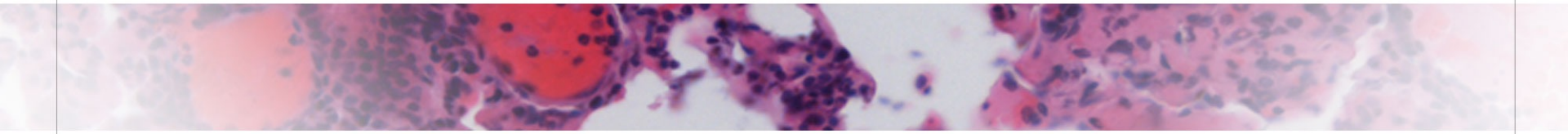
American Society *of* Hematology
Helping hematologists conquer blood diseases worldwide



WUCART7 1001 Phase 1/2 Dose-Escalation/Dose-Expansion Study of Anti-CD7 Allogeneic CAR-T Cells (WU-CART-007) in Relapsed or Refractory (R/R) T-Cell Acute Lymphoblastic Leukemia/ Lymphoblastic Lymphoma (T-ALL/LBL)

Armin Ghobadi[1], *Ibrahim Aldoss*[2], *Shannon L. Maude*[3], *Deepa Bhojwani*[4], *Alan S. Wayne*[4], *Ashish Bajel*[5], *Rawan Faraman*[6], *Ryan J. Mattison*[7], *Bhagirathbhai Dholaria*[8], *Michael P. Rettig*[1], *Ken Jacobs*[9], *Ouiam Bakkacha*[9], *John Muth*[9], *Angela Pannunzio*[9], *Brett Ramsey*[9], *Eileen McNulty*[9], *Matthew L. Cooper*[9], *Jan Davidson-Moncada*[9], *and John F. DiPersio*[1]

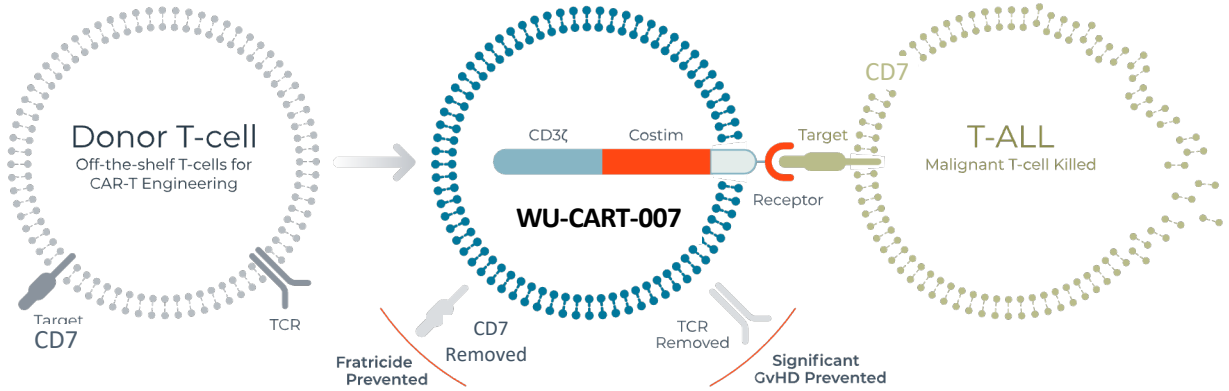
[1]*Washington University School of Medicine, Saint Louis, MO;* [2]*City of Hope, Duarte, CA;* [3]*The Children's Hospital of Philadelphia, Philadelphia, PA;* [4]*Children's Hospital of Los Angeles, Los Angeles, CA;* [5]*Clinical Haematology, Royal Melbourne Hospital, Parkville, Australia;* [6]*Bone Marrow Transplant and Cellular Therapies, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL;* [7]*Carbone Comprehensive Cancer Center, Madison, WI;* [8]*Vanderbilt University Medical Center, Nashville, TN;* [9]*Wugen, St Louis, MO*

Introduction

- T-acute lymphoblastic leukemia/lymphoblastic lymphoma (T-ALL/LBL) are challenging hematologic cancers.
- T-ALL/LBL is a highly aggressive disease with high rates of relapse and mortality in both children and adults.
- T-ALL/LBL is a high unmet need with very limited treatment options in the refractory and relapse cases.
- CD7 is expressed in >95% of T-ALL/LBL patients at both diagnosis and recurrence.
- While CAR-T therapies have been effective in treating B-cell leukemias, specific challenges exist when targeting T-cell disease.

WU-CART-007: A Dual Edited CD7-Targeted CAR-T for Treatment of T-cell Malignancies

Problem	Solution: WU-CART-007
CD7⁺ CAR-T vs. CD7⁺ CAR-T killing (**friendly-fire**)	CRISPR deletion of CD7 to prevent friendly fire
An autologous product would contain **malignant T-cells**	Allogeneic healthy donor to prevent malignant cell contamination of product
Allogeneic T-cells induce **Graft-versus-Host Disease (GvHD)**	CRISPR deletion of TCR and mitigate GvHD risk



WU-CART-007 1001 Clinical Study

- WU-CART-007 is a CD7-targeted CAR-T cell product with CRISPR/Cas9 deletion of CD7 and T-cell receptor alpha constant (TRAC), to prevent fratricide and enable the use of healthy donor allogeneic T-cells, respectively (Leedom, *et al.* ASH 2021).
- This off-the-shelf allogeneic CAR-T cell product is being developed for the treatment of $CD7^+$ malignancies.
- WU-CART-007 1001 (NCT04984356) is a global first-in-human, Phase 1/2 single-agent study of WU-CART-007 in patients with R/R T-ALL/LBL.

WU-CART-001 1001 Eligibility Criteria

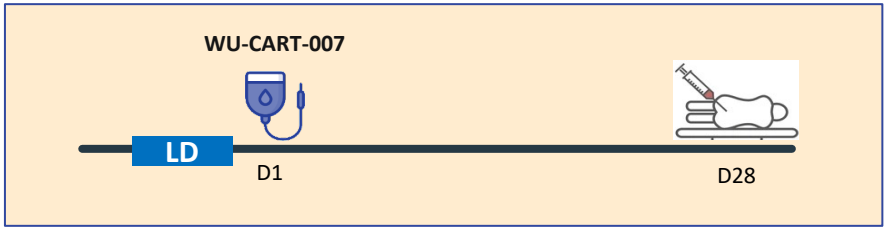
Key Inclusion Criteria

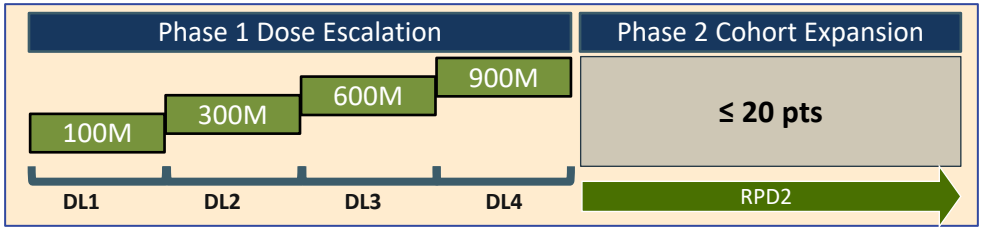
- Patients, **12 year or older**, with evidence of **relapsed or refractory T-ALL or T-LBL**, as defined by World Health Organization (WHO) classification with **bone marrow with ≥ 5% lymphoblasts**, or evidence of **extramedullary disease** at screening.
- **Relapsed or refractory disease** defined as at least one of the following criteria:
    - Primary refractory: failure to achieve CR after induction chemotherapy, per investigator.
    - Early Relapse: relapsed disease within 12 months of initial diagnosis.
    - Late Relapse (relapsed refractory disease): relapsed disease after 12 months of initial diagnosis AND failure of re-induction therapy after disease recurrence.
    - Relapsed or refractory disease after allogeneic transplant.
- **ECOG** Status of 0 or 1

Key Exclusion Criteria

- Treatment with any prior anti-CD7 therapy.
- Unresolved toxicities from prior anticancer therapy, defined as having not resolved to baseline or to CTCAE Grade ≤1, except for nausea or alopecia, or to the levels dictated in the inclusion/exclusion criteria.
- Patient has previously participated in any investigational research study and is being screened for participation within a period of 5 half-lives of the last dose of the investigational therapy.
- Active or latent hepatitis B or active hepatitis C, or any uncontrolled infection at Screening.
- Grade 2 to 4 acute or extensive chronic GvHD requiring systemic immunosuppression.

WU-CART-001 1001 Study Design





Lymphodepletion Conditioning Chemotherapy (sLD) Phase 1 Dose Escalation:

- Fludarabine 30 mg/m²/day ×3 (Days -5, -4, and -3)
- Cyclophosphamide 500 mg/m²/day ×3 (Days -5, -4, and -3)

Enhanced Lymphodepletion Conditioning Chemotherapy (eLD) Phase 2 Cohort Expansion:

- Fludarabine 30 mg/m²/day ×4 (Days -6, -5, -4, and -3)
- Cyclophosphamide 1000 mg/m²/day ×3 (Days -5, -4, and -3)

Phase 1

Primary Endpoint

- Safety, dose-limiting toxicities (DLT), and maximum tolerated dose (MTD) or maximum administered dose (MAD)
- Define the Recommended Phase 2 Dose (RP2D) of WU-CART-007 in T-ALL/LBL

Phase 2

Primary Endpoint

- To investigate the Composite Complete Remission Rate (CRc) of WU-CART-007 in R/R T-ALL/LBL patients

Secondary Endpoint

- To investigate the duration of response (DOR) of WU-CART-007 in relapsed or refractory T-ALL/LBL patients

Patient and Disease Characteristics

Patient Characteristics	DL1 100x10^6 n=3	DL2 300x10^6 n=3	DL3 600x10^6 n=6	DL4 900x10^6 n=3	Cohort Expansion 900x10^6 n=10	Total n=25
Median Age (y, range)	26 (26-49)	33 (21-49)	33.5 (25-61)	35 (20-68)	29.5 (14-44)	31.5 (14-69)
Female (%, n)	66% (2)	0% (0)	33% (2)	0% (0)	40% (4)	32% (8)
Primary Induction Failure (%, n)	33% (1)	33% (1)	67% (4)	0% (0)	10% (1)	28% (7)
Median Prior Lines of Treatment (range)	5 (1-5)	5 (1-7)	3 (2-6)	4 (3-4)	3 (2-5)	4 (1-7)
Post-HSCT (%, n)	0% (0)	33% (1)	17% (1)	66% (2)	50% (5)	36% (9)
Median Baseline % BM Blast (range)*	60% (43-85)	77% (68-85)	60% (47-63)	18% (5-30)	73% (23-91)	63.2% (5-95)

*BM: Bone marrow; EMD: Extra medullary disease; *7 patients had EMD only (no BM blasts) disease at baseline; data cut 11/28/2023..*

WU-CART-007 1001 Safety Assessment

WU-CART-007 demonstrated manageable safety.

- Treatment-related adverse events of ≥ Gr 3 were observed in 14/25 (56%) patients.
- Cytokine Release Syndrome (CRS) was observed in 21/25 (84%) patients.
- Most (64%; 16/25) patients had Gr 1-2 CRS events, (12%; 3/25) had Gr 3 CRS events, and (8%; 2/25) had Gr 4 CRS events.

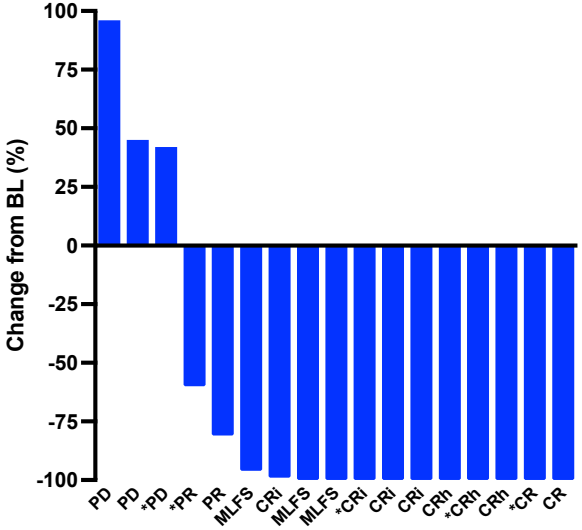
  Grade 4 CRS events were manageable with supportive care and completely resolved within 7 and 13 days, respectively.
- Grade 1 ICANS was reported in a patient at DL3, which resolved spontaneously.
- No GvHD events were reported.
- 3 patients had Gr 5 events - one of which was temporally related and occurred in the setting of disease progression.

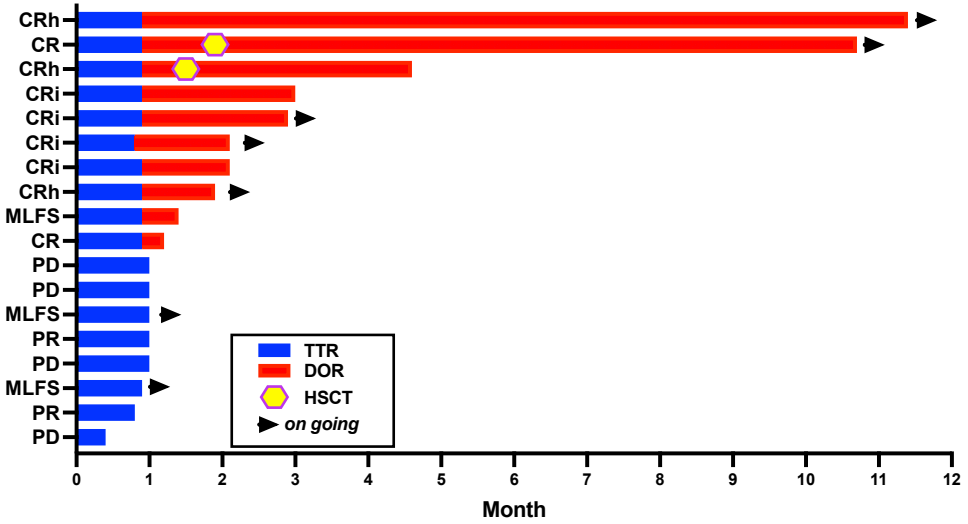
Treatment-Related AESI	DL1 (n=3)		DL2 (n=3)		DL3 (n=6)		DL4 sLD (n=3)		Expansion (n=10)		ALL (n=25)	
	G1-G2	Gr ≥3	G1-G2	Gr ≥3	G1-G2	Gr ≥3	G1-G2	Gr ≥3	G1-G2	Gr ≥3	G1-G2	Gr ≥3
CRS	2 (67%)	0	2 (67%)	1 (33%)	3 (50%)	0	3 (100%)	0	6 (60%)	4 (40%)	16 (64%)	5 (20%)
HLH	0	0	0	2 (67%)	0	0	0	0	1 (10%)	1 (10%)	1 (4%)	3 (12%)
ICANS	0	0	0	0	1 (33%)	0	0	0	0	0	1 (4%)	0
GvHD	0	0	0	0	0	0	0	0	0	0	0	0
Prolonged Cytopenia/ T-cell Aplasia*	0	0	0	0	0	0	0	0	0	0	0	0
EBV Viremia/Viremia	0	0	0	0	0	0	0	0	1 (10%)	1 (10%)	1 (4%)	1 (4%)

**Prolonged Cytopenia (including T-cell aplasia): persistent ≥ Gr 3 cytopenia lasting more than 30 days starting in the absence of disease; AESI: Adverse Events of Special Interest; Data cut 11/28/2023.*

Efficacy assessment at active dose (DL ≥ 2)

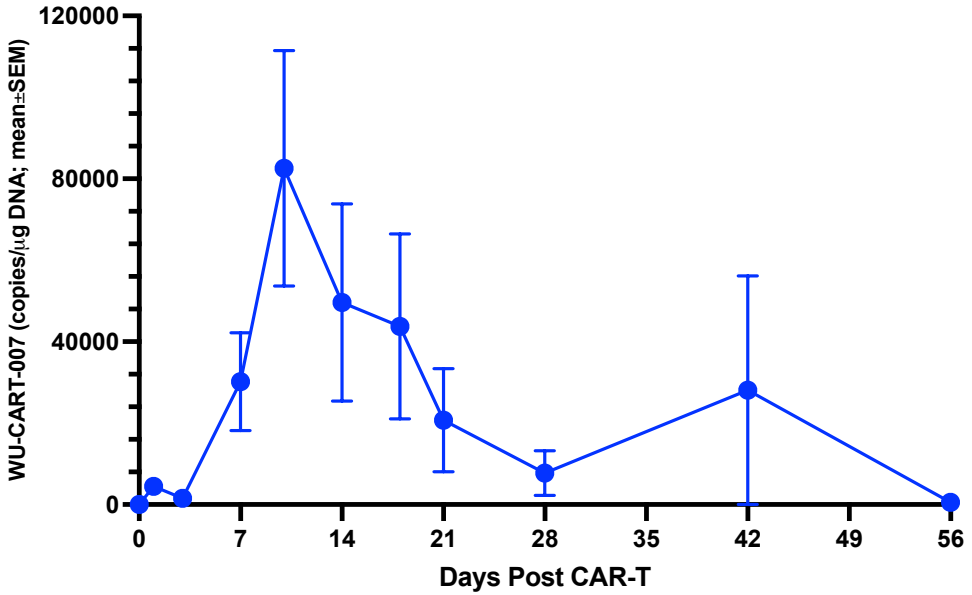
- Objective Response Rate (CRi, CRh, CR, MLFS, PR) **ORR 78%** (14/18)
- **CRc** (CR, CRh, CRi, MLFS) **67%** (12/18) [MRD^{neg} 91% (10/11)]





Composite complete remission rate (CRc); **Evaluable pts n=18, four patients are not evaluable for efficacy** (Three pt. died of causes unrelated to disease progression and did not have a disease evaluation; third pt. did not meet inclusion criteria for T-ALL/LBL); **Of evaluable pts one pt. had PD noted in CNS and is not represented on waterfall plot**. One pt sample for MRD assessment was not available; *EMD disease per Lugano criteria; *data cut 11/28/2023.*

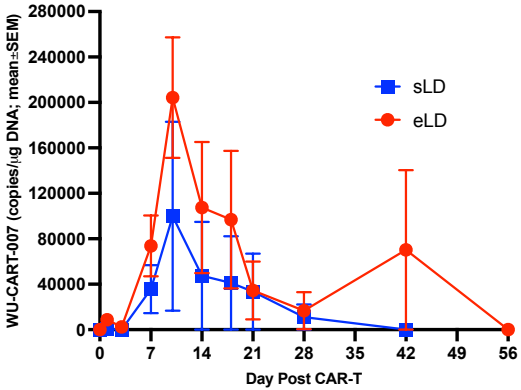
WU-CART-007 PK Analysis



- WU-CART-007 expansion peaks at Day 10 (82,523 copies/μg of DNA) and can be detected out to Day 56.
- No patient developed drug product-specific anti-HLA antibodies.
- No anti-drug antibody detected on any patients (n = 18; *3 DL1, 3 DL2, 6 DL3, 6 DL4*) to date.

Recommended Phase 2 Dose: Efficacy Assessment

- Enhanced lymphodepletion leads to increased WU-CART-007 proliferation and persistence
- Enhance lymphodepletion leads to **100% ORR at RP2D** (900 x 10^6 WU-CART-007 cells)

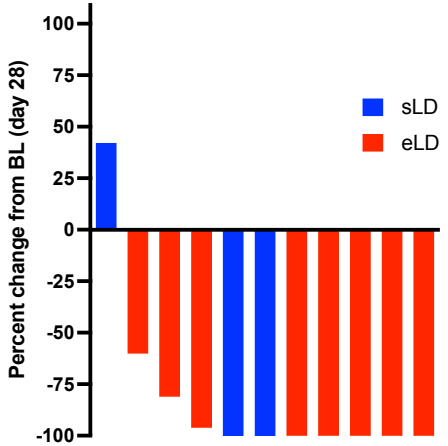


WU-CART-007 Expansion Peak (Day 10)

eLD: 204219 copies/μg of DNA.

sLD: 99898 copies/μg of DNA

	900 sLD (n=3)		900 eLD (n=10)	
AESI	**All**	**Gr ≥3**	**All**	**Gr ≥3**
ICANS	0	0	0	0
CRS	3 (100%)	0	10 (100%)	4 (40%)
HLH	0	0	2 (20%)	1 (10%)
GvHD	0	0	0	0
Prolonged Cytopenia/ T-cell Aplasia	0	0	0	0
EBV Viremia	0	0	2 (20%)	1 (10%)
Fungal Infection	0	0	1 (10%)	1 (10%)



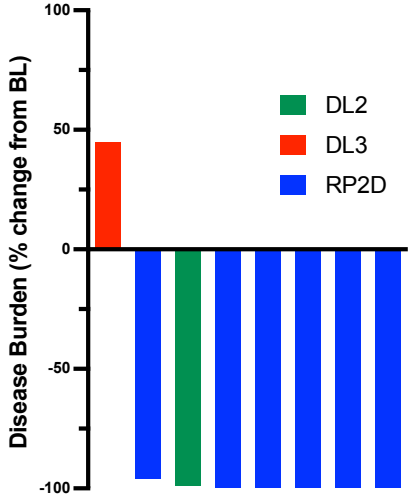
Lymphodepletion	ORR	CRc
sLD (n=3)	66% (2)	66% (2)
eLD (n=8)	100% (8)	75% (6)

*Composite complete remission rate (CRc; evaluable pts n=11); **Two patients are not evaluable for efficacy**. (Both pts. died of causes unrelated to disease progression and did not have a disease evaluation); EMD disease per Lugano criteria; sLD: lymphodepletion; eLD: enhanced lymphodepletion; *data cut 11/28/2023.*

Subgroup Analysis of Relapsed Post-HSCT Patients

In the post-HSCT setting **ORR 100% at RP2D** (900 x 10^6 WU-CART-007 cells)

Patient Characteristics	N = 9
Age (Median, Range)	35 (16-49)
Female	22% (2)
T-ALL	89% (8)
Primary Induction Failure	0 (0)
Prior Lines of Treatment (Median, Range)	4 (3-7)
Prior Allogeneic Stem Cell Transplant	100% (9)
Baseline % BM Blast (Median, Range)	68% (5-91)



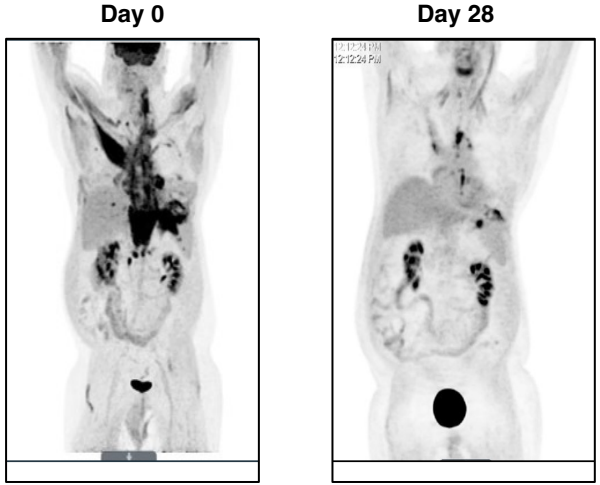
Adverse Events of Special Interest	Relapsed Post-HSCT (n = 9; n[%])	
	All	Gr ≥3
ICANS	0	0
Cytokine Release Syndrome	9 (100%)	2 (22%)
GvHD	0	0

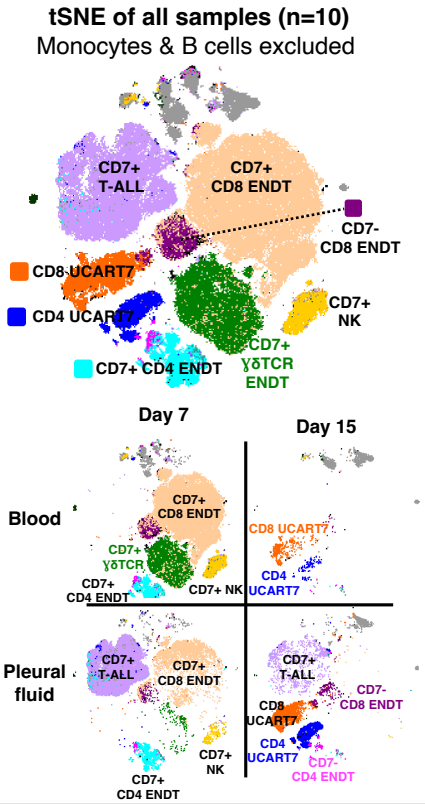
Relapsed Post-HSCT (n = 8)*	All	RP2D
ORR	88% (7/8)	100% (6/6)
CRc	88% (7/8)	100% (6/6)

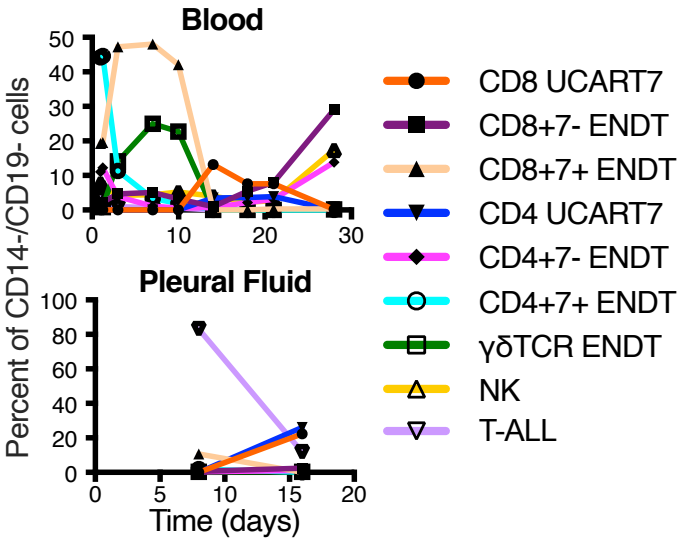
*One post-HSCT patient not evaluable for efficacy. (Pt. died of causes unrelated to disease progression and did not have a disease evaluation); EMD disease per Lugano criteria; *data cut 11/28/2023.*

WU-CART-007: Pt. 01-201

44-year-old male T-LBL relapsed after 4 lines of therapy including allo-HCT







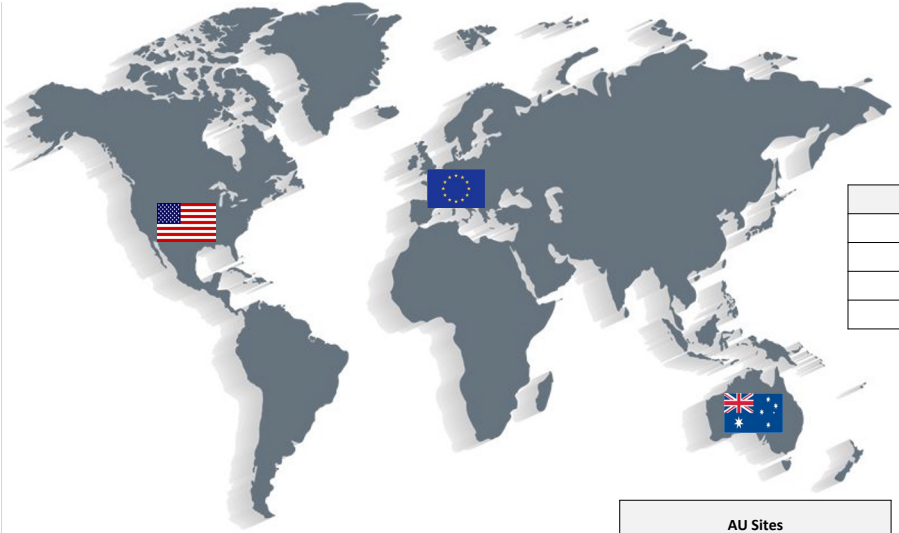
Conclusions

- WU-CART-007 has demonstrated an acceptable safety profile and encouraging anti-leukemic activity in difficult to treat patients.
- WU-CART-007 is an effective treatment option in the post-HSCT setting.
- This program advances CAR-T cell therapy in heavily pre-treated patients with R/R T-ALL/LBL.
- The WU-CART-007 1001 study is ongoing.

Acknowledgements

Thank you to all the patients, families, caregivers, and investigators.

US Sites
Washington University, St Louis
City of Hope National Medical Center
University of Wisconsin Medical Center
Children's Hospital of Los Angeles
Children's Hospital of Philadelphia
Moffitt Cancer Center
Vanderbilt Ingram Cancer Center



EU Sites
Erasmus MC (NL)
Princess Maxima Centrum (NL)
Hôpital Universitaire Robert Debré (FR)
Hôpital St Louis, Paris (FR)

AU Sites
Peter MacCallum Cancer Centre