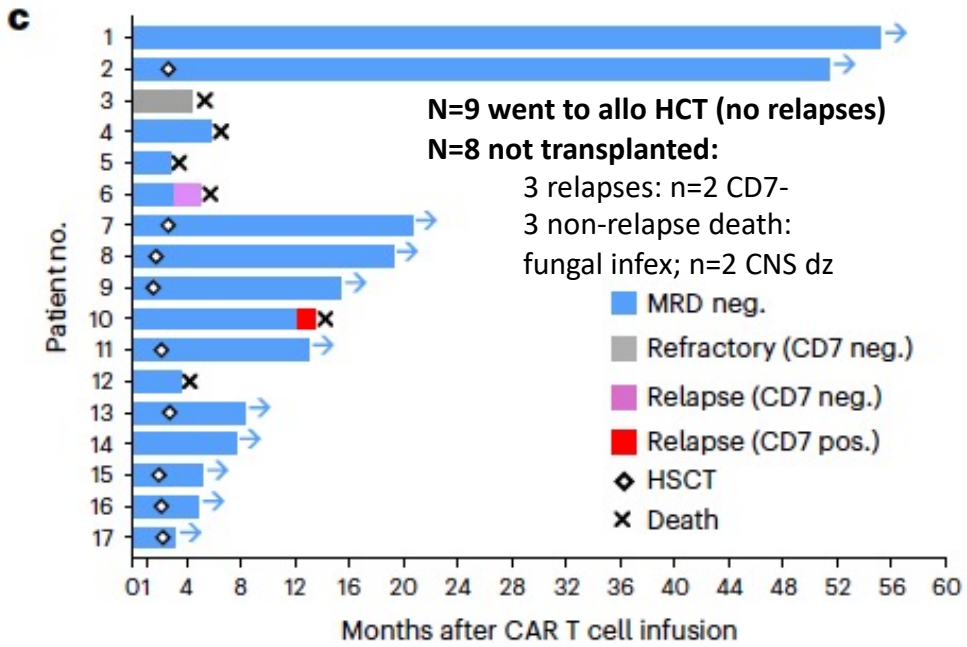
Chiesa R, et al. N Engl J Med 2026;394:152-165

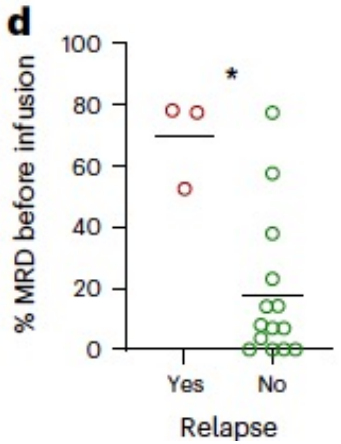
Fratricide-resistant (PEBL) auto CD7-CART in T-ALL

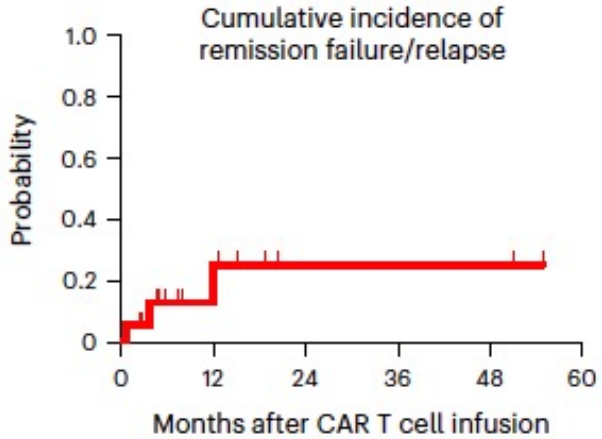












Oh, B.L.Z., Shimasaki, N., Coustan-Smith, E. *et al.* Fratricide-resistant CD7-CAR T cells in T-ALL. *Nat Med* 30, 3687–3696 (2024)

CD7 CART in T-cell malignancies – autologous cells

Publication	Target	Diagnosis	Pts w/ T-cell malignancy	Age	Type of CART	Lympho-depletion	Cell dose	Response	Survival	Toxicities	Infection/ CMV & EBV
Lu, et al. Blood 2022	CD7	T-ALL & T-LBL	N=20	22 (3-47)	Nat. select. auto or allo (if prior allo)	Flu 30mg/m^2 Cy 300mg/m^2 x3d	0.5- 2x10^6 per kg	@Day+28: 95% CR/CRi in BM: (19/20) 56% CR in EM (5/9)	N=14 underwent consolidative allo HCT – no relapses; 4/6 w/o allo HCT remain in remission @ 142 days; n=2 died (n=1 each PD and GVHD)	CRS: 95% (G1-2:90%; G3: 5%); ICANS: 10% (all G1); no T-cell aplasia	N=1 CMV; no EBV; n=2 bacterial sepsis
Zhang et al. CCR 2022	CD7	T-ALL & T-LBL	N=8	36 (15-68)	NB-derived fratr. res. auto T cells	Flu 30mg/m^2 x3d Cy 500mg/m^2 x2d	1.0-1.5x10^6 per kg	@30 days: 75% CR (6/8) @3 months: 87.5% CR (7/8)	N=1 died of infection; 4/8 relapsed; 3 remain in remission at 3,8 and 12 months w/o allo HCT	100% CRS (G1-2: 87.5%; 12.5% G4); no T-cell aplasia	CMV/EBV N/A N=1 (12.5% G5 abdominal infection)
Oh et al. Nat Med 2024	CD7	T-ALL	N=17	16 (2-71)	PEBL	Flu/Cy	0.5x10^6 per kg	@1 months: 95% MRD- CRR (16/17)	@mFU 15 mo n=11 alive and in CR; n=2 w/o allo HCT 6 died (n=3 relapse)	76% CRS (all <G3); 12% ICANS (all G1);	30% >G3 infection; at least 1 G5 fungal infection)

CD7 CART in T-cell malignancies – allogeneic cells

Publication	Target	Diagnosis	Pts w/ T-cell malignancy	Age	Type of CART	Lympho-depletion	Cell dose	Response	Survival	Toxicities	Infection/ CMV & EBV
Pan, et al. JCO 2021	CD7	T-ALL	N=20 (T-ALL)	20 (3-45)	Allo	Flu 30mg/m^2 Cy 250mg/m^2 (30mg/kg if no	5 x 10^5 per kg or 1 x 10^6 per kg	90% CR (85% MRD- CR)	9 of 11 w/o HCT, remain in CR at mFU 7.0mo; n=2 died (n=1 each PD & gal PNA)	CRS: 100% (G1-2: 90%; G3: 5%; G4: 5%); ICANS: 15% (all G1); no T-cell aplasia; 60% early GVH	N=5 w/ CMV and/or EBV; n=1 G5 fungal PNA.
Hu et al, NEJM 2023	CD7	AML, T-ALL, T-LBL	N=2 T-/ n=1 T-L						U 15 months 3 died (n=2 infection; l PD); imated 1y OS 68% % CI 43-100); 1y DFS 54% (95% CI: 29-100).	CRS: 90% (all G1-2); No ICANS; N=1 CAR-related GVHD; no T-cell aplasia	90% CMV and/or EBV reactivation w/ 1 EBV+ PTLD; N=5 bact. or fungal infections (n=2 G5)
Chiesa et al NEJM 2023/NEJM 2026	CD7	T-ALL	N=11	13 (13-15)	Base-edited donor T cells (TCRB1, CD7, CD52)	Flu 150mg/m^2 Cy 120mg/m^2 Alemtuzumab 1mg/kg x1d	0.2x10^6 per kg or 2.0x10^6 per kg	@28 days ORR 82%	N=1 died of fungal pneumonia (D+33); all n=9 in CR went to allo and alive	CRS: 100% (all G1-2); ICANS: 33% (all G1); no GVHD	CMV n=2; N=1 each E.coli bacteremia, Candidal bacteremia aspergillus PNA
Ghobadi, et al.Res Sq 2024/ Blood 2025	CD7	T-ALL/ T-LBL	N=28 (n=13 RP2D)	14-69	Allo CD7KO, TRAC del	Flu 30mg/m^2 Cy 500mg/m^2 x3d or enhanced (Flu x4d; Cy 1000mg/m2)		CR 72.7% @R2PD (8/11); ORR 91%	DOR 6.6m	CRS 88.5% (19.2 G3/4); 7.7% ICANS (G1); 11.1% G5 (inx/ MOF)); n=1 GVHD	N=1 G5 fungal infection; n=1 G5 sepsis; 19.2% G3/4 infections; n=1 G5 encephalopathy

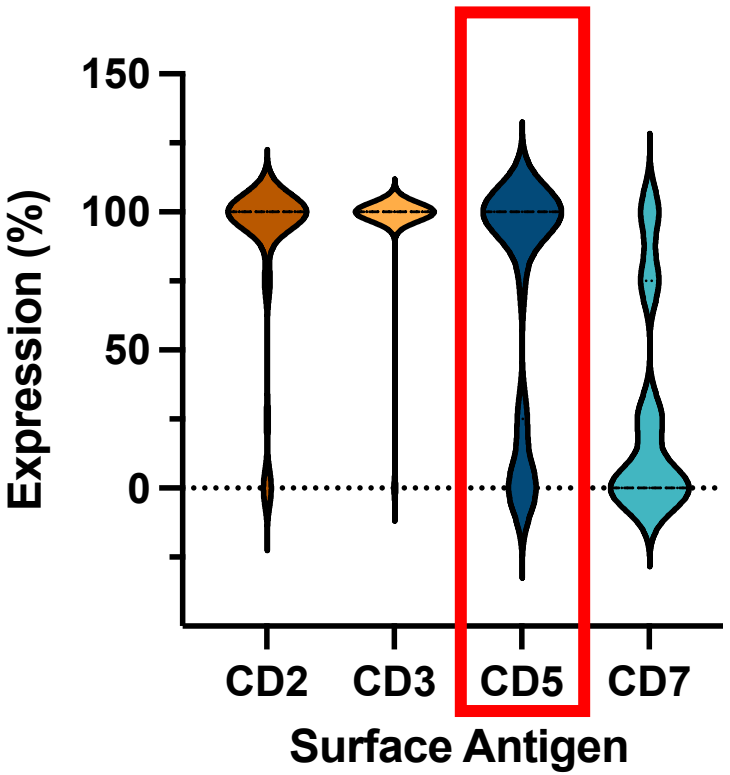
Summary:

High response rates in T-ALL and T-LBL at 1 month with most patients undergoing allo HCT after CART Rx.

Infectious complications, are more common.

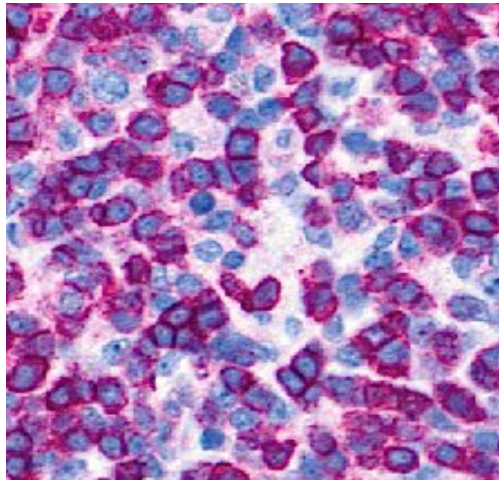
Concerns regarding durability of response w/o allo HCT, this nevertheless is a promising bridging therapy.

Targeting CD5

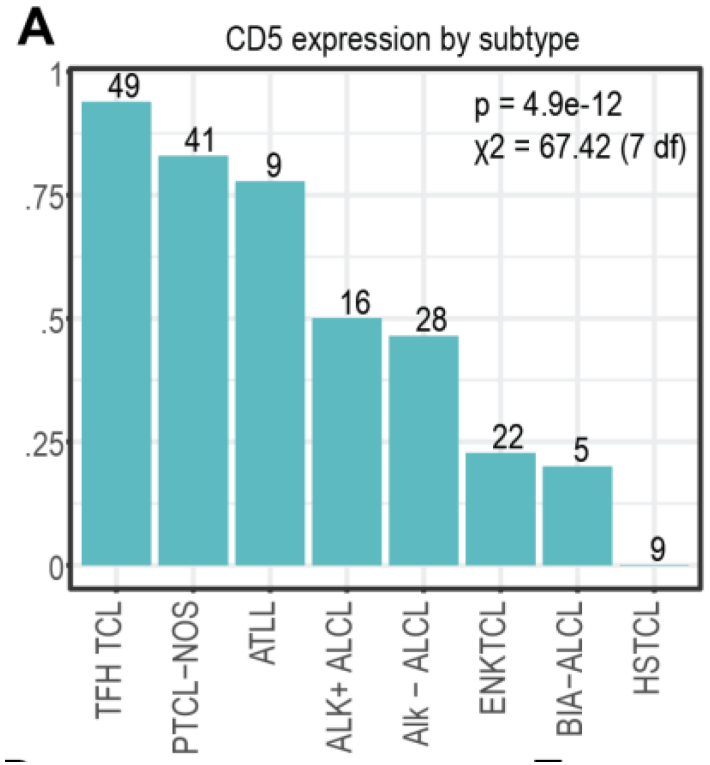


Courtesy: Stefano Pileri

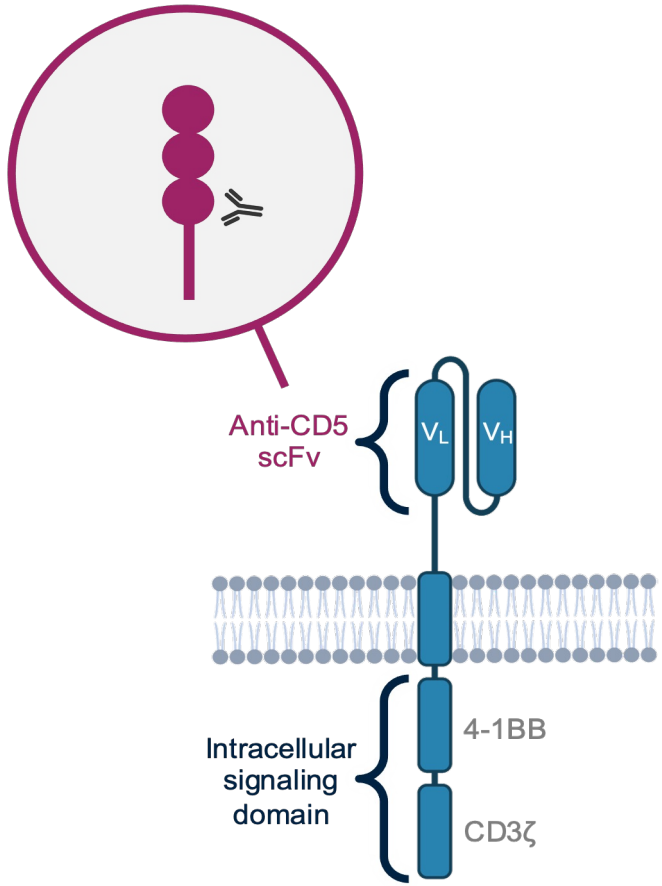
T cell lymphoma



CD5



Anti-CD5 CAR

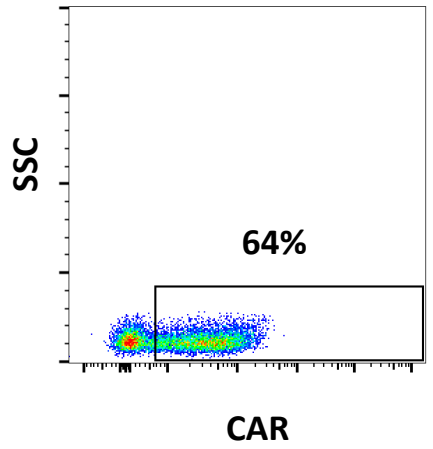


Elghawy O, et al. Cancers 2024;
Patel R, et al. Science Immunology, 2024

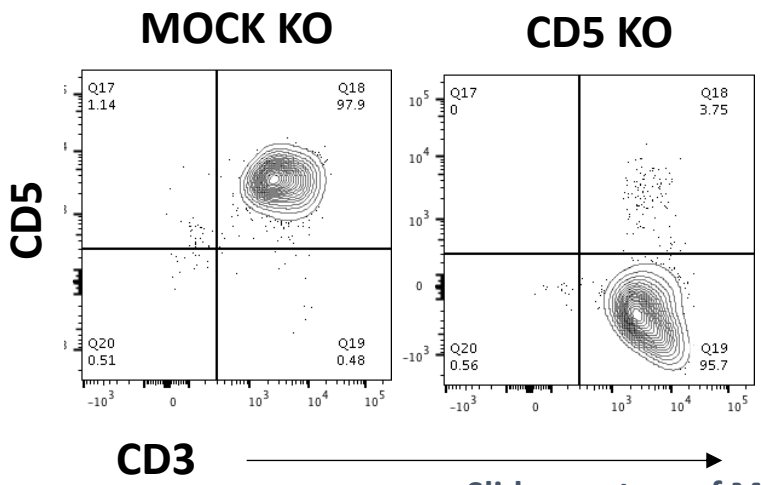
Highly efficient CRISPR/Cas9 CD5 knock out and CAR expression

Challenge #1: T-cell fratricide

CAR5 expression

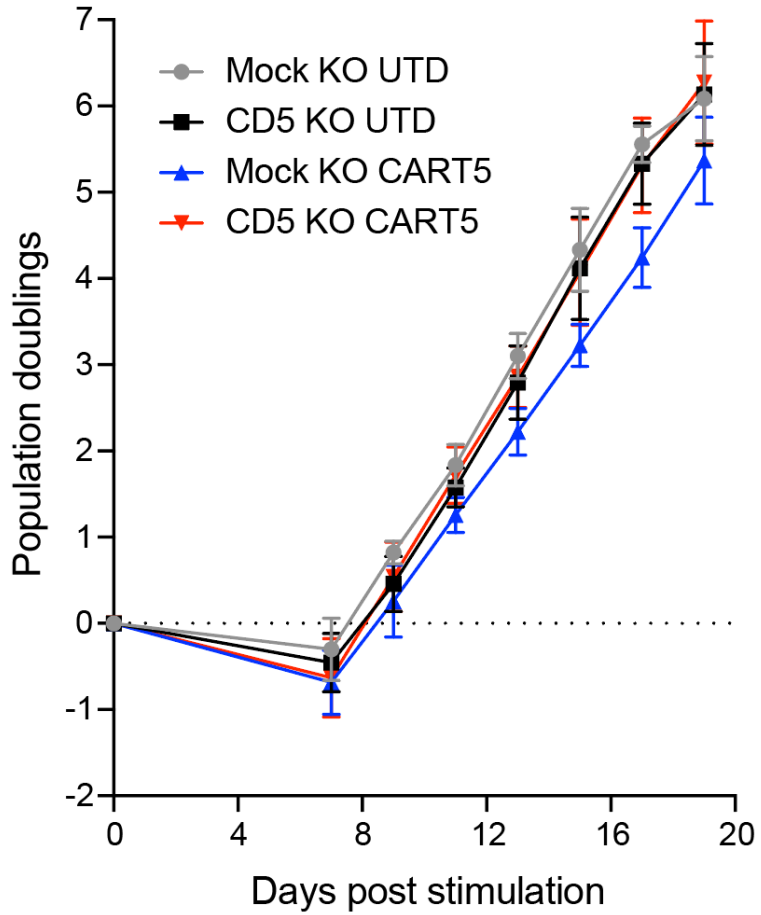


CD5 expression



Slide courtesy of Marco Ruella (modified)

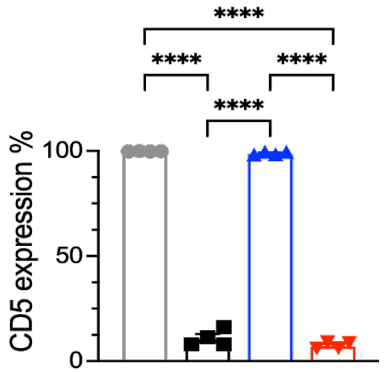
CART population doublings



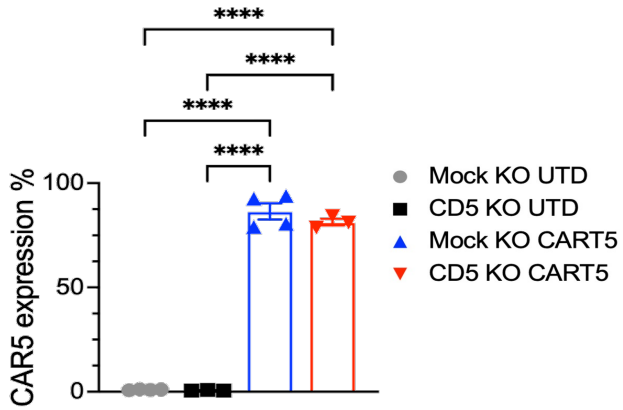
Chun I. et al Blood, 136, Suppl. 1, Pages 51-52

CD5 knock out leads to less activated & differentiated CART

CD5 expression

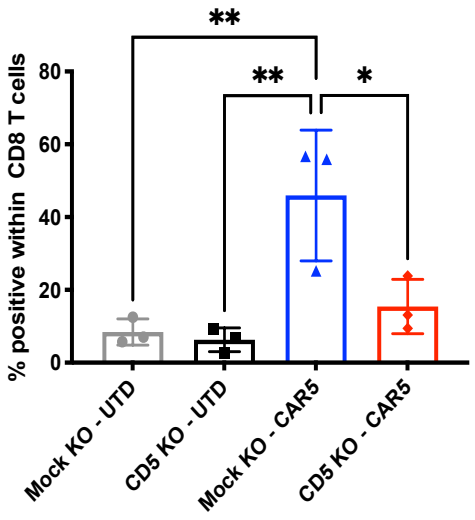


CAR5 expression

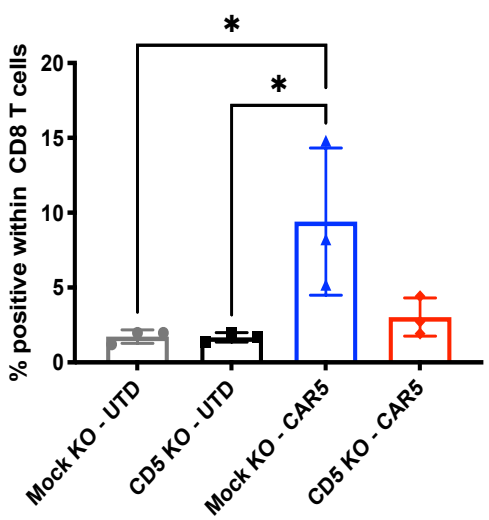


Exhaustion markers

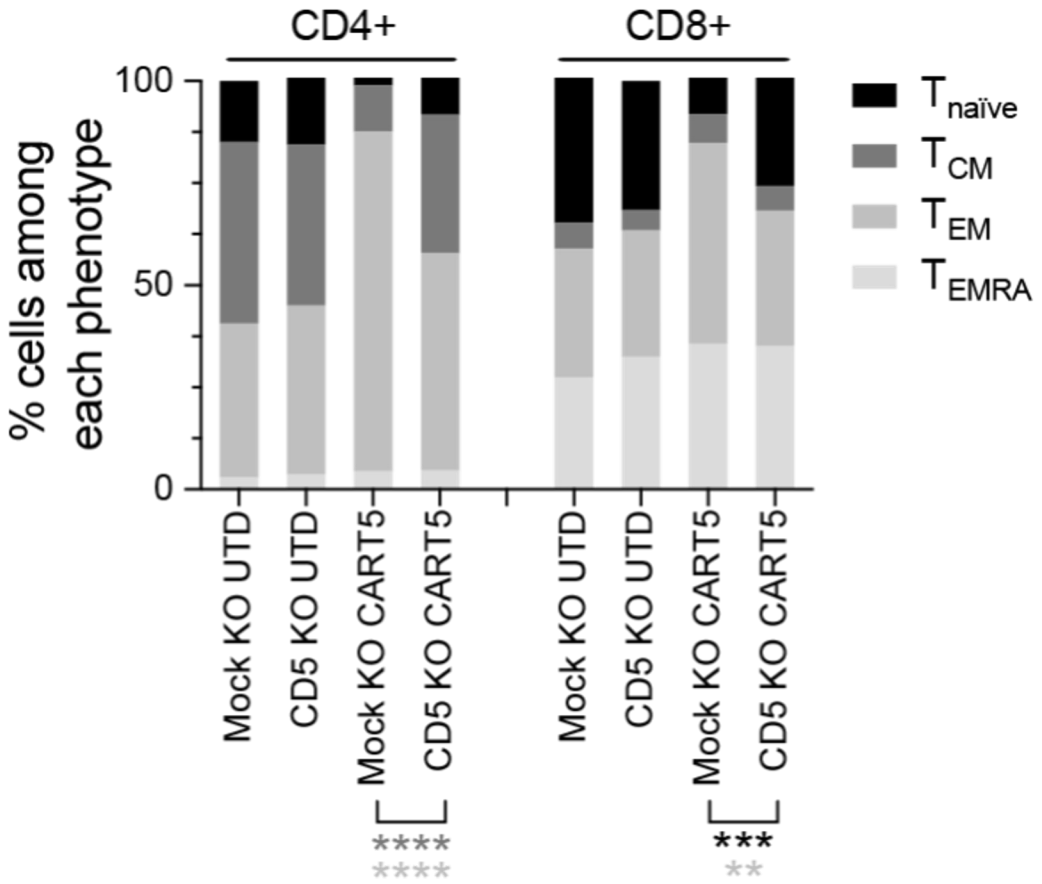
Lag3+



PD1+

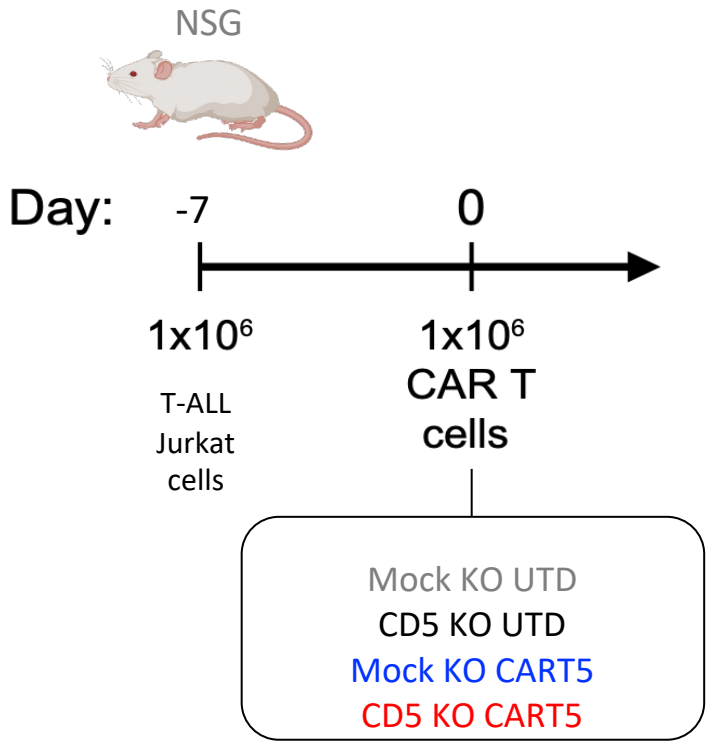


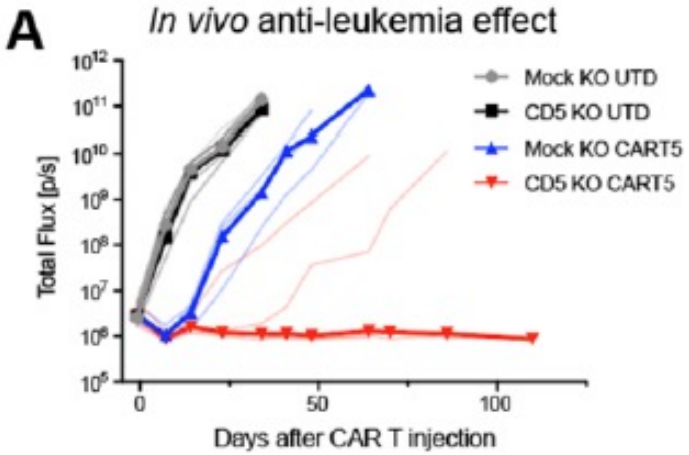
Memory phenotypes

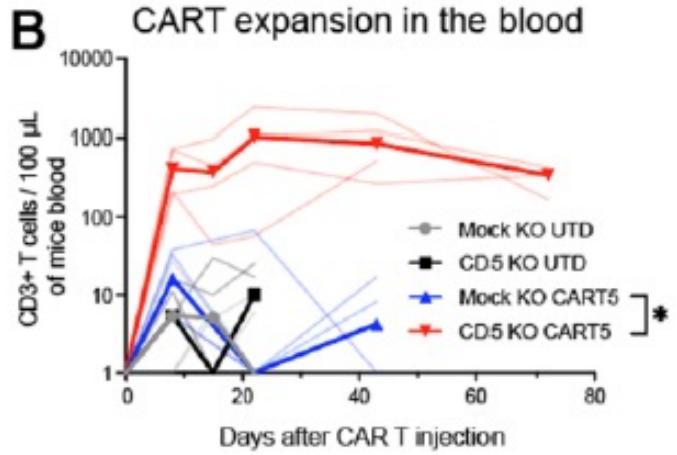


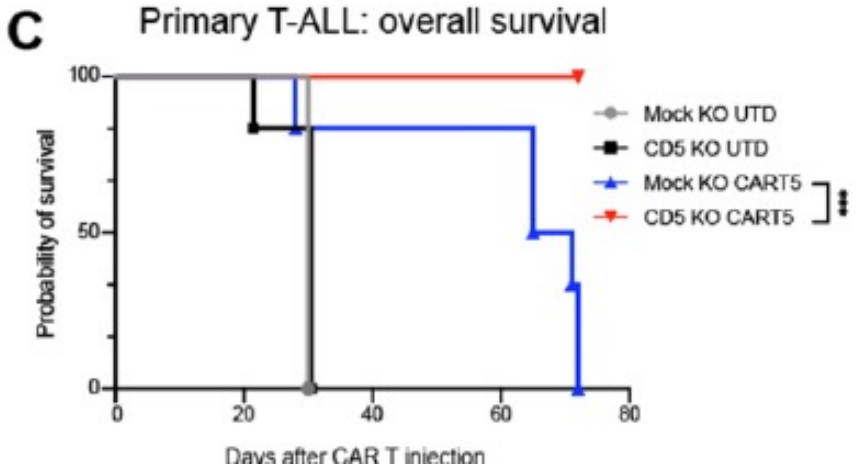
Patel RP, Science Immunology, 2024 Jul 19;9(97)

CD5 KO enhances CART5 against T-cell NHL







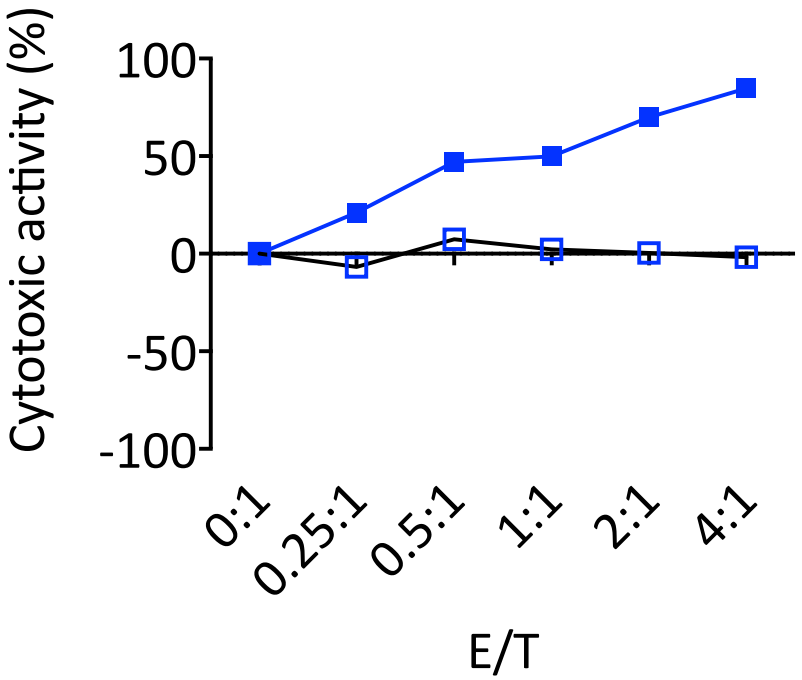


Patel RP, Science Immunology, 2024 Jul 19;9(97)

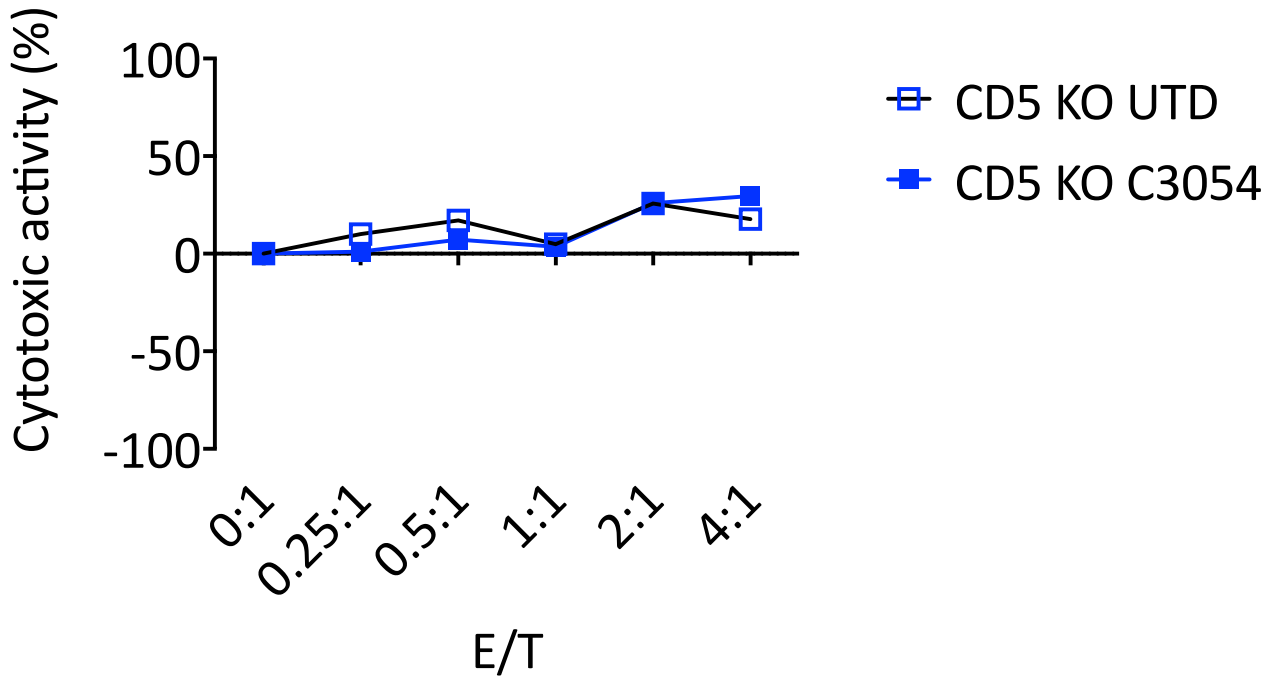
CART5 can kill CD5+ but not CD5KO normal T cells

Challenge#2:
Killing Healthy T cells

CD5+ normal T cells: *killed*



CD5 KO normal T cells:
ignored

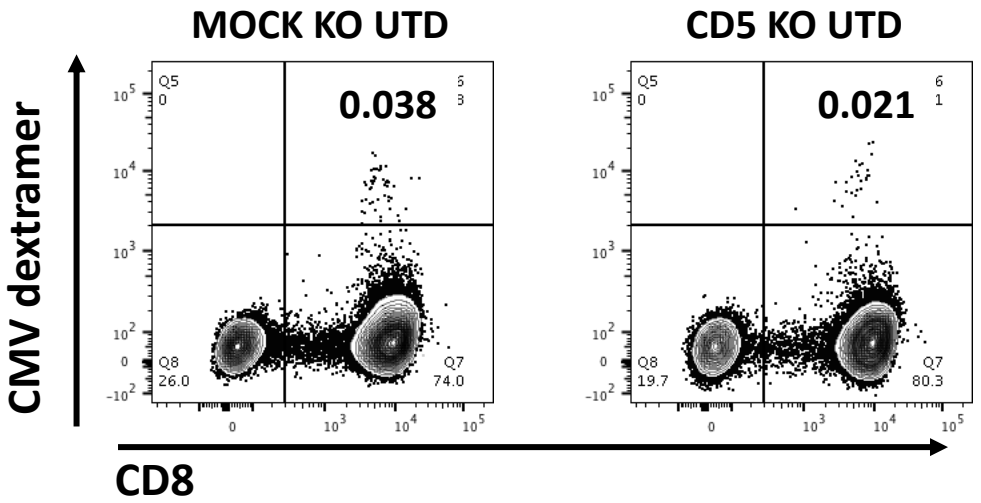


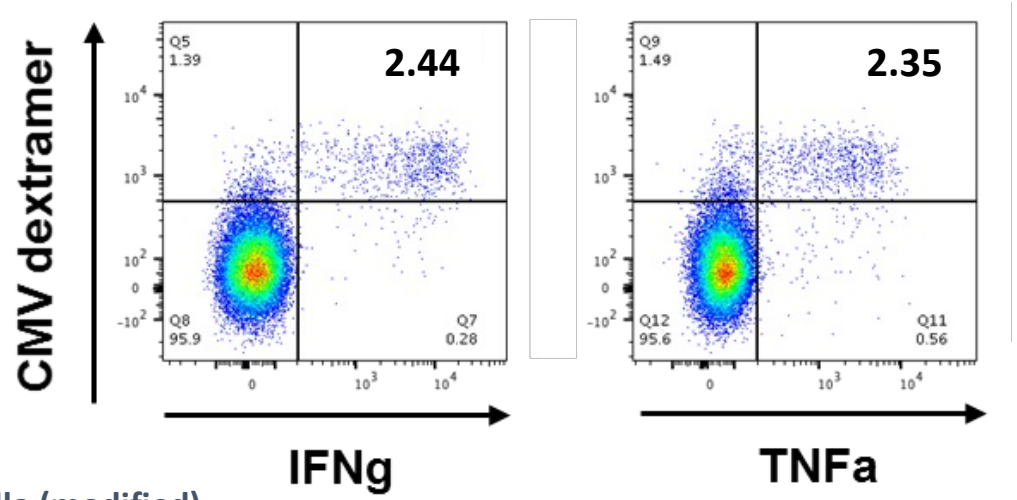
Slide courtesy of Marco Ruella (modified)

Patel RP, Science Immunology, 2024 Jul 19;9(97)

CD5KO untransduced T cells recognize CMV

Challenge#2:
Killing Healthy T cells



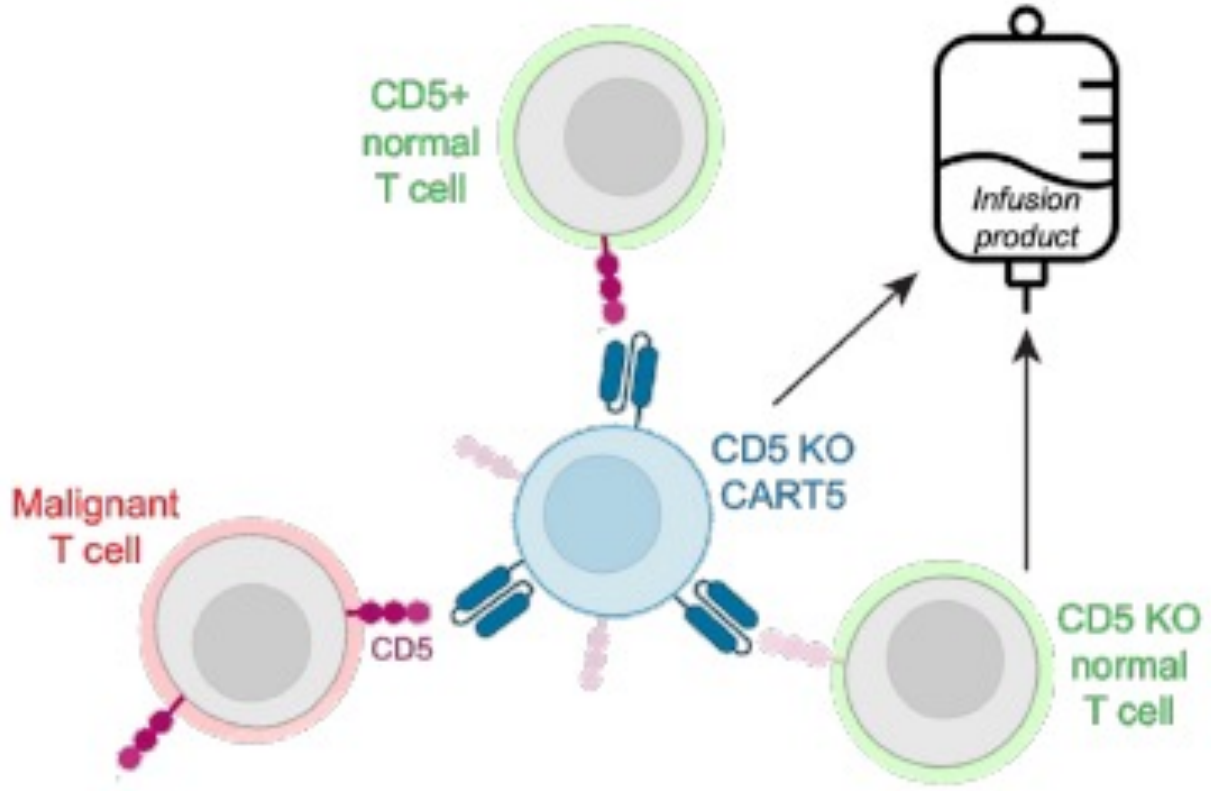


Slide courtesy of Marco Ruella (modified)

Patel RP, Science Immunology, 2024 Jul 19;9(97)

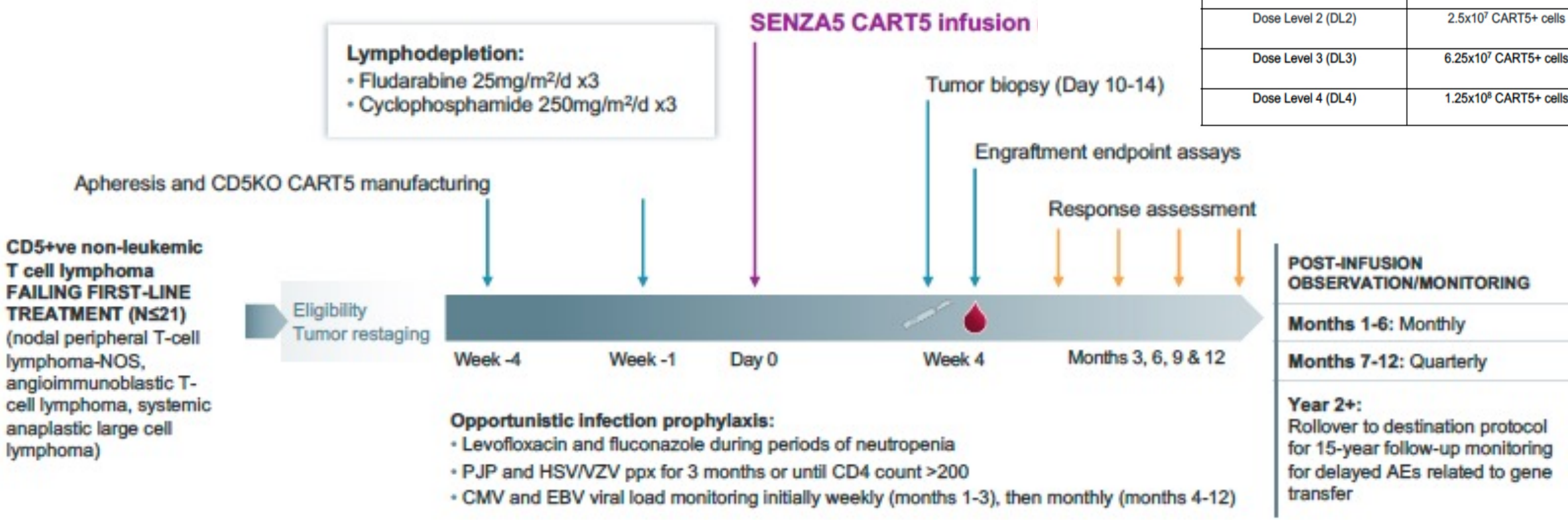
CD5KO CART5 are designed to enhance efficacy and reduce toxicity

- **No fratricide**
- **Enhanced expansion and persistence**
- **Enhanced efficacy**
- **Transduction of CD5KO untransduced cells may help restore T-cell mediated immunity faster**



Viper 101 Phase I Clinical Protocol

Dose Level	CART5+ Dose Level[2] (per patient)
Dose Level -1 (DL-1)[1]:	$3x10^6$ CART5+ cells
Dose Level 1 (DL1):	$1x10^7$ CART5+ cells
Dose Level 2 (DL2)	$2.5x10^7$ CART5+ cells
Dose Level 3 (DL3)	$6.25x10^7$ CART5+ cells
Dose Level 4 (DL4)	$1.25x10^8$ CART5+ cells



PRIMARY OBJECTIVES

- Recommended phase II dose
- Safety

SECONDARY OBJECTIVES

- Manufacturing feasibility
- Overall response rate
- Progression-free survival
- Overall survival
- Duration of response

EXPLORATORY OBJECTIVES

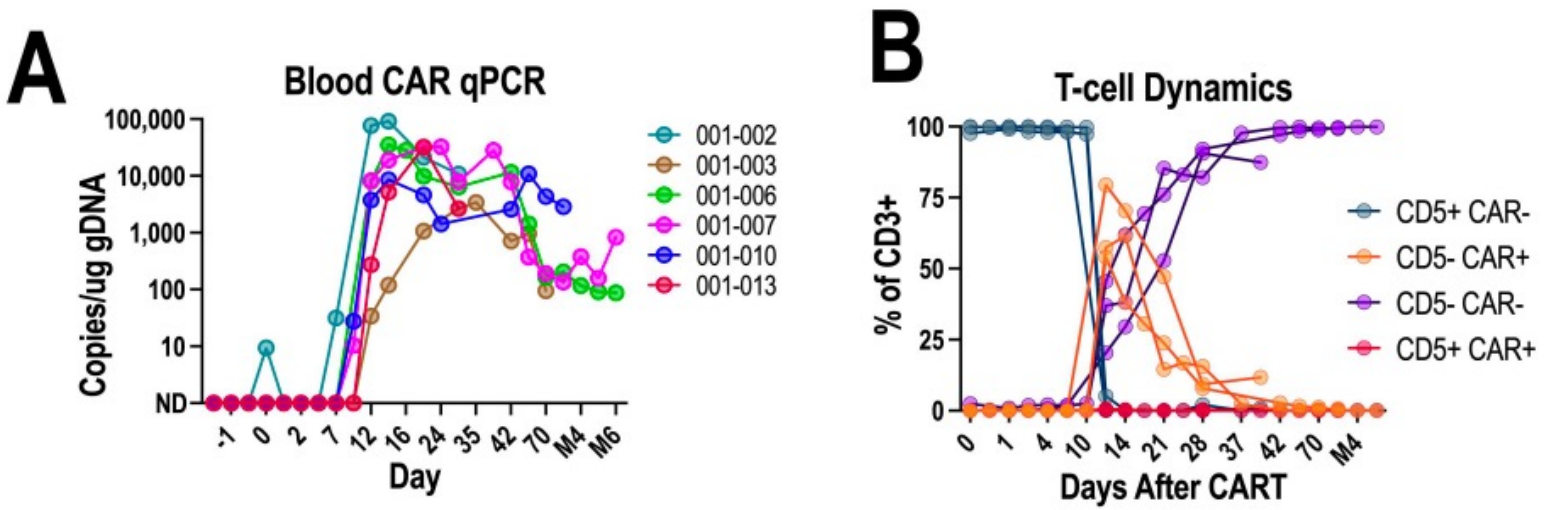
- Persistence and trafficking
- T cell cytopenia
- CD5KO T cell functionality

ClinicalTrials.gov ID NCT06420089

VIPER 101 – Prelim Results

Table 1. Study Enrollment and Demographics

Patient ID	Diagnosis	Sex & Age	Dose Level	Race
001-002	AITL	F, 75	DL1: 1e7 CAR+	White
001-003	PTCL-NOS	M, 58	DL-1: 3e6 CAR+	Black or African American
001-006	PTCL-NOS	M, 70	DL-1: 3e6 CAR+	Asian
001-007	PTCL-TFH	M, 55	DL-1: 3e6 CAR+	White
001-009	PTCL-NOS	M, 50	Not Treated	White
001-010	MF	M, 65	DL-1: 3e6 CAR+	White
001-012	AITL	M, 72	DL-1: 3e6 CAR+	White
001-013	MF	M, 71	DL-1: 3e6 CAR+	Black or African American
001-014	MF	F, 39	Pending Treatment	Black or African American
002-003	PTCL-NOS	M, 65	DL-1: 3e6 CAR+	White Hispanic



Barta SK, Schuster SJ, … Ruella M. *Blood* 2025; 146 (Supplement 1): 4174.

VIPER 101 – Prelim Results

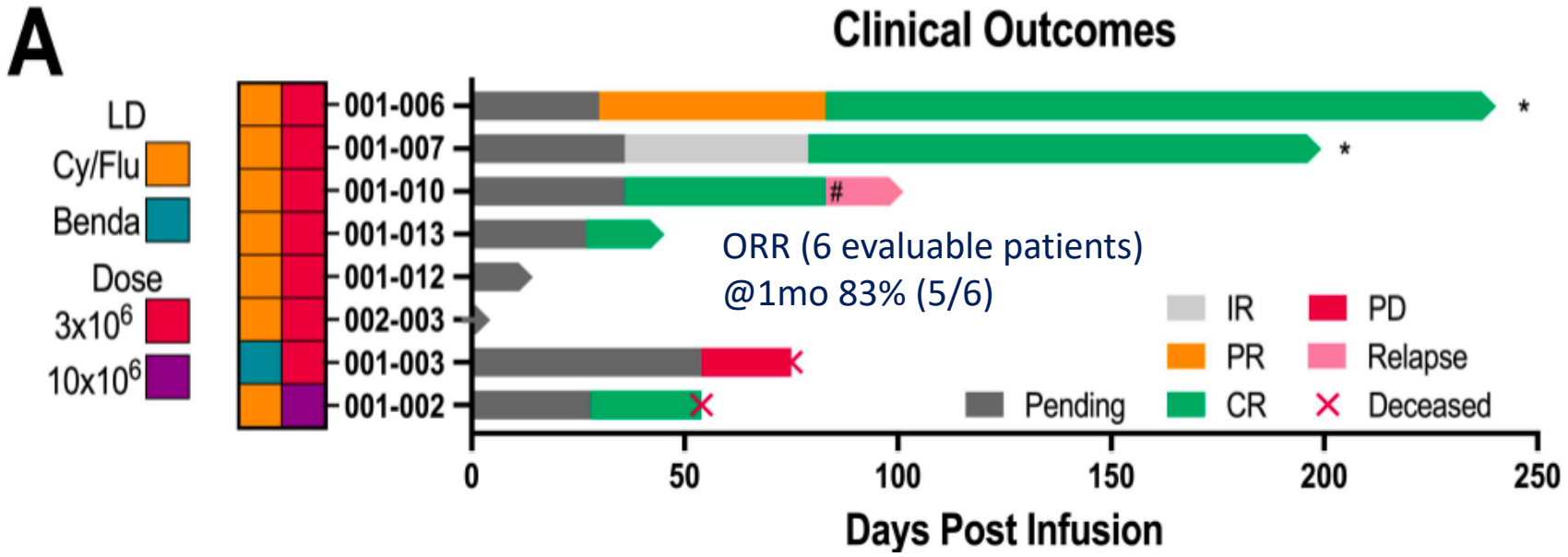
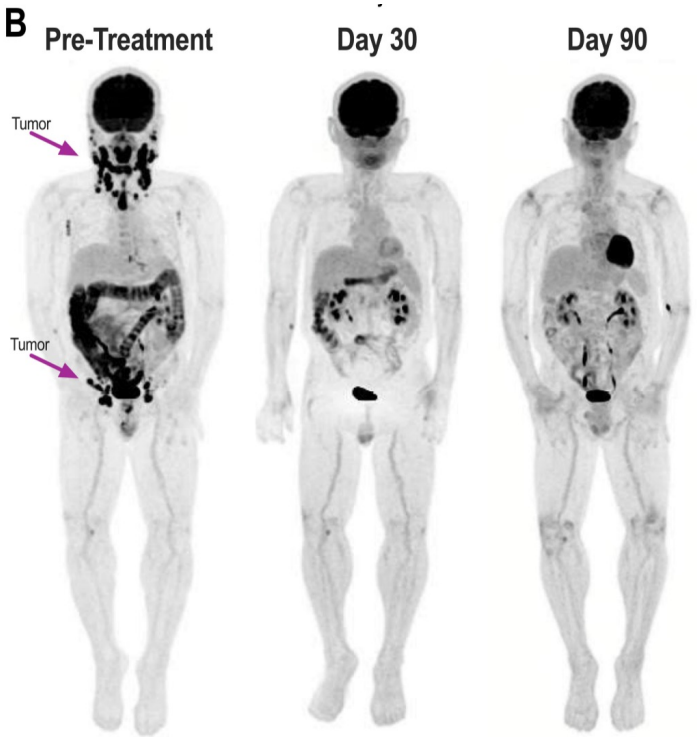


Table 2. Adverse Events

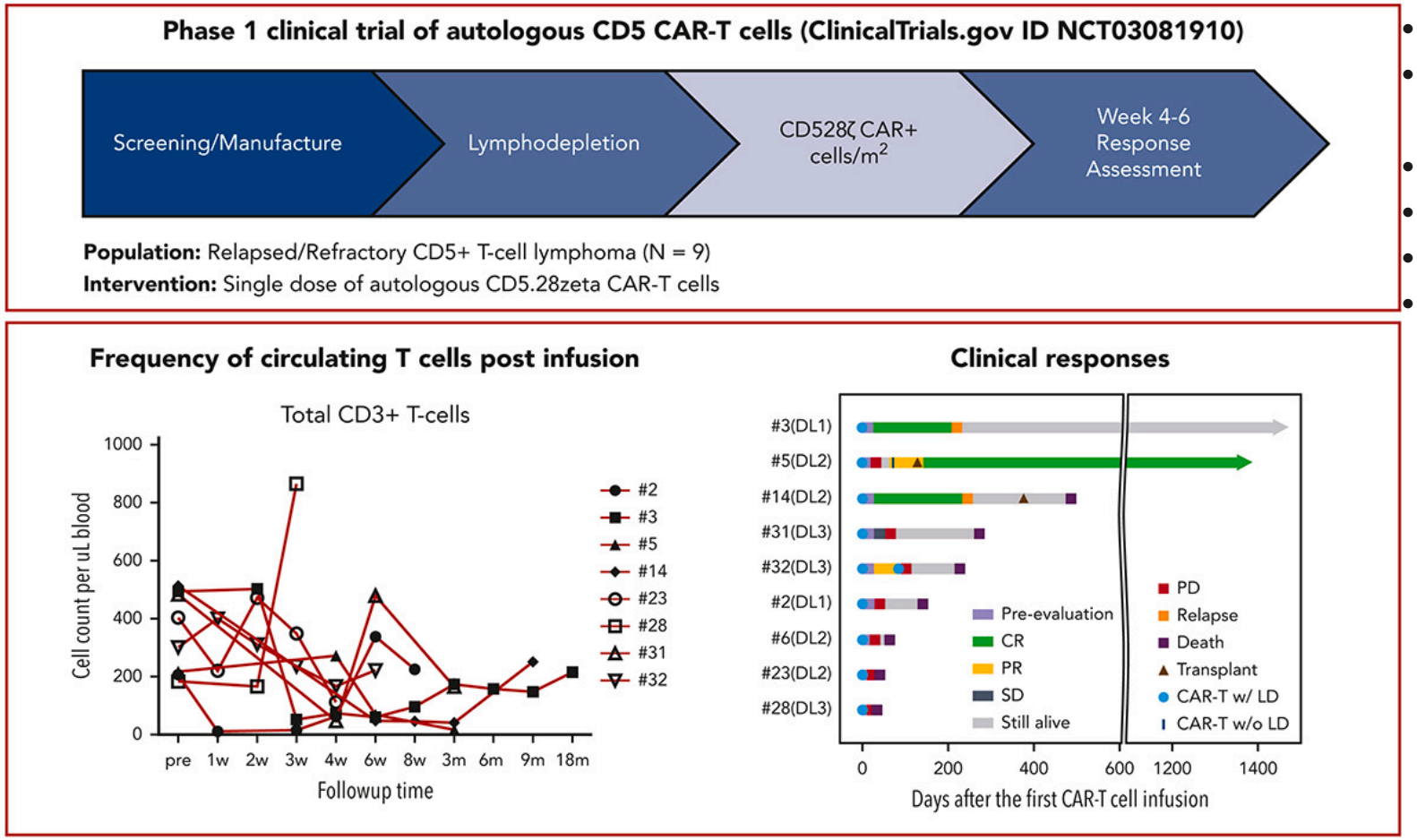
	Grade 1		Grade 2		Grade 3		Grade 4	
Adverse Event	DL-1 (n=5)	DL1 (n=1)	DL-1 (n=5)	DL1 (n=1)	DL-1 (n=5)	DL1 (n=1)	DL-1 (n=5)	DL1 (n=1)
Anemia	1 (20%)	0 (0%)	3 (60%)	1 (100%)	3 (60%)	0 (0%)		
Cytokine Release Syndrome	5 (100%)	1 (100%)	0 (0%)	1 (100%)				
Diarrhea	1 (20%)	1 (100%)						
Dry Mouth	2 (40%)	0 (0%)	2 (40%)	1 (100%)				
Fatigue	1 (20%)	1 (100%)						
Fever	3 (60%)	0 (0%)						
Headache	2 (40%)	0 (0%)						
Hypotension*	1 (20%)	0 (0%)	4 (80%)	0 (0%)	1 (20%)	0 (0%)	1 (20%)*	0 (0%)
Lymphocyte Count Decreased			1 (20%)	0 (0%)	1 (20%)	0 (0%)	1 (20%)	0 (0%)
Maculo-Papular Rash	1 (20%)	0 (0%)	1 (20%)	1 (100%)				
Nausea			1 (20%)	0 (0%)				
Neutropenia	4 (80%)	1 (100%)	4 (80%)	1 (100%)	5 (100%)	1 (100%)	5 (100%)	1 (100%)
Tachycardia	1 (20%)	0 (0%)	1 (20%)	0 (0%)	1 (20%)	0 (0%)		
Thrombocytopenia	4 (80%)	1 (100%)	4 (80%)	1 (100%)	5 (100%)	1 (100%)	5 (100%)	1 (100%)
WBC Decreased	4 (80%)	0 (0%)	4 (80%)	0 (0%)	5 (100%)	0 (0%)	4 (80%)	0 (0%)
Weight Loss	1 (20%)	0 (0%)	0 (0%)	1 (100%)				

*Grade 4 hypotension associated with pulmonary embolism event and progressive disease
Data as of October 8th, 2025

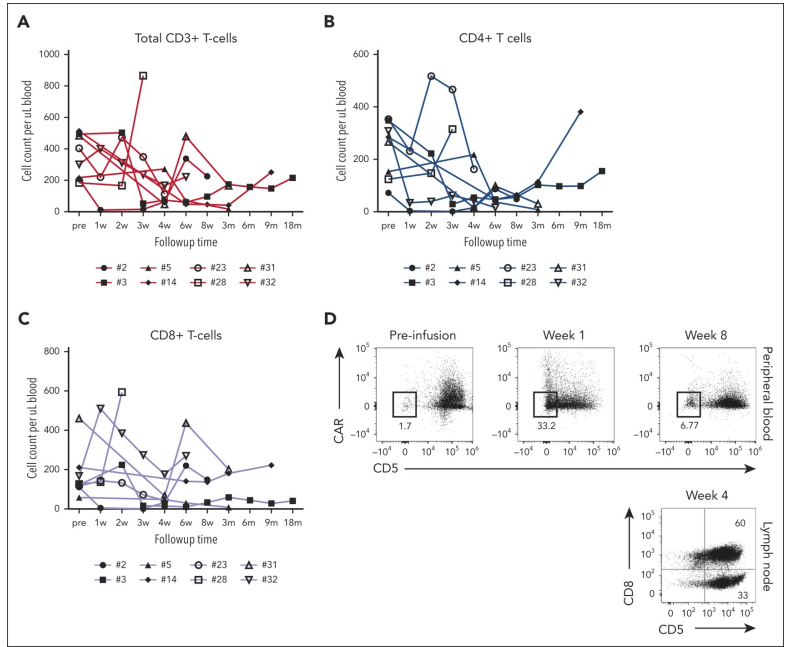


Barta SK, Schuster SJ, … Ruella M. *Blood* 2025; 146 (Supplement 1): 4174.

Antitumor efficacy and safety of unedited autologous CD5.CAR T cells in RR mature T-cell lymphomas



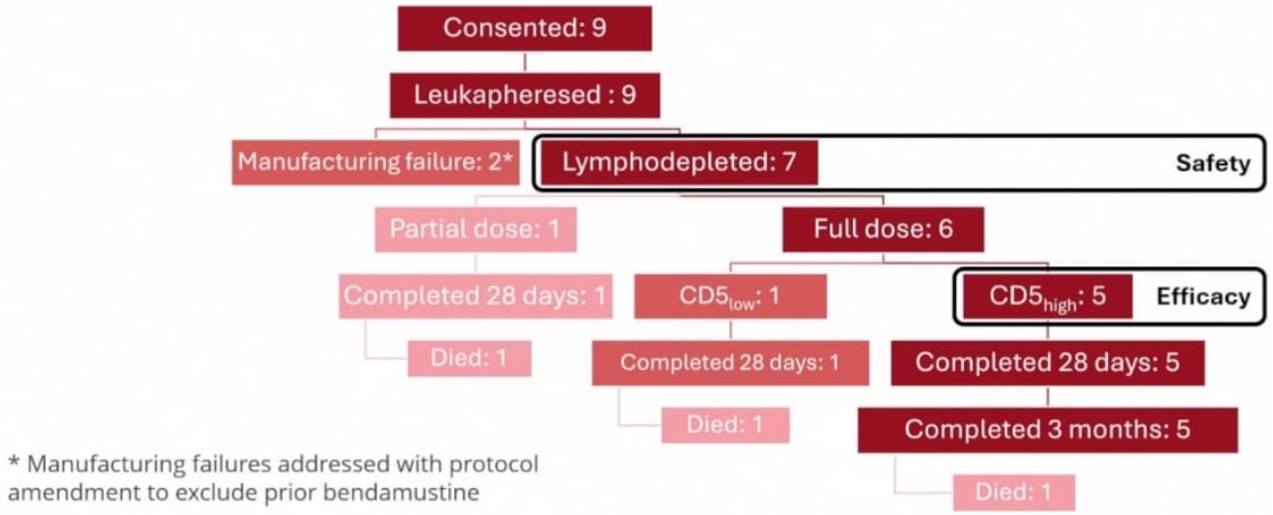
- N=17 enrolled
- Product successfully manufactured for 13/14 (93%) & administered to 9 (69%) patients.
- ORR 44%, CR in 2/9 (22%)
- The most common grade 3+ AEs were cytopenias.
- No grade 3+ CRS or ICANS.
- N=2 died during the immediate toxicity evaluation period due to rapidly progressive disease.



Hill et al. Blood 2023

Phase 2 study of MB-105, a CD5.CAR T therapy for patients with relapsed/refractory T cell lymphoma

Consort diagram



* Manufacturing failures addressed with protocol amendment to exclude prior bendamustine

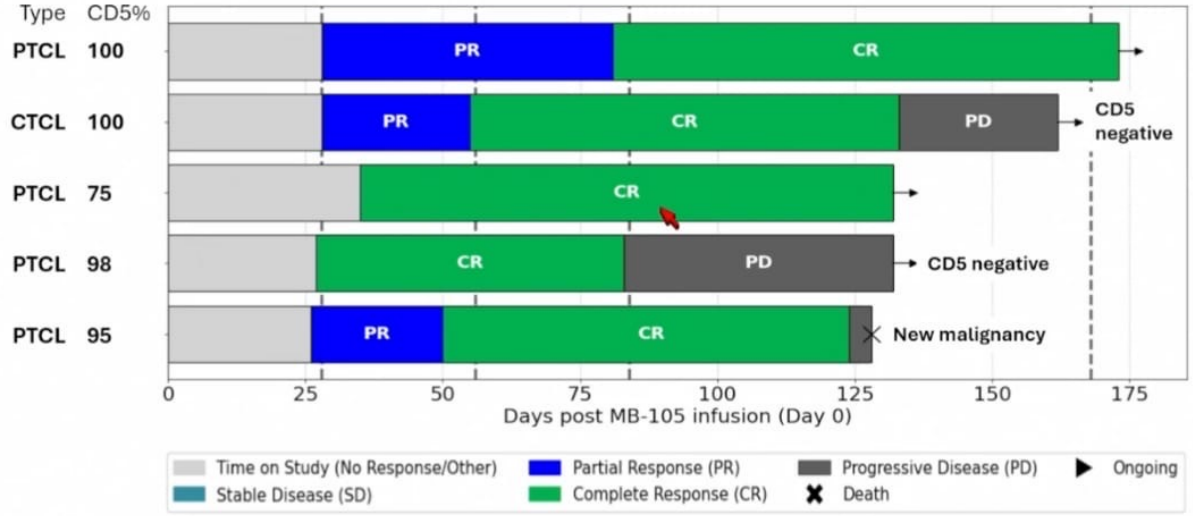
Demographics and baseline characteristics

Characteristic, n (%)	Treated patients (n=7)
Age (years)	
Median (range)	70 (60-76)
Sex female	3 (43)
Race	
White	5 (71)
Black	1 (14)
Other	1 (14)
Karnofsky 90-100	5 (71)
Karnofsky 70-80	2 (29)
Type of lymphoma	
PTCL	5 (71)
PTCL-NOS	3 (43)
AITL	2 (29)
CTCL (all MF)	2 (29)

Iyer S, et al. Interim analysis of safety & efficacy in a Ph 2 study of MB-105, a CD5.CAR T therapy for patients with RR T cell lymphoma. *Blood* 2025; 146 (Suppl 1): 775.

Phase 2 study of MB-105, a CD5.CAR T therapy for patients with relapsed/refractory T cell lymphoma

Efficacy: swimmer plot



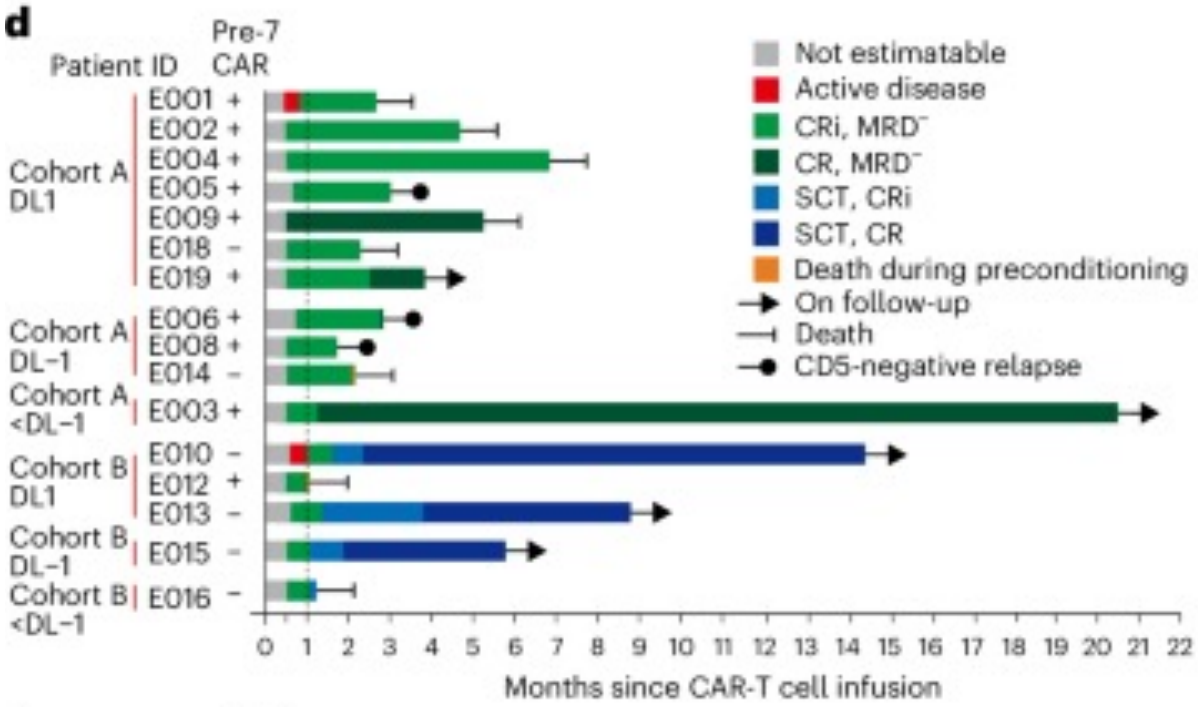
Treatment-emergent adverse events in >1 patient

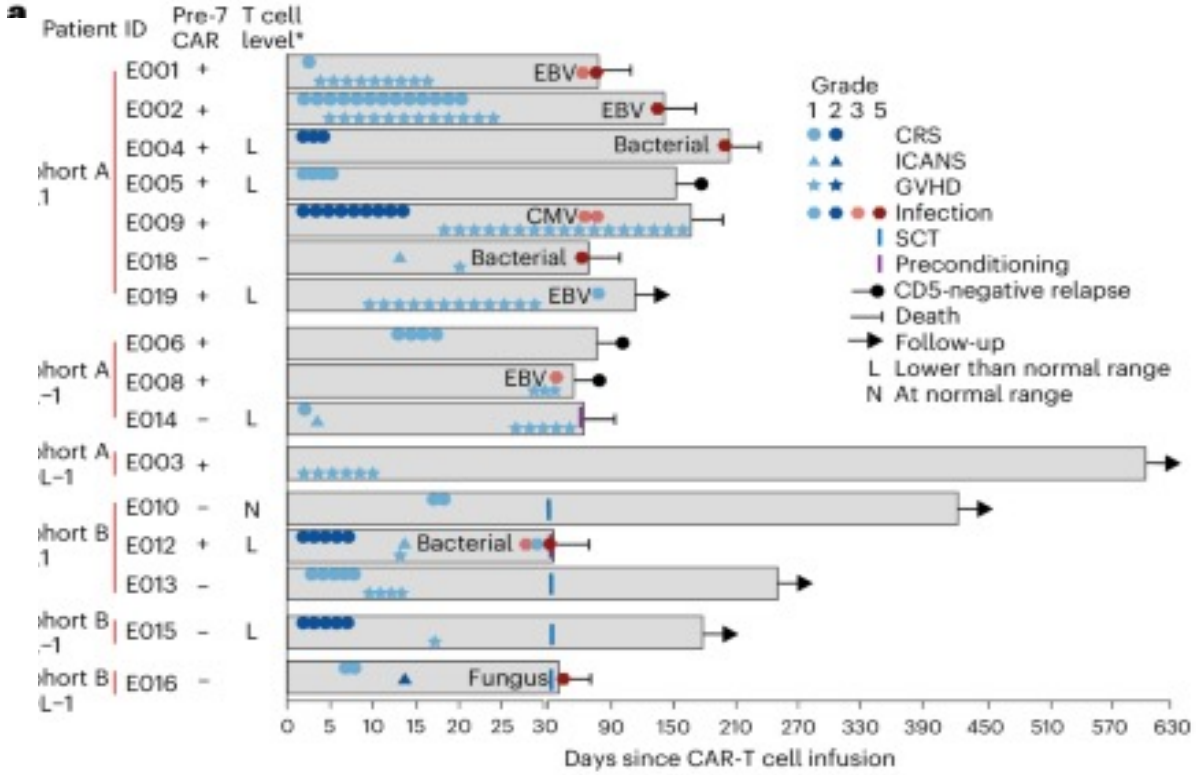
Hematologic TEAEs (n=7)		
Preferred Term n (%)	Grade 3-4	All
Anaemia	3 (43)	5 (71)
Neutropenia	2 (29)	4 (57)
Neutrophil count decreased	3 (43)	3 (43)
Thrombocytopenia	3 (43)	3 (43)
Platelet count decreased	1 (14)	2 (29)
Blood creatinine increased	0	2 (29)
Hypokalaemia	0	3 (43)

Non-hematologic TEAEs (n=7)		
Preferred Term n (%)	Grade 3-4	All
Cytokine release syndrome	**0**	**4 (57)**
Fatigue	0	4 (57)
Dizziness	0	3 (43)
Hypotension	2 (29)	3 (43)
Pyrexia	0	3 (43)
Deep vein thrombosis	2 (29)	3 (43)
Oedema peripheral	0	2 (29)
Constipation	0	2 (29)
Dehydration	0	2 (29)
Dry mouth	0	2 (29)
Febrile neutropenia	2 (29)	2 (29)
Polyomavirus viraemia	0	2 (29)
Pruritus	0	2 (29)

Iyer S, et al. Interim analysis of safety & efficacy in a Ph 2 study of MB-105, a CD5.CAR T therapy for patients with RR T cell lymphoma. *Blood* 2025; 146 (Suppl 1): 775.

Allogeneic CD5-specific CAR-T therapy for relapsed/refractory T-ALL





Pan, J., Tan, Y., Shan, L. *et al.* Allogeneic CD5-specific CAR-T therapy for relapsed/refractory T-ALL: a phase 1 trial. *Nat Med* 31, 126–136 (2025).

CD5 CART in T-cell malignancies

Publication	Target	Diagnosis	Pts w/ T-cell malignancy	Age	Type of CART	Lympho-depletion	Cell dose	Response	Survival	Toxicities	Infection/ CMV & EBV reactivation
Hill, et al. Blood 2024	CD5	Mature T-cell NHL	N=17 enrolled; 13/14 manufactured; n=9 infused	63 (29-71)	Auto	Flu 30mg/m^2 Cy 250mg/m^2 (30mg/kg if no prior allo) x3d	1 x 10^7/m^2; 5x 10^7/m^2; 2x10^8/m^2; 1-2 doses	ORR: 44% (all CR; 4/9)	N=7 died: n=5 died of PD; n=1 toxicity from salvage therapy; n=1 TRM; 2 alive @ 41 and 48 months (both had relapsed)	CRS: 44% (all G1-2); ICANS? 11% (G2); no T-cell aplasia.	1 w/ CMV and BK.; no EBV; n=1 bacteremia
Pan et al, Nat Med 2025	CD5	T-ALL	N=16 (n=10 had prior CD7 CART)	10 (7-15)	Donor T-cells	Flu 30mg/m^2 Cy 250mg/m^2 x3d	1.0x10^6 per kg	3 months BOR 100% mFU 14.3mo	3 of 4 s/p allo HCT alive; 2/12 w/o HCT alive in 3 relapsed (CD5-; ed of infection)	CRS: 75% (all G1-2); ICANS: 25% (all G1-2); 68% GVHD; N=2 G5 TMA; T-cell aplasia: 10/16 "below normal" T-cell counts	N=5 CMV/EBV incl. n=1 G3 EBV PTLD; n=1 G3 CMV PNA; n=2 G5 EBV; n=1 G2 mucor/asp.; n=1; n=3 bacterial inf
Lin, et al. Blood Cancer Journal 2024	CD5	T-NHL (n=2 AITL; n=1 SPTCL)	N=3	22 (3-47)	Auto w/ tEGFR safety switch	Flu 30mg/m^2 Cy 300mg/m^2 x3d	1x10^6 per kg	3/3 (n=1 CR; n=2 PR)	N=1 (CR) died of MOF d+124; n=1 PR underwent alloHCT; n=1 PD @ D+182	CRS: 100 % (all G1-2); no ICANS; n=3 G3-4 skin rash	N/A

Summary:

Largest experience in T- cell NHL.

Response rates are lower in NHL than in ALL/LBL.

Infectious complications esp. s/p allo CART.

Durability of response is a concern.

nature medicine

Article

https://doi.org/10.1038/s41591-024-03326-7

TRBC1-CAR T cell therapy in peripheral T cell lymphoma: a phase 1/2 trial

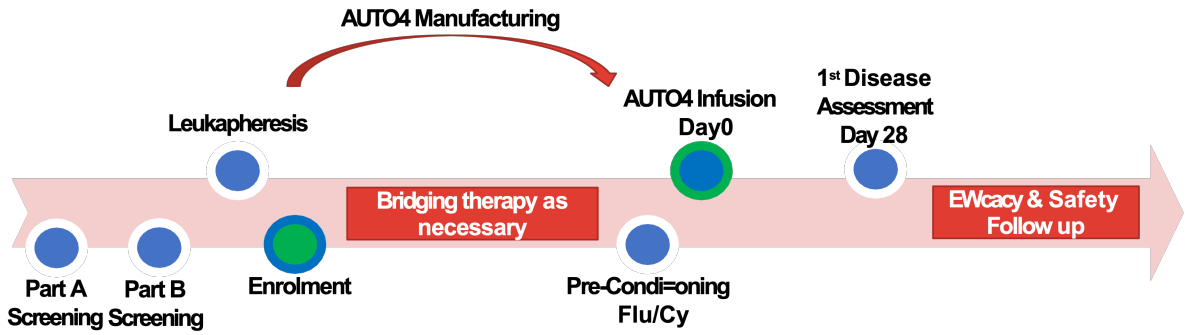
Received: 18 January 2024

Accepted: 30 September 2024

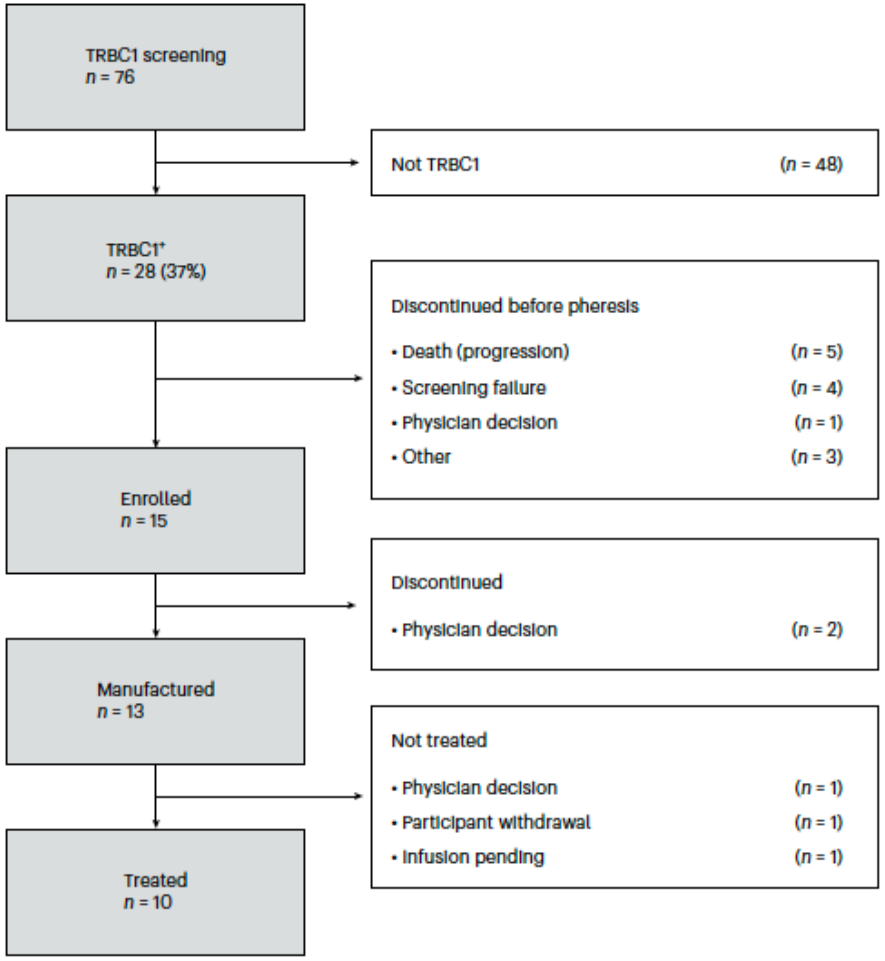
A list of authors and their affiliations appears at the end of the paper

AUTO4 = Anti-TRBC1 CAR T cells with a 41BB-ζ endodomain

AUTO4 Study design



- Part A: Lymphoma tissue screening for TRBC1 or TRBC2 expression using NGS
- Part B: Study screening for patients determined to have TRBC1+ Lymphoma

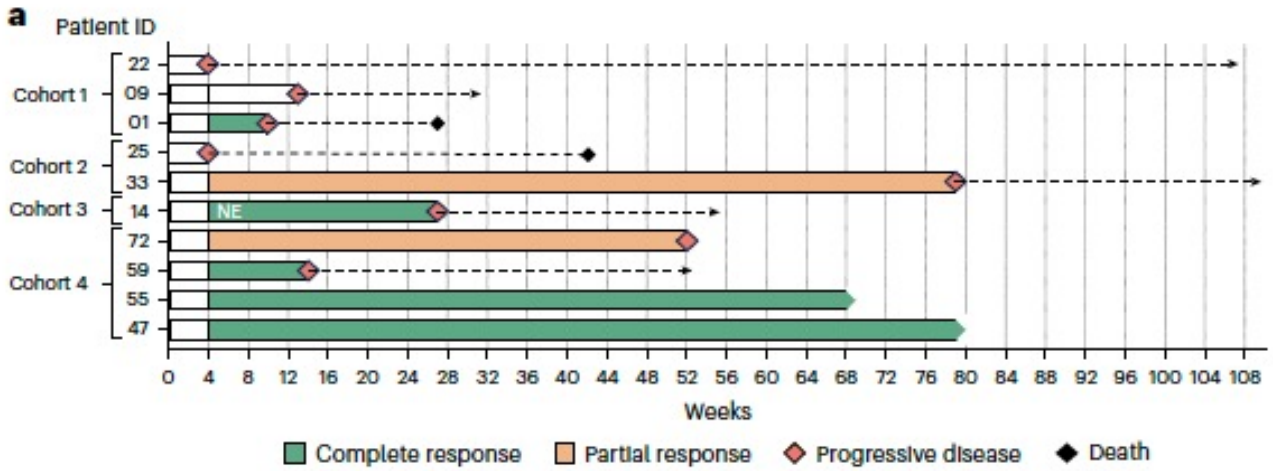


Cwynarski, K. *et al.* TRBC1-CAR T cell therapy in peripheral T cell lymphoma: a phase 1/2 trial. *Nat Med* (2024)

LibraT1 study – AUTO4 in PTCL

Table 1 | Patient characteristics

Patient ID	Cohort dose	Histologic subtype	Age (years)	Sex	No. of prior lines	Prior ASCT	Bridging
22	25×10^6	PTCL-NOS	34	Female	5	N	Y
01	25×10^6	AITL	57	Male	2	N	Y
09	25×10^6	AITL	61	Female	2	Y	N
33	75×10^6	PTCL-NOS	35	Female	1	N	Y
25	75×10^6	PTCL-NOS	53	Male	4	N	Y
14	225×10^6	ALCL	47	Male	3	Y	Y
72	450×10^6	PTCL-NOS	44	Male	2	Y	Y
55	450×10^6	AITL	63	Male	3	N	Y
59	450×10^6	PTCL-NOS	58	Male	3	N	N
47	450×10^6	AITL	61	Male	2	N	Y



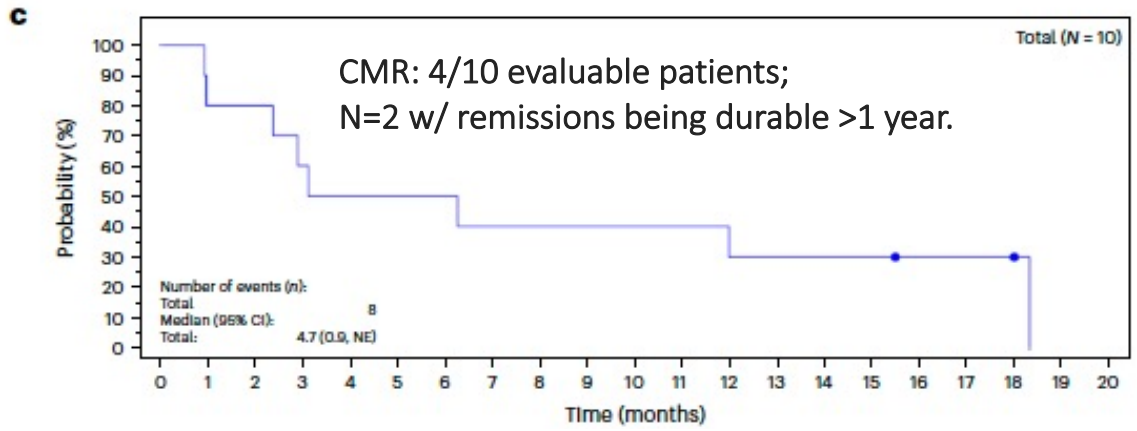


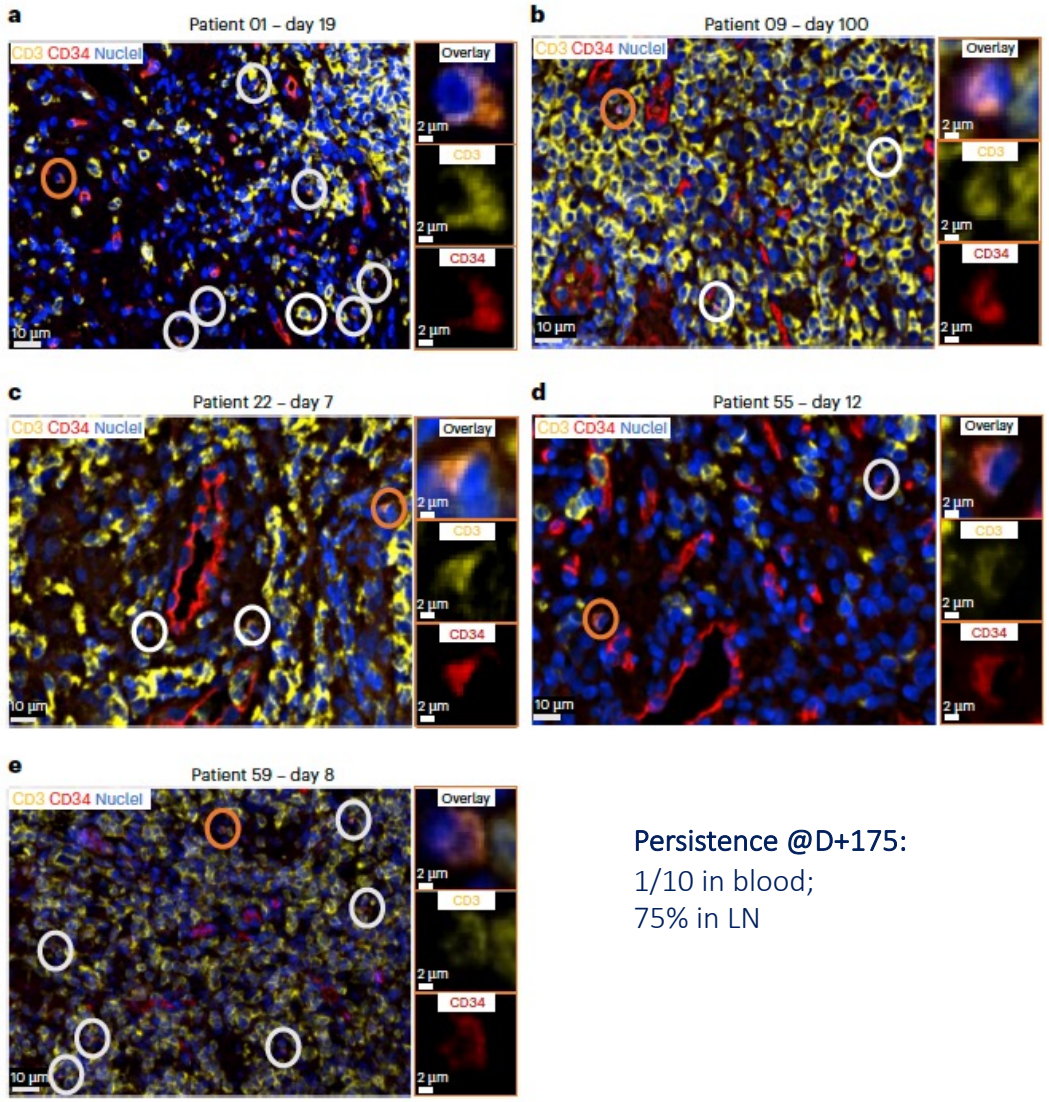
Table 2 | Summary of adverse events

	25×10^6 (n=3)	75×10^6 (n=2)	225×10^6 (n=1)	450×10^6 (n=4)	Total (n=10)
DLT	0	0	0	0	0
Any-grade neutropenia	3 (100%)	2 (100%)	0	3 (75%)	8 (80%)
Any-grade infections	3 (100%)	1 (50%)	1 (50%)	1 (25%)	6 (60%)
Any-grade CRS	0	0	0	4 (100%)	4 (40%)
Grade 3 CRS	0	0	0	1 (25%)	1 (10%)
Any-grade ICANS	0	0	0	0	0

Cwynarski, K. *et al.* TRBC1-CAR T cell therapy in peripheral T cell lymphoma: a phase 1/2 trial. *Nat Med* (2024)

AUTO4 - Lack of expansion and persistence on the peripheral blood

- Only n=1 at the highest dose level had detectable transgene in PB 10 min after infusion, dropping by day 7 & further by day 13. Day 123 was the latest time point in which CAR T cells were detectable by ddPCR.
- No CAR T cells were detected by flow cytometry.
- Notably, some evidence for **reverse targeting of AUTO4 CAR T cells by normal TRBC1+ T cells** could be detected in vitro
- **All five of five patients** with posttreatment lymph nodes accessible to biopsy both IF and ddPCR **confirmed infiltration of AUTO4 CAR T cells** at these tumor sites.



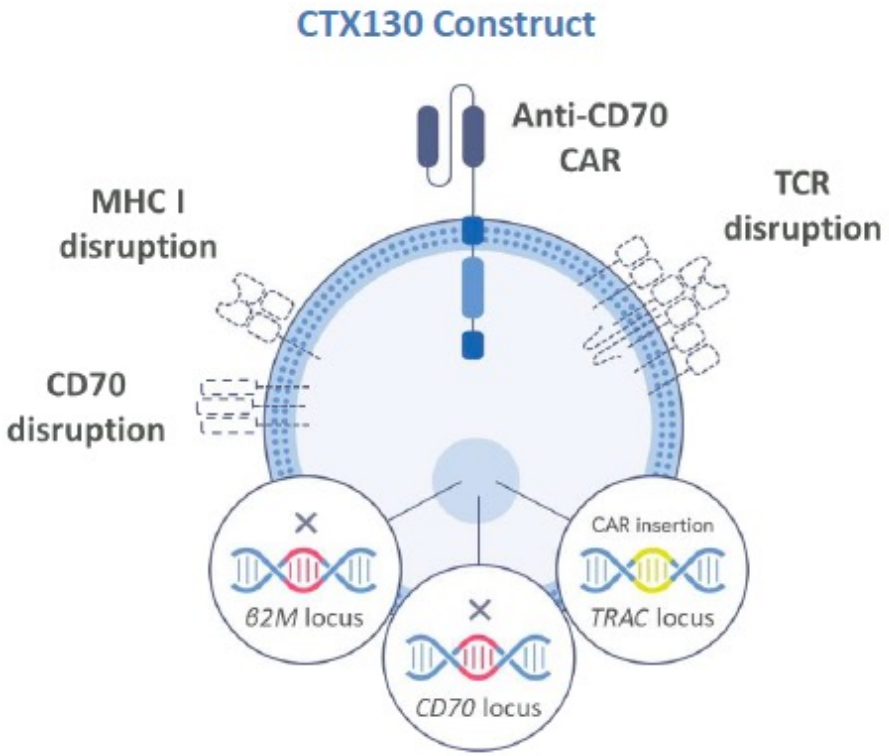
Persistence @D+175:
1/10 in blood;
75% in LN

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 Prica, 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 Mendonez, Alissa Keegan, Steven M Horwitz*

CTX130:

- Allogeneic T cells;
- CRISPR/Cas9 gene edited with TRAC, B2MG, and CD70 disruption;
- anti-CD70 CAR.



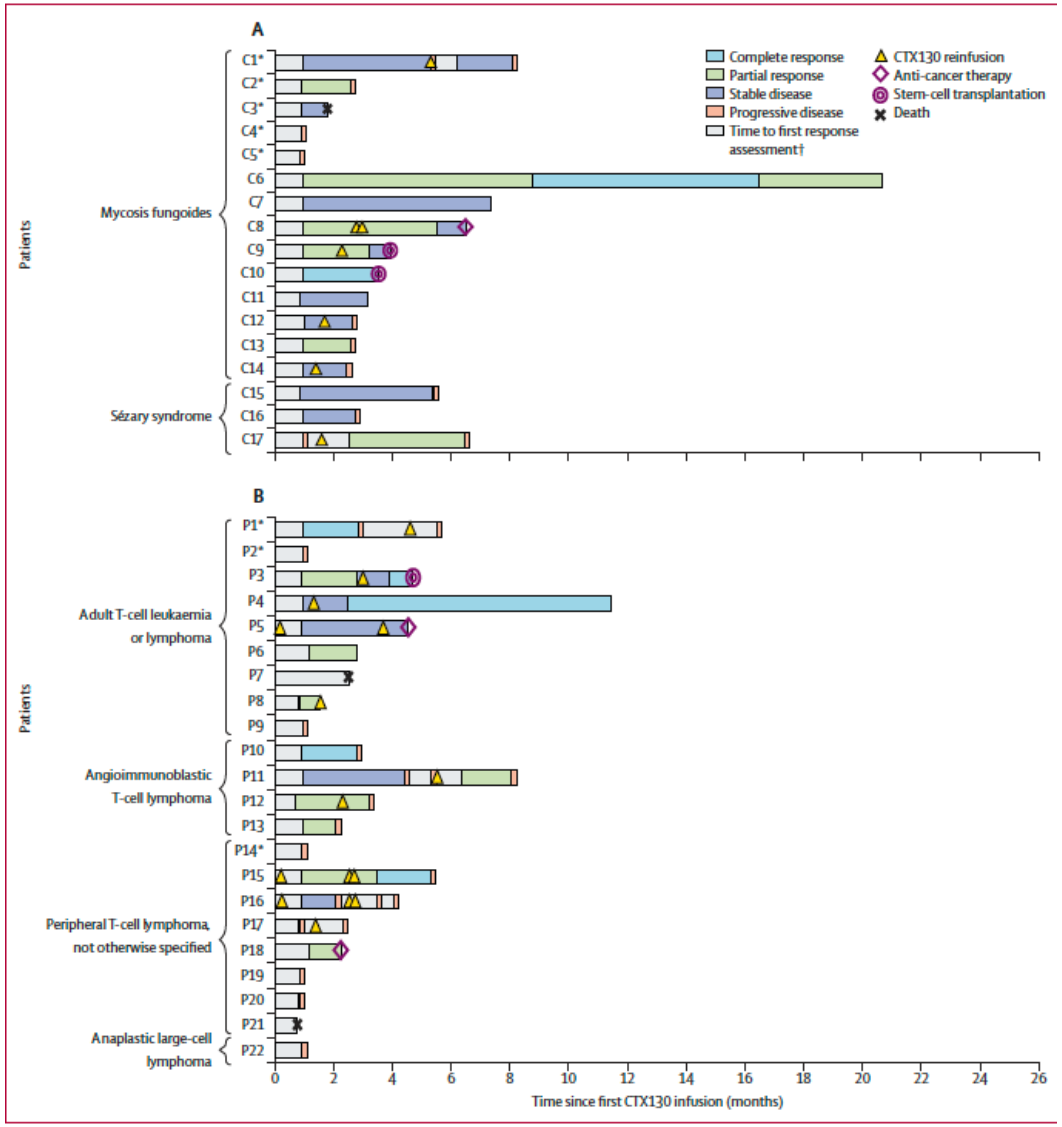
COBALT-LYM:

- 41 patients with either PTCL or CTCL
- 39 (95%) received CTX130.
- Median FU 7·4 months (IQR 3·1–12·2).
- Median number of previous lines of anticancer therapy was 2·5 (IQR 1·3–4·0) for patients w/ PTCL and 5·0 (IQR 5·0–7·0) for patients w/ CTCL.

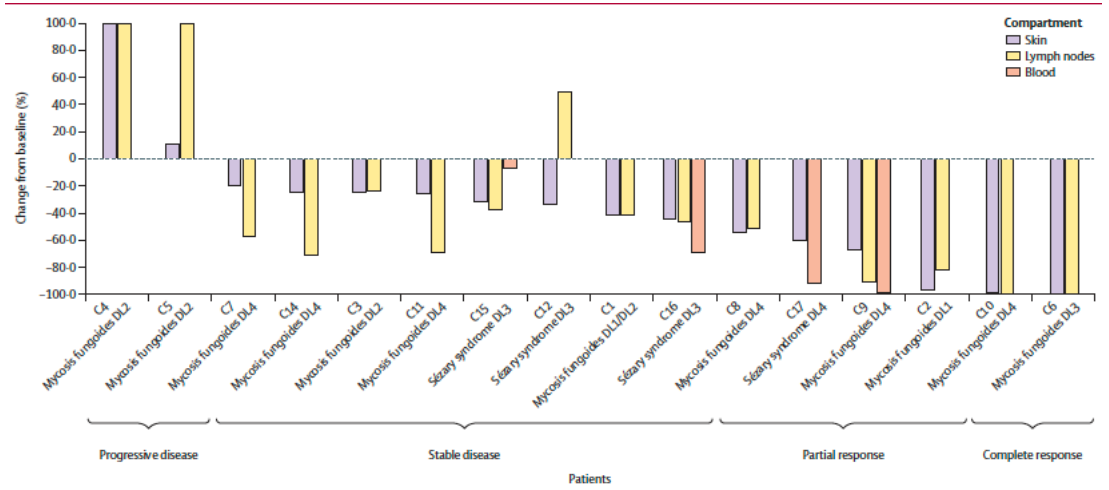
Iyer, SP et al. The Lancet Oncology, Volume 26, Issue 1, 110 - 122

COBALT-LYM trial - results

Swimmer plot for A) CTCL and B) PTCL



Waterfall plot for skin response (mSWAT) in CTCL



ORR 46.2% [95% CI 30·1–62·8] (18/39).
At DL3+, ORR 51·6% [33·1–69·8]) (16/31) w/ 19·4% CR.
MF/SS: ORR 50.0% [21·1–78·9]) @ DL3+ (N=2 CR)
DOR @ DL3+ in PTCL, 2·5 months (95% CI 1·1 to non-evaluable)

	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Cytokine release syndrome	10 (26%)	13 (33%)	2 (5%)	1 (3%)	0
Immune effector cell-associated neurotoxicity syndrome	2 (5%)	2 (5%)	0	0	0
Haemophagocytic lymphohistiocytosis	0	0	2 (5%)	0	1 (3%)
Grade ≥3 infection	NA	NA	7 (18%)	1 (3%)	2 (5%)
CTX130 infusion-related reaction	1 (3%)	1 (3%)	0	0	0
Cardiac failure	0	0	1 (3%)	0	1 (3%)

Data are n (%). NA=not applicable.

***Table 3*: Adverse events of special interest**

Iyer, SP et al. The Lancet Oncology, Volume 26, Issue 1, 110 - 122

Summary and Conclusions

CAR-T for T cell NHL has arrived.

PLUSES

- High response rates @ 1 months
- CRS and ICANS are limited
- No significant T-cell aplasia

MINUSES

- Significant infectious toxicities and EBV reactivation
- Unusual toxicities have been seen – prolonged cytopenias; skin rash; GI toxicities
- Relapses commonly due to antigen loss

Next steps:

We need to better understand on-target, off tumor effects; what makes long-term responders; how to address antigen loss by malignant T-cells

Penn Medicine

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Eugenio Fardella
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Al Garfall
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Vittoria Biotherapeutics
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Bruce Peacock
Adam Snook
Aditya Nimmagadda
Rosemary Mazanet
Stephen Yang
Kimberly Brown

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Patients and their families

THANK YOU!

The "Penn Lymphoma Bunch"