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Engineering macrophages for cancer immunotherapy

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AACR 2024

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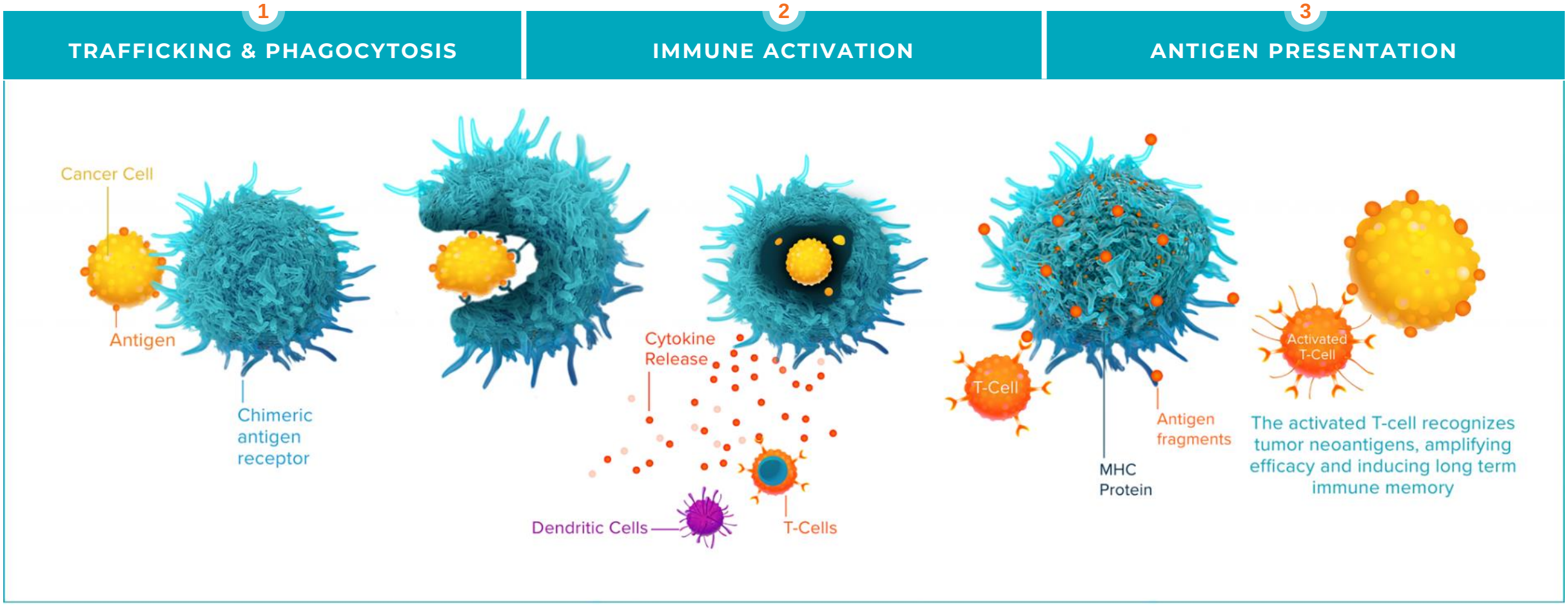
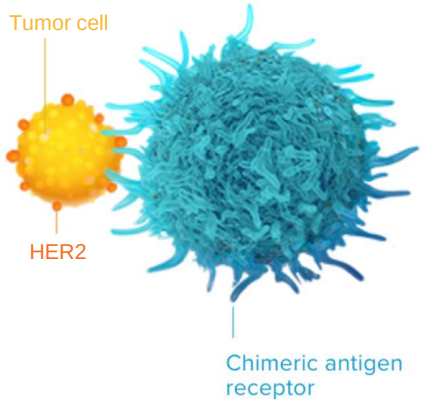
CAR-M: A differentiated mechanism of action

Potential to address the challenges of treating solid tumors with cell therapies

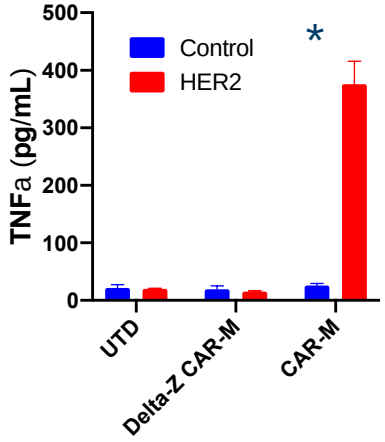


MHC: Major Histocompatibility Complex
CAR-M: chimeric antigen receptor macrophages and monocytes

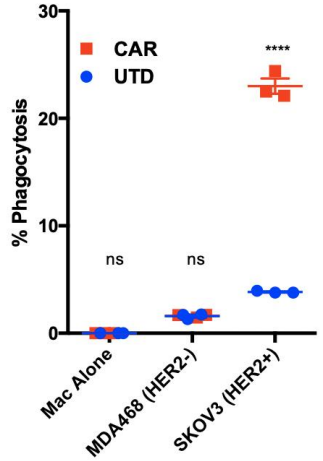
CARs redirect macrophage and monocyte effector function



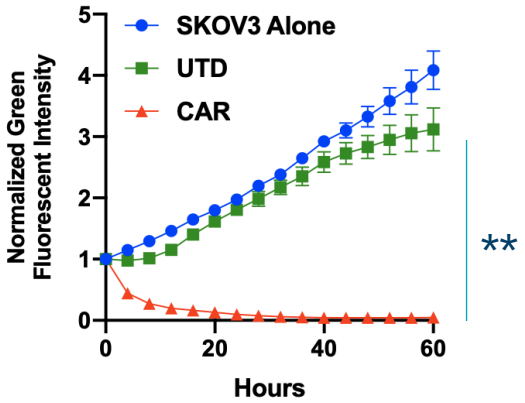
CAR-M Cytokine Production



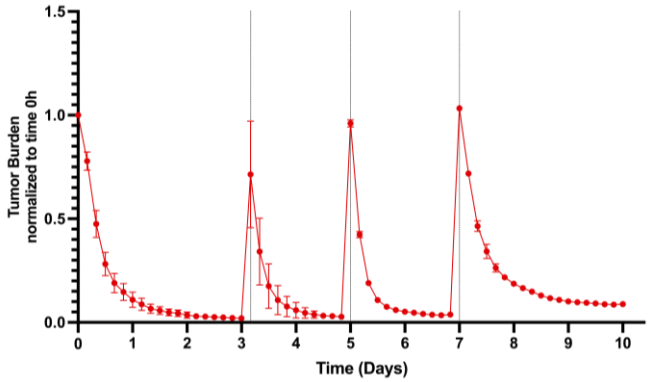
CAR-M Phagocytosis



CAR-M Killing



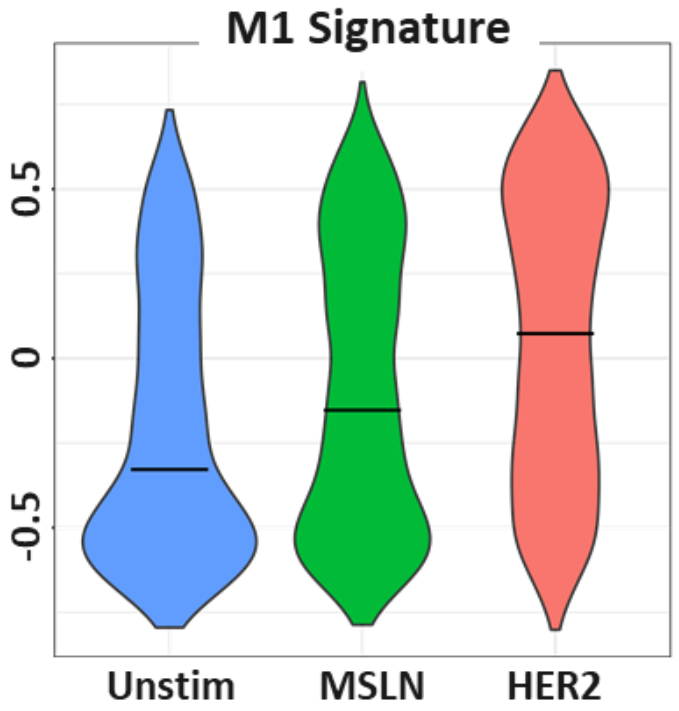
CAR-M Serial Killing

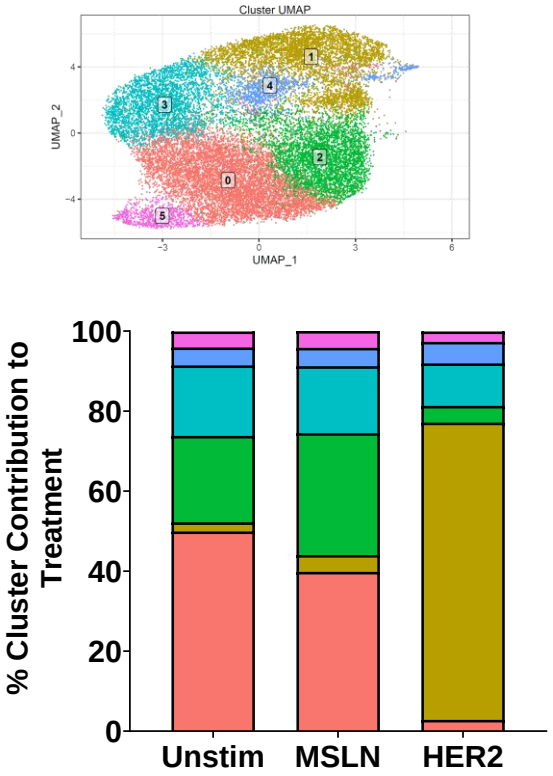


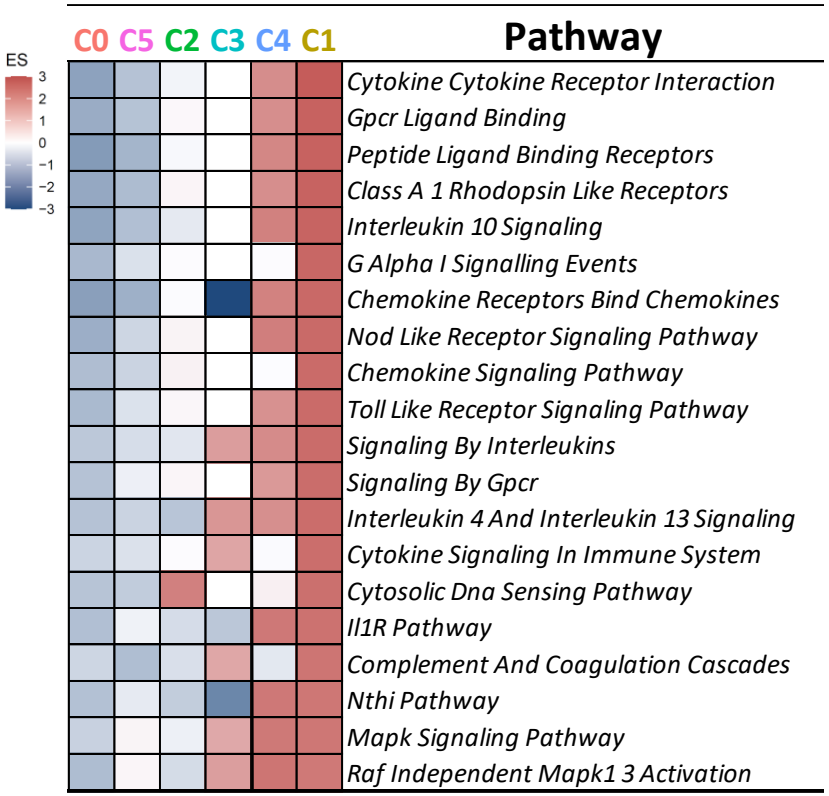
Klichinsky M, et al. Nature Biotechnology. 2020.

CAR engagement triggers an M1 gene expression program

Anti-HER2 CAR-M stimulation with HER2 leads to gene expression changes associated with M1 macrophage phenotype.



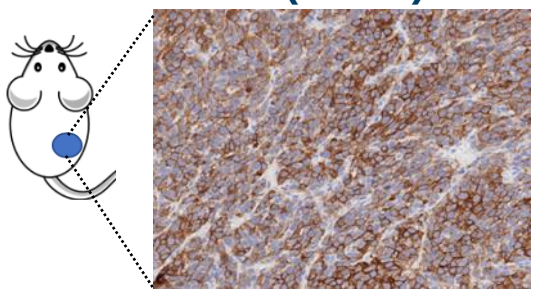




Ball M, et al. SITC. 2022.

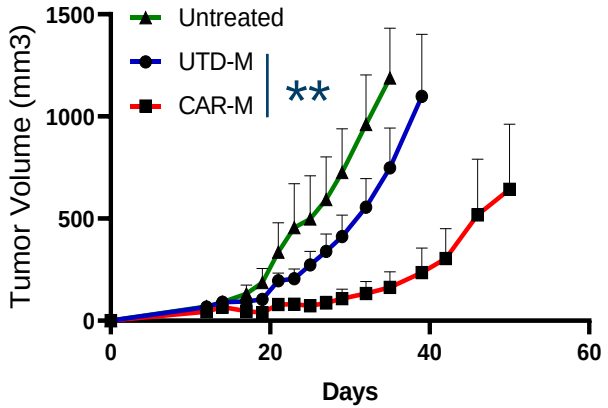
CAR-M shrink tumors, modulate the TME, and induce systemic T cell responses in immunocompetent models

CT26 (HER2)

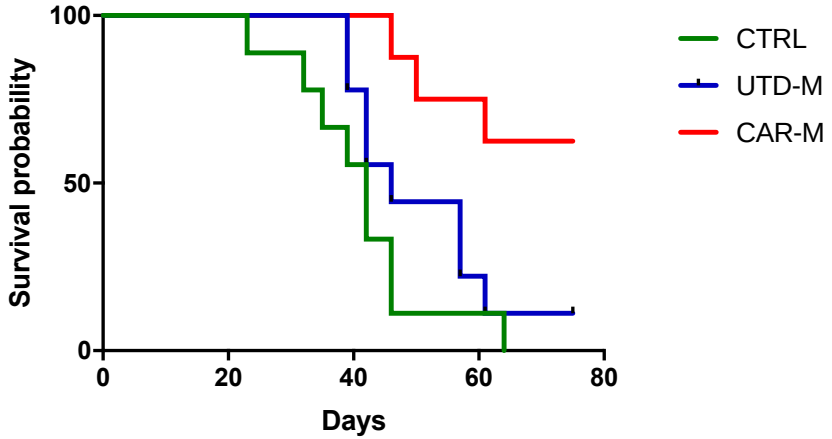


HER2 IHC: HER2 3+

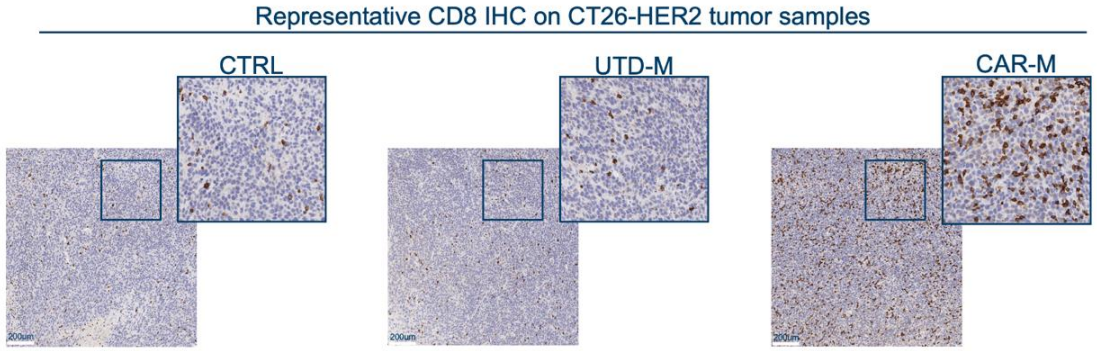
Average tumor growth curves:

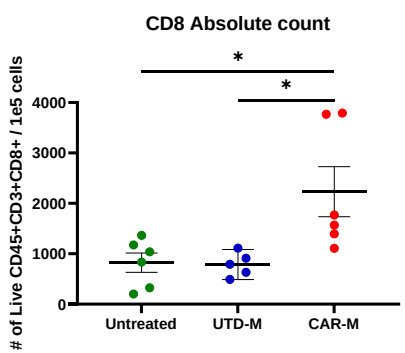


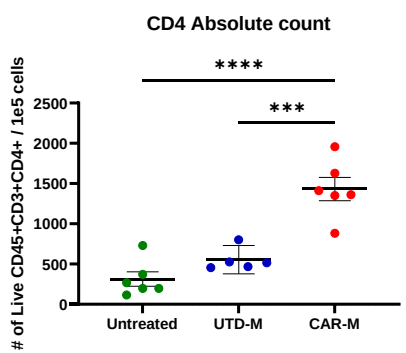
Kaplan Meier Survival Curve:

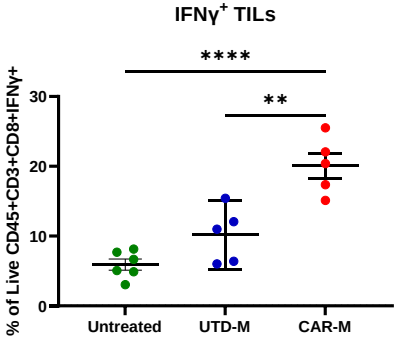


CAR-M modulate the TME – CD8+ T cell infiltration



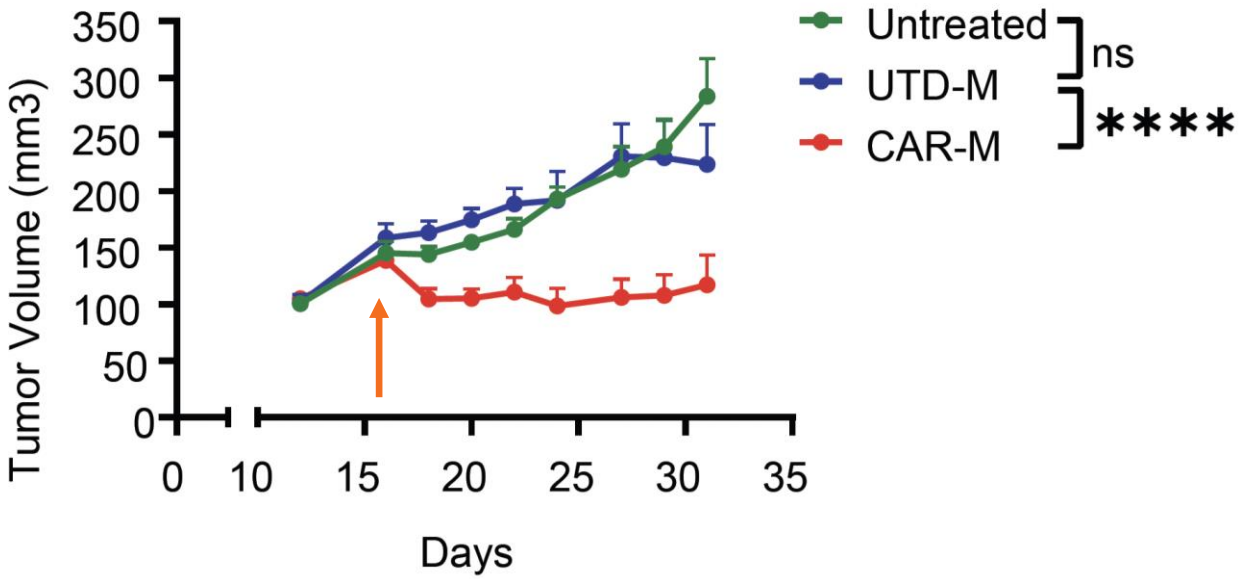




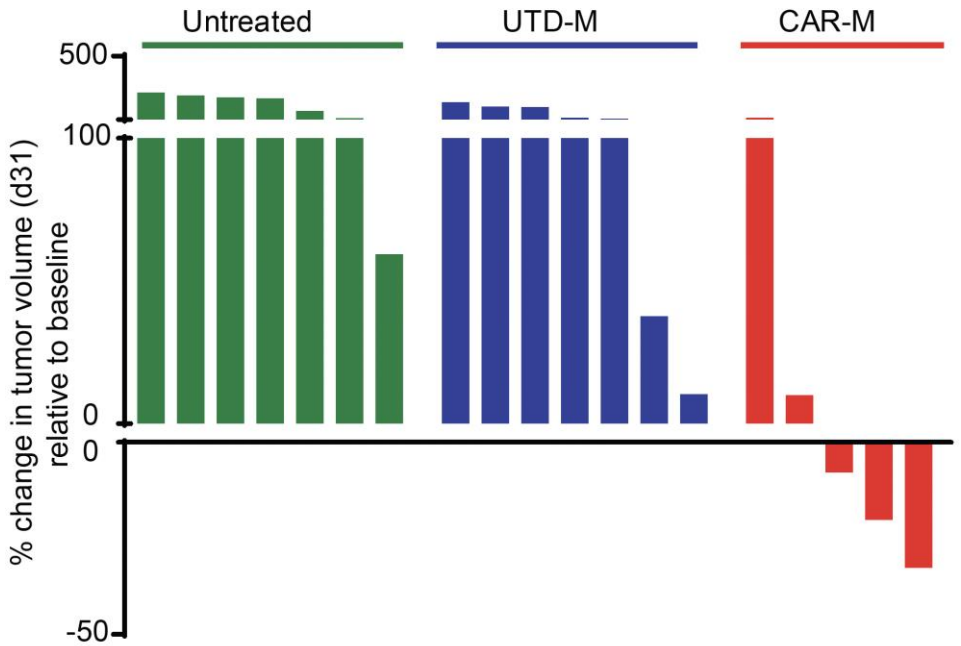


Anti-HER2 CAR-M controlled tumor growth in an orthotopic 4T1-HER2 mammary fat pad model

Average tumor growth curves



Tumor change: Day 31 vs. Baseline



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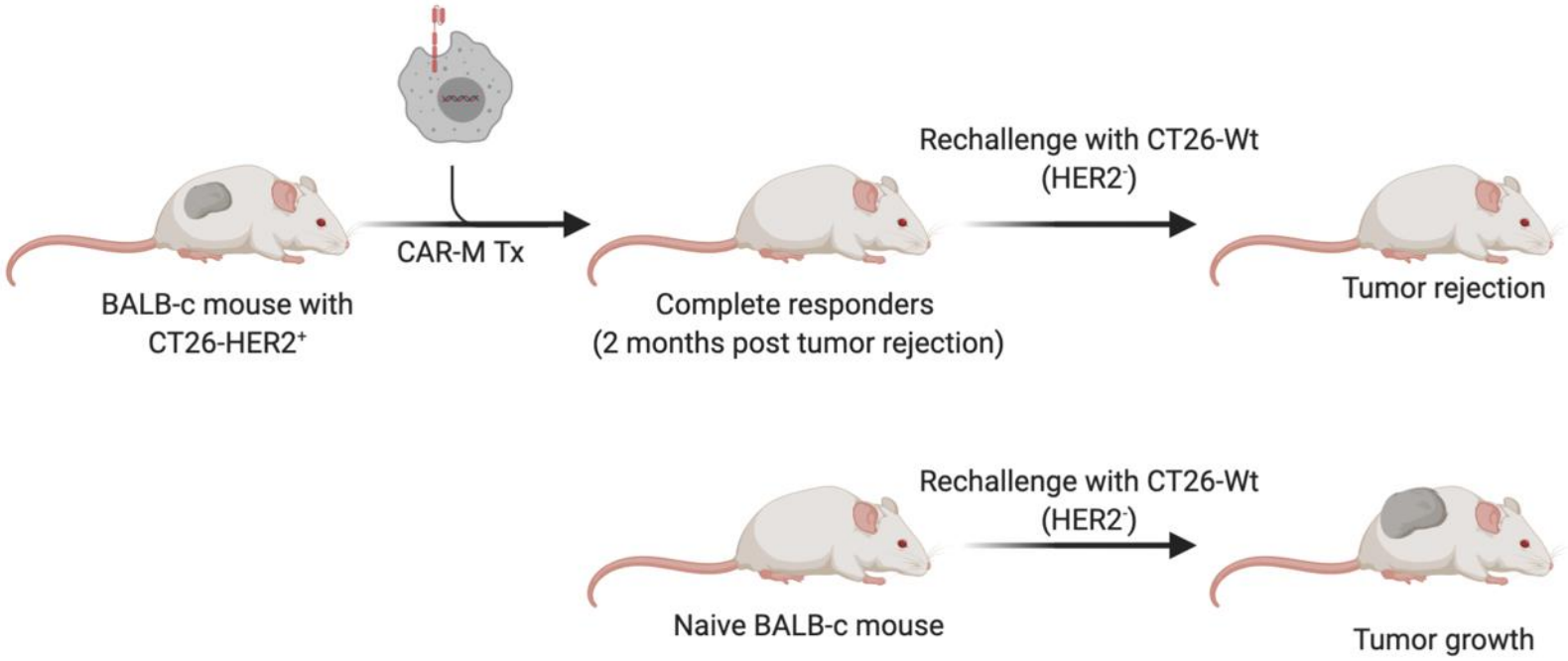
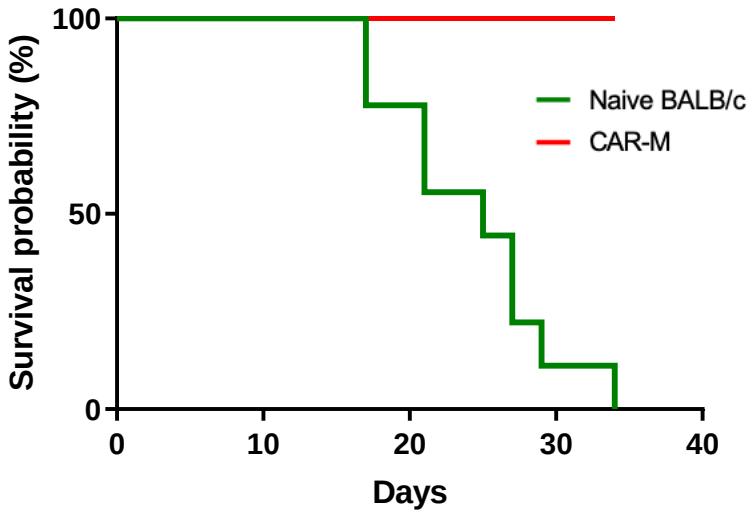
CAR-M Therapy Protects Mice Against Tumor Recurrence and Prevents Antigen Negative Relapse



CT26 Wt (HER2-) rechallenge: Kaplan Meier Survival Curve



CT-0508: HER2 Targeted CAR-Macrophage

Well-tolerated and active therapy in safety study sets the stage for further development of anti-HER2 CAR-M

Highlights

Study Status

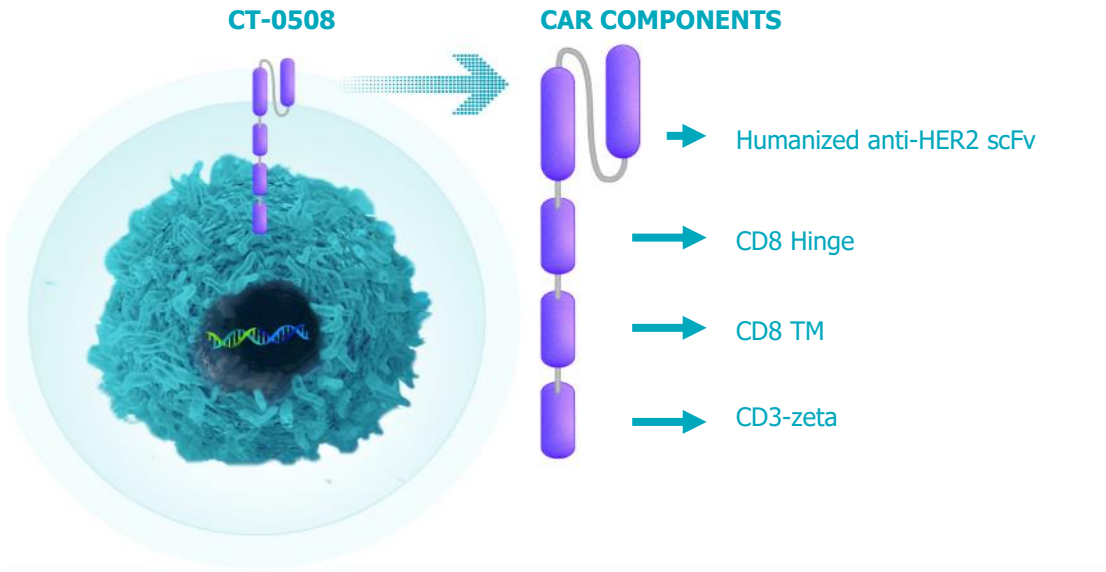
- Study 101 Group 1 (fractionated dosing): 9 patients
- Study 101 Group 2 (bolus dosing): 5 patients
- Study 101 sub-study (pembrolizumab combination): 6 patients
- Determined to ceased further development in late March 2024

Key Study Takeaways To Date - Monotherapy

- Generally well-tolerated
- No tolerability differences between fractionated and bolus dosing
- Demonstrated manufacturing feasibility
- Clear MoA and anti-tumor activity observed in HER2 3+ patients
- Dose, trafficking, and persistence a key limitation
- Patient population with exhausted T cells – a key barrier

Upcoming Activities

- Complete Study 101 pembrolizumab sub-study Regimen 2
- Additional Study 101 pembrolizumab sub-study data expected 2Q ‘24



	CT-0508 Product Description
Cells	Autologous monocyte derived macrophages
Vector	Ad5f35
Phenotype	M1
CAR	1st Generation

MOA: Mechanism of Action

CT-0508 Study 101: First in Human Phase 1 Clinical Design

Assessing safety, tolerability, feasibility and TME impact of CT-0508 monotherapy

HER2 2+/3+ solid tumors (n≈27)

G-CSF mobilization and apheresis, CAR-Macrophage manufacture, bridging therapy, baseline staging

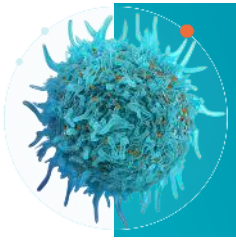
Group 1: CT-0508 fractionated dose D1,3,5 (n=9)

Group 2: CT-0508 bolus dose D1 (n≤9)

Pembro Sub-study: CT-0508 + pembrolizumab (n≥9)

Demonstrated manufacturing feasibility, safe administration, cell trafficking from blood to tumor, cells resided in tumor for up to 4 weeks, positively modulated TME[1]

Anticipate presenting data from Pembro Sub-study in 2Q 2024



PRIMARY OUTCOMES[2]

- Safety and tolerability
- Manufacturing feasibility

SECONDARY OUTCOMES & ADDITIONAL ANALYSES[2]

- ORR (RECIST 1.1)
- PFS
- Trafficking
- TME activation
- T cell recruitment/activation
- T cell expansion/clonality

Biopsy performed at screening, Day 8, Week 4 and Week 6 or 7 RECIST v1.1
Note: In late March 2024, Carisma made the decision to cease further development of CT-0508, including monotherapy and in combination with pembrolizumab
ORR: Objective Response Rate; PFS: Progression-Free Survival
1. Data from Reiss, et al. SITC 2022; and Klichinsky, et al. CAR-TCR 2023. 2. Outcomes are specific to Group 1 and Group 2 study.

CT-0508 Study 101 monotherapy patient demographics (n=14)

Heavily pre-treated pts with HER2 2+/3+ solid tumors

Summary of Participant and Tumor Characteristics			
Characteristic	**N = 14**	**Characteristic**	**N = 14**
Median age (range), years	58 (45, 81)	Tumor Type, n (%) Breast Cancer Esophageal Cancer Salivary Carcinoma Cholangiocarcinoma Ovarian Cancer	 8 (57.1) 2 (14.3) 2 (14.3) 1 (7.1) 1 (7.1)
Gender, n (%) Male Female	 4 (28.6) 10 (71.4)		
Race, n (%) White	 14 (100)	Median Number of Prior Cancer Therapies, n (range)	5 (2, 12)
ECOG PS, n (%) 0 1	 9 (64.3) 4 (28.6)	Median Number of Prior Anti-HER2 Therapies, n (range) Subjects with Prior Anti-HER2 Therapy	2 (0, 9) 13 (92.9)
HER2 Overexpression, n (%) IHC 3+ IHC 2+/FISH+	 9 (64.3) 5 (35.7)	Prior Radiotherapy, n (%) Yes	 9 (64.3)
Microsatellite Instability (MSI)* MSS/MSI-Low MSI-High Unknown	 13 (92.9) 0 (0) 1 (7.1)	Tumor Mutational Burden (TMB)* Low (<10 mut/Mb) High (≥10 mut/Mb) Unknown	 11 (78.6) 2 (14.3)† 1 (7.1)

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* MSI-high and TMB high are known biomarkers associated with improved response to immune checkpoint

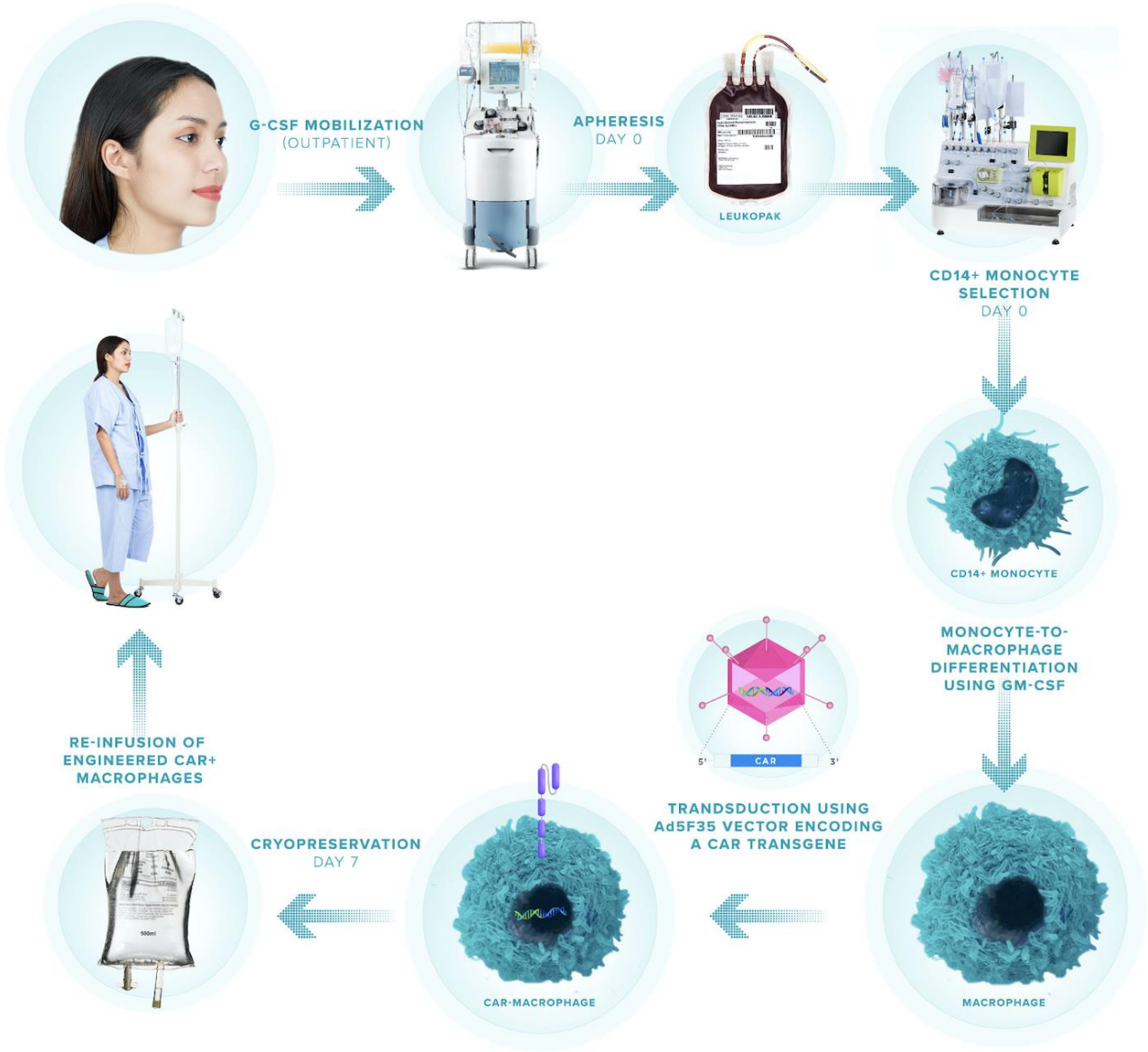
† 1 patient had received 11 lines of prior therapy and 1 patient has demonstrated HLA-A and HLA-C loss of Heterozygosity

CT-0508 Manufacturing Process

- **Source**: autologous mobilized peripheral blood monocytes
- **Mfg time**: ~1 week
- **Vein to vein**: ~3 weeks
- **Vector**: Ad5f35
- **Process**: Automated
- **Format**: Cryopreserved
- **Manufacturing Partners:**

Miltenyi Biotec

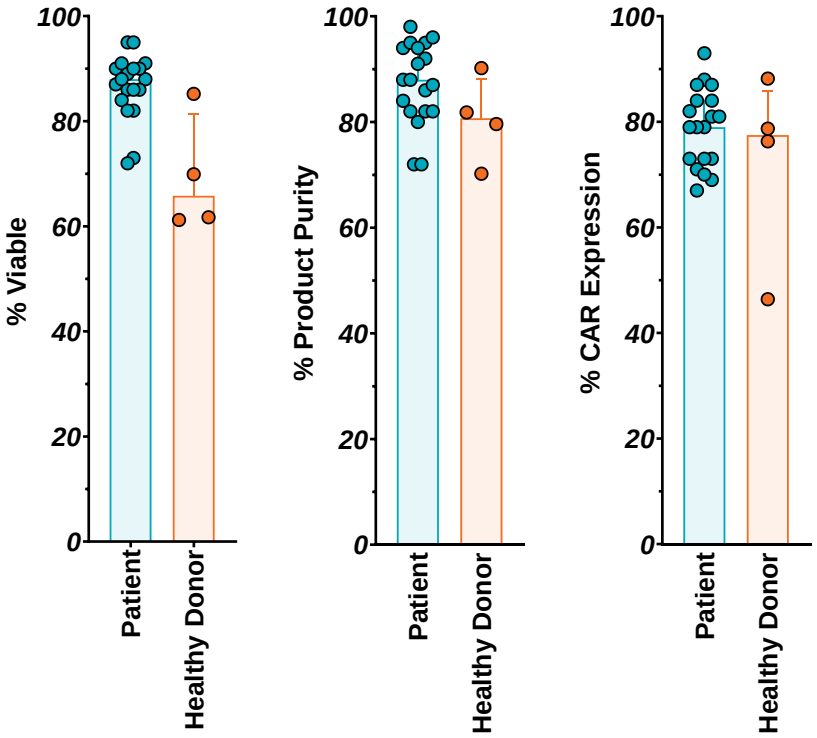
NOVARTIS



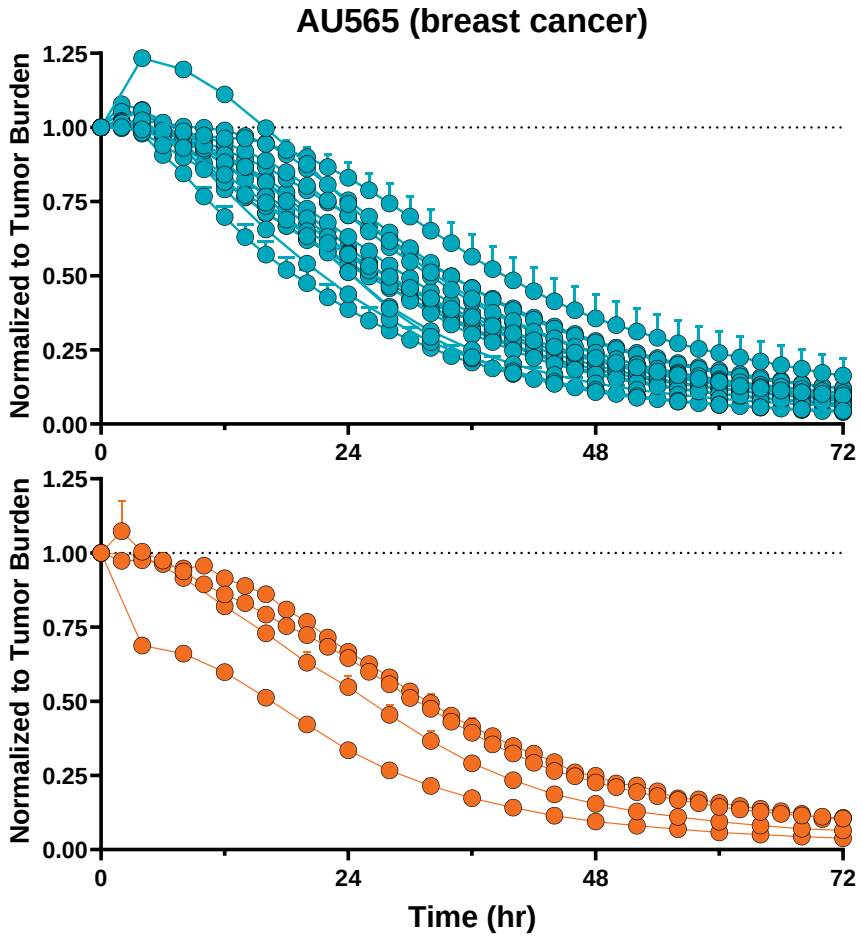
High viability, purity, CAR expression, killing, and phagocytosis with patient derived CT-0508

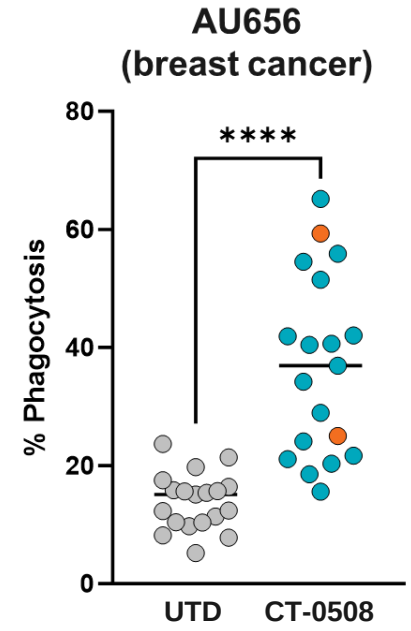
High viability, purity, and CAR Expression

Patient Derived CT-0508
Healthy Donor Derived CT-0508



All CT-0508 batches kill and phagocytose HER2+ tumor cells





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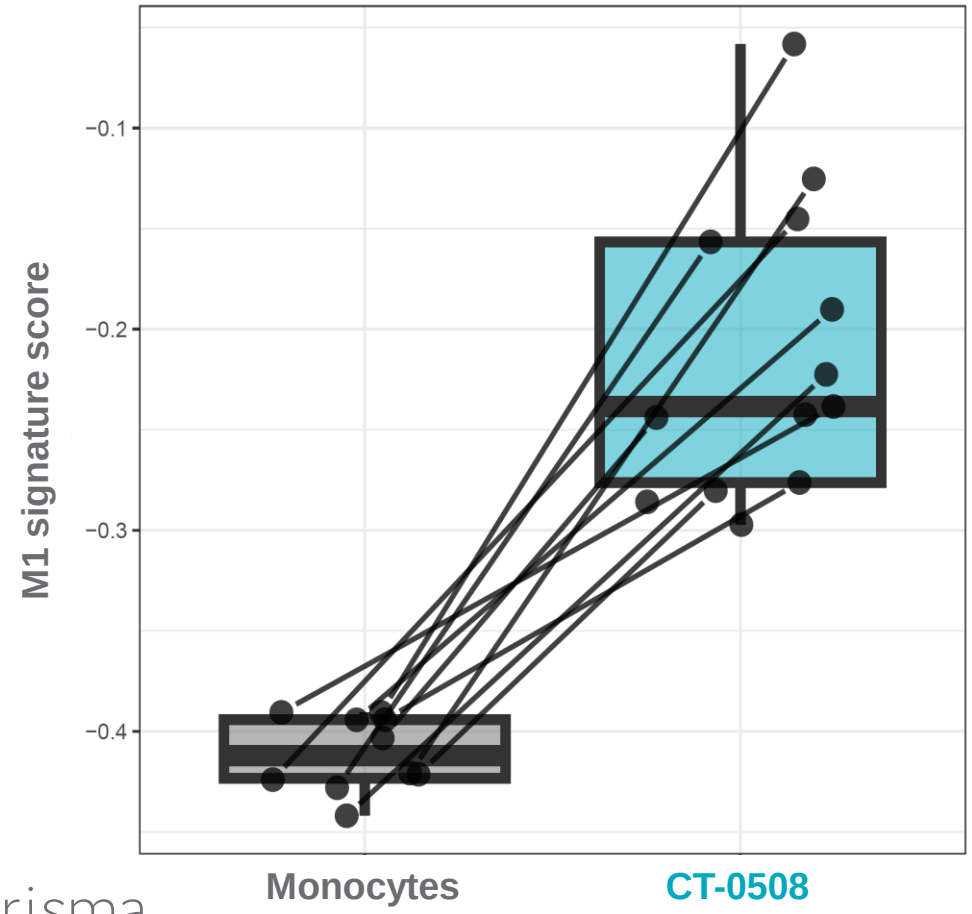
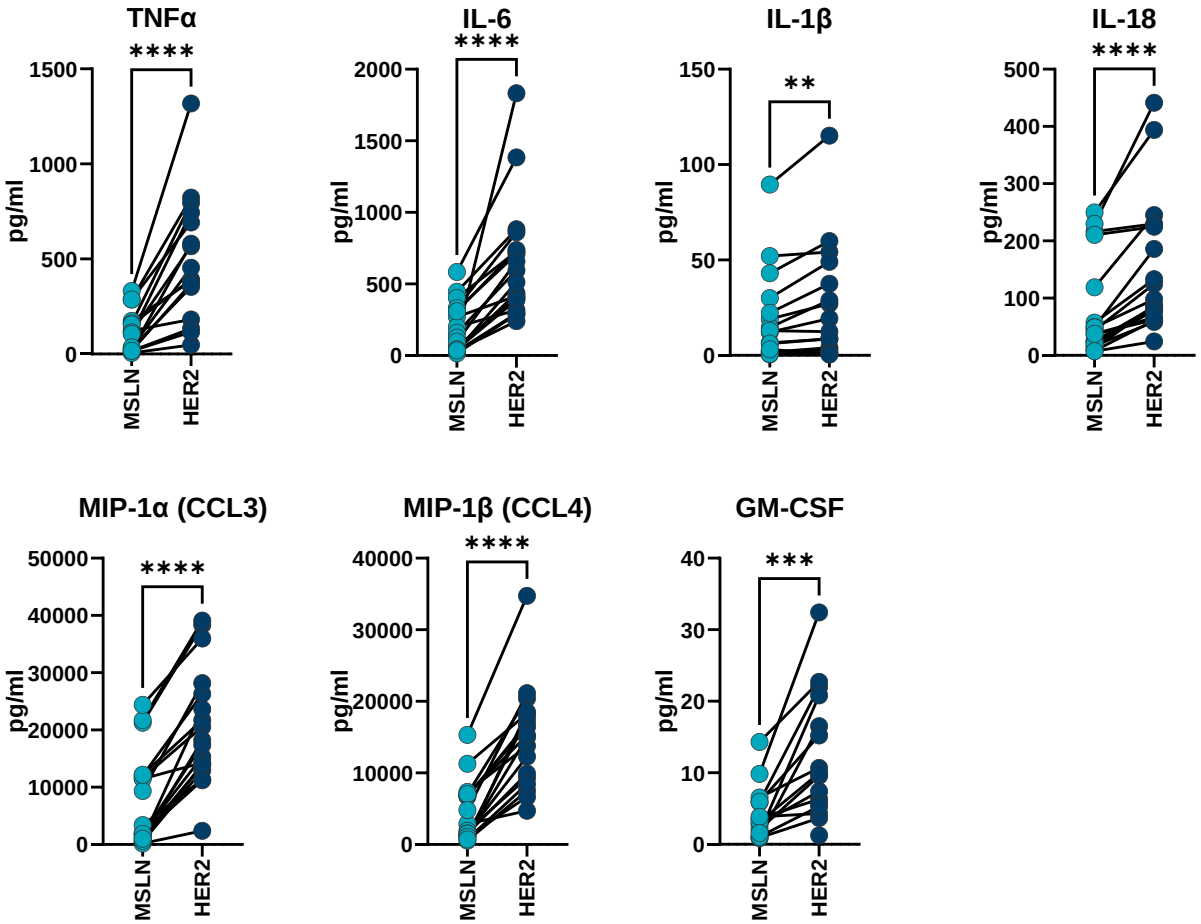
CT-0508 adopted an inflammatory phenotype and produced cytokines in response to HER2 stimulation

M1 markers were increased in CT-0508 for every batch produced



Individual patient CT-0508 cytokine concentrations



Median dose of 1.66 x 10^9 CAR macrophages administered

CT-0508 dose per patients in monotherapy group:

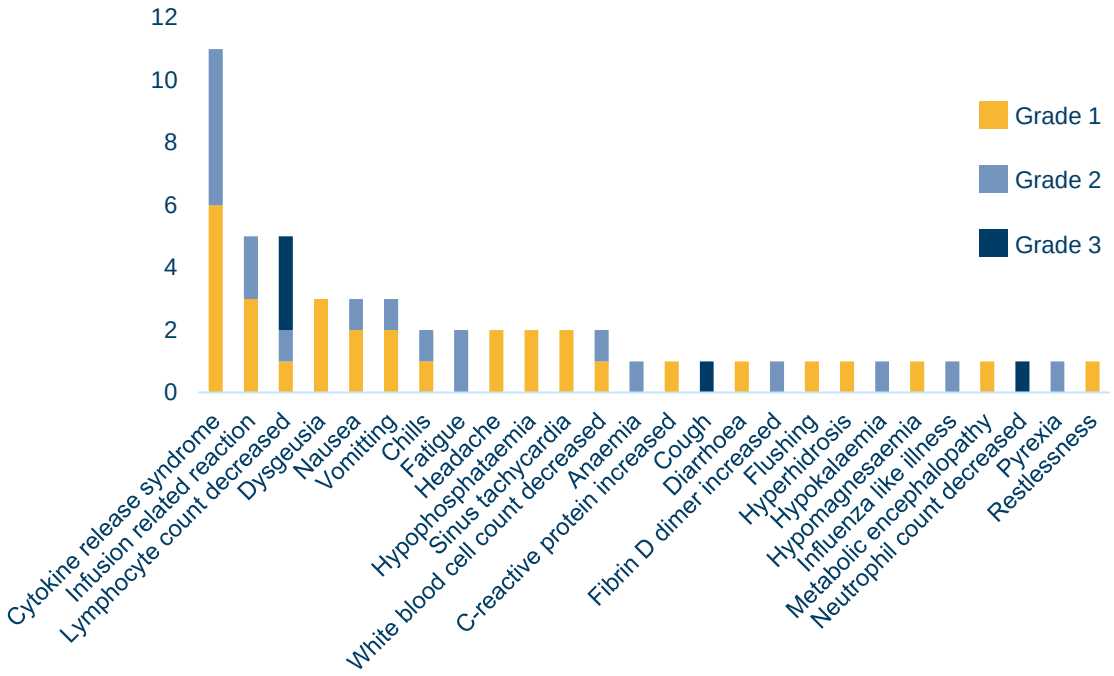
Group	Median # of cells infused	n
Group 1	1.61 x 10^9	9
Group 2	2.10 x 10^9	5
Total	**1.66 x 10^9**	**14**

- Maximum dose administered: 4.6x10^9
- No dose limiting toxicity seen on study
- No correlation between dose and safety profile

CT-0508 is Well Tolerated with No Dose Limiting Toxicities

Preliminary data supports a safe and tolerable product profile

Number of Adverse Events



Adverse Event Data by Patient

	G1: Fractionated	G2: Bolus	Combined
Patients Treated	N=9 (%)	N=5 (%)	N=14 (%)
Cytokine release syndrome (CRS)	**6** (67)	**3** (60)	**9** (64)
Grade 1-2	**6** (67)	**3** (60)	**9** (64)
Grade 3-4	**0** (0)	**0** (0)	**0** (0)
Infusion Reaction	**2** (22)	**1** (20)	**3** (21)
Grade 1-2	**2** (22)	**1** (20)	**3** (21)
Grade 3-4	**0** (0)	**0** (0)	**0** (0)
Immune effector cell-associated neurotoxicity syndrome (ICANS)	**0** (0)	**0** (0)	**0** (0)
SAEs Related To Treatment[1]	**2** (22)	**3** (60)	**5** (36)

Similar safety profile between Group 1 and Group 2

No severe CRS or ICANS

Majority of adverse events were Grade 1-2

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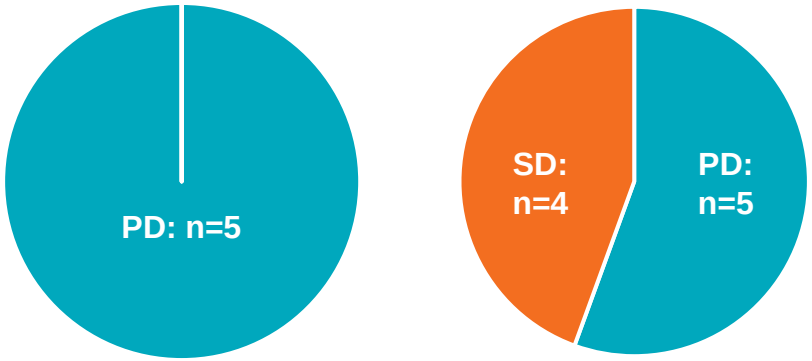
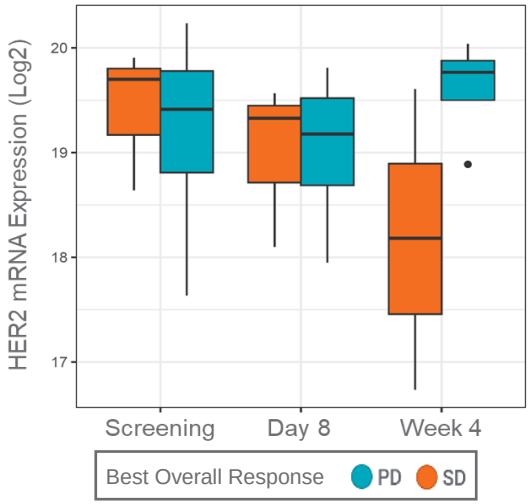
Data from Reiss, et al. SITC 2022; and Klichinsky, et al. CAR-TCR 2023. Includes data from combined Group 1 and Group 2.
1. All SAEs related to treatment were due to hospitalization for monitoring of either Grade 2 CRS or Grade 2 infusion reaction.

Patients with HER2 3+ tumors had increased anti-tumor activity

Correlation between HER2 status and Best Overall Response



Trend Toward Decrease in HER2+ Tumor Cells in Patients with Stable Disease (SD)



KEY TAKEAWAYS

- Best Overall Response of Stable Disease per RECIST 1.1 in 4 of the 14 evaluated participants (28.6%)*+
- Stable Disease was enriched in HER2 3+ subpopulation (n=4/9, 44.4% SD)
- Stable Disease correlated with CT-0508 induced TME remodeling, T cell activation, and baseline T cell exhaustion levels

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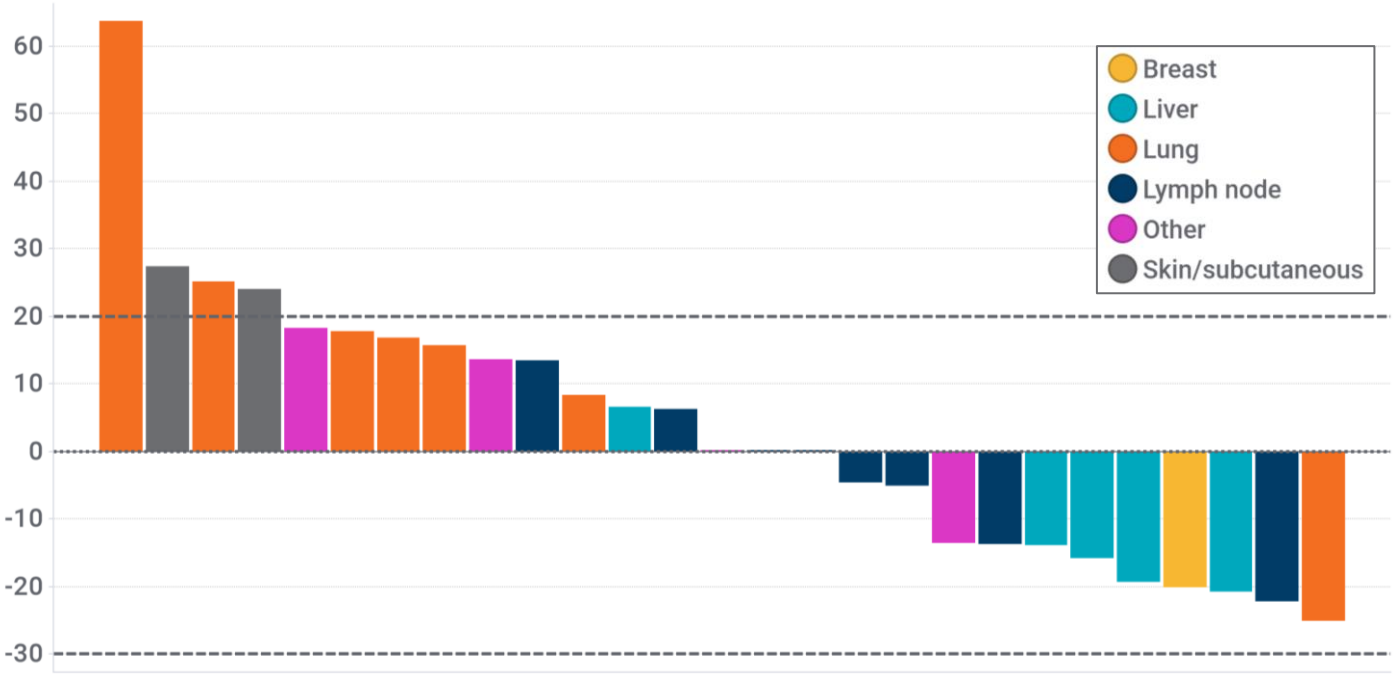
Data from Reiss, et al. SITC 2022; and Klichinsky, et al. CAR-TCR 2023. Includes data from combined Group 1 and Group 2.
SD=Stable Disease; PD = Progressive Disease; TME: Tumor Microenviroment
*Best Overall Response (RECIST 1.1); As of 08/02/2023, all patients discontinued to disease progression.
+1 patient in group 1 discontinued the study 2 weeks post infusion and never got a scan post infusion for re-staging, hence data is unavailable for this patient.

40.7% of all target lesions had reduced in size on at least 1 scan

Best changes in individual target lesions by anatomic site:

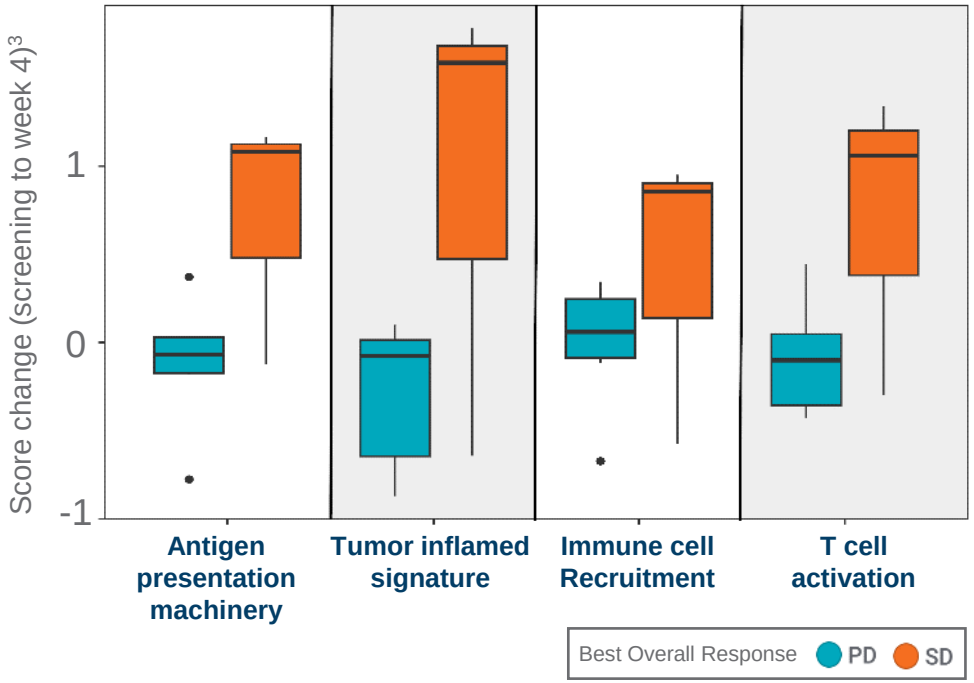


Each column represents a single target tumor lesion, not a patient.

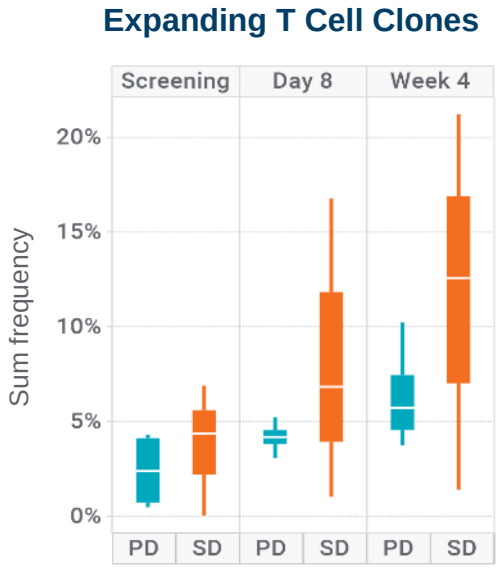
Target lesion reduction by anatomic site:

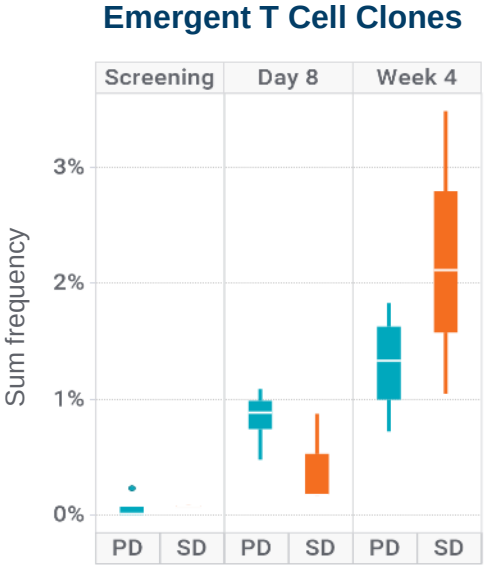
Anatomic Location	Frequency of tumor lesions that reduced on treatment on at least 1 scan
Breast	1/1 (100%)
Liver	4/5 (80%)
Lung	1/7 (14.3%)
Lymph Node	4/8 (50%)
Other	1/4 (25%)
Skin/Subcutaneous	0/2 (0%)
All Lesions	11/27 (40.7%)

CT-0508 induced TME remodeling, expanded T cell clonality, and emergence of novel T cell clones



TME activation, based on multiple gene sets, was enriched in patients that had Stable Disease





Accumulation of peripherally expanded and emergent T cell clones was increased in patients that had Stable Disease

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Data from Reiss, et al. SITC 2022; and Klichinsky, et al. CAR-TCR 2023. Includes data from combined Group 1 and Group 2.
SD=Stable Disease; PD = Progressive Disease, TME: Tumor Microenviroment

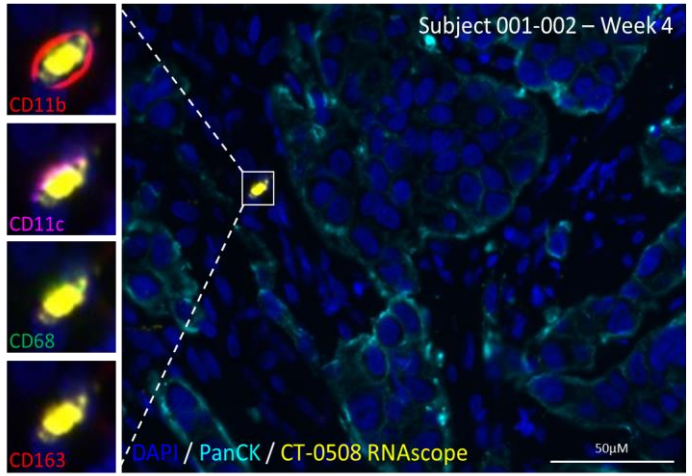
Dose, trafficking and persistence were key limiting factors

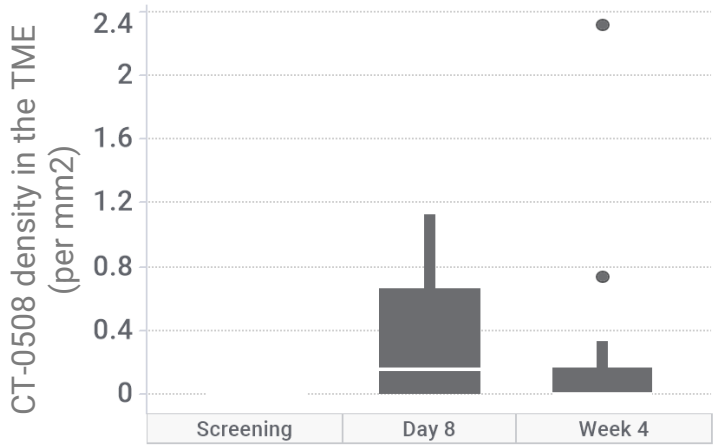
CT-0508 detection was more prevalent in Day 8 biopsies compared to week 4 biopsies.

Group 1			Group 2		
Pt	Day 8	Week 4	Pt	Day 8	Week 4
1	-	+	10	N/A	N/A
2	+	+	11	N/A	N/A
3	+	-	12	+	-
4	-	+	13	+	-
5	+	N/A	14	+	-
6	+	-			
7	+	-			
8	+	-			
9	-	-			

- CT-0508 was detected within the TME at Day 8 of 11 of the 12 participants (92%).
- CT-0508 was detected within the TME at Week 4 of 3 of the 11 participants (27%)

CT-0508 levels were relatively small in tumor biopsies





* RNAscope technology was combined with multiplex IHC allowing detection of multiple myeloid markers in addition to the CAR construct in the patients' biopsies; Data not available for 2 patients

CT-0525: Multiple Potential Improvements Over CT-0508

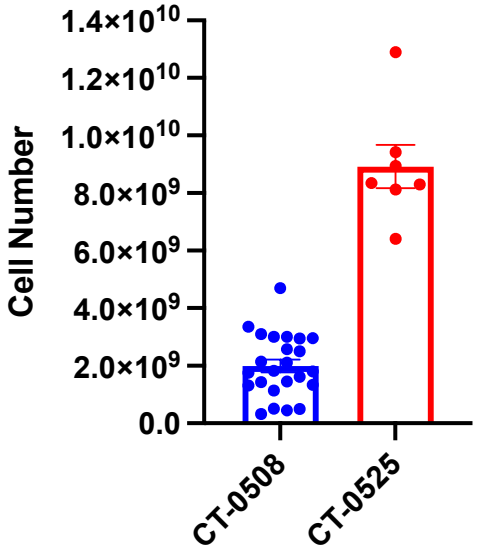
Pre-clinical models demonstrate increased cell potency with ~2,000-fold increased exposure over CT-0508

5X
Cell Number

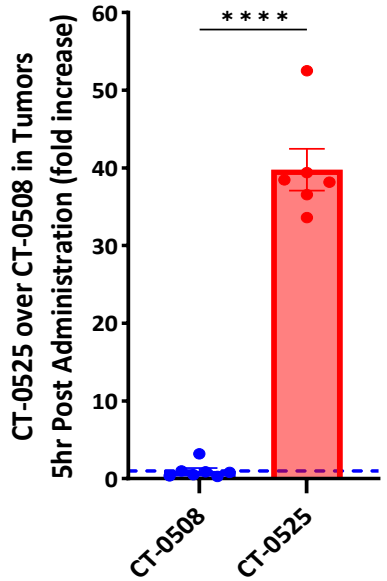
40X
Tumor Infiltration

10X
Persistence

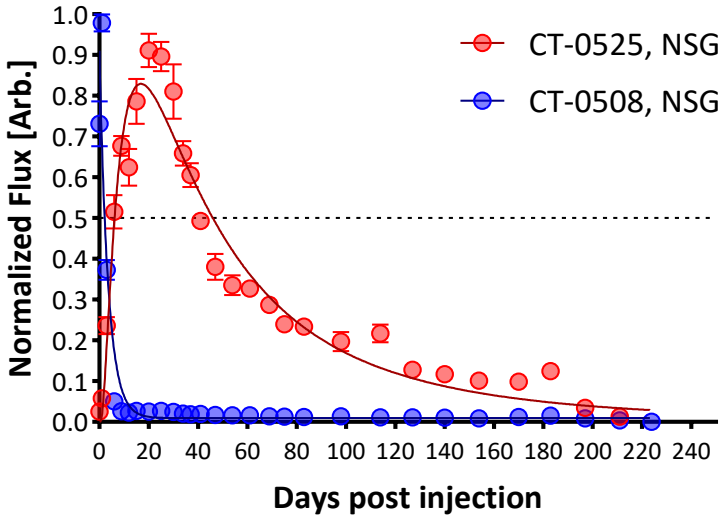
Cells Produced from Single Apheresis:



Trafficking in solid tumor model:



CT-0525 half-life is ~45 days:



CT-0525: HER2 Targeted CAR-Monocyte (Macrophage Precursor)

Ability to increase dose up to 5x, enhance trafficking and persistence, and manufacture more rapidly

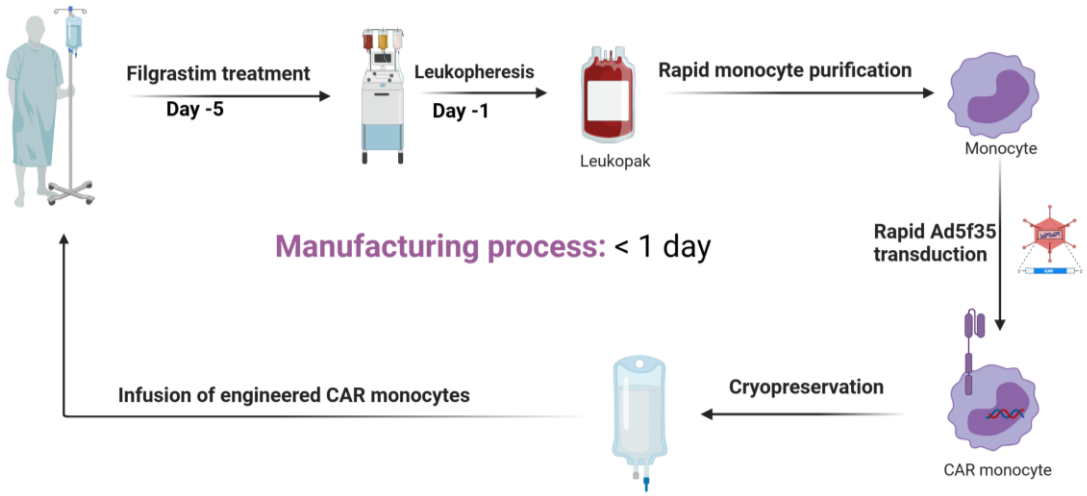
Highlights

Manufacturing Advantages Over CAR-Macrophage

Potential Biological Advantages Over CAR-Macrophage

IND Cleared
First patient expected to be treated in 2Q 2024
Initial data expected in 4Q 2024

CAR-Monocyte Rapid Manufacturing Process



CT-0525 Study 102: Phase 1 Clinical Trial Design

Assessing safety, tolerability, and manufacturing feasibility of CT-0525; additional analyses on TME impact

HER2 2+/3+ solid tumors (n≥6)

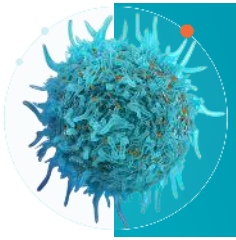
G-CSF mobilization and apheresis, CAR-Monocyte manufacture, bridging therapy, baseline staging

Cohort 1: Up to 3 billion cells of CT-0525 in bolus dose D1 (n≥3)

Cohort 2: Up to 10 billion cells of CT-0525 in bolus dose D1 (n≥3)

Initial data in 4Q 2024

Potential subsequent development plans could include combination with a T cell checkpoint inhibitor, and additional dose-ranging and dose schedule (among others)



PRIMARY OUTCOMES

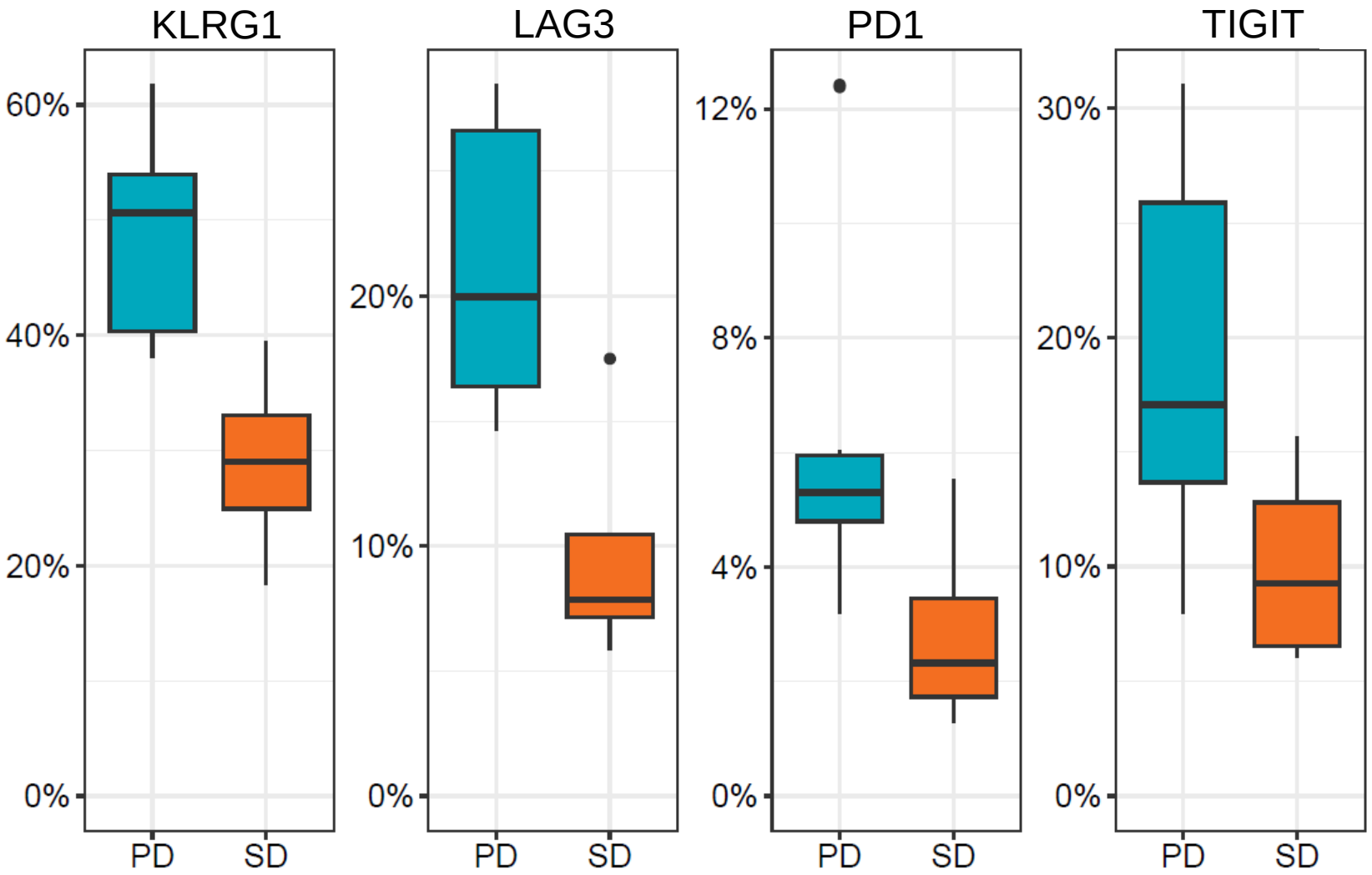
- Safety and tolerability
- Manufacturing feasibility

SECONDARY OUTCOMES[1]

- In vivo cellular kinetics profile (levels, persistence, trafficking)
- ORR (RECIST 1.1)
- DOR

Biopsy performed at screening, Day 8, and Week 6
ORR: Objective Response Rate; DOR: Duration of Response
1: Other tertiary/exploratory outcomes are being explored

Patients with lower CD8 T cell exhaustion at baseline achieved a better clinical outcome w/ CT-0508 monotherapy

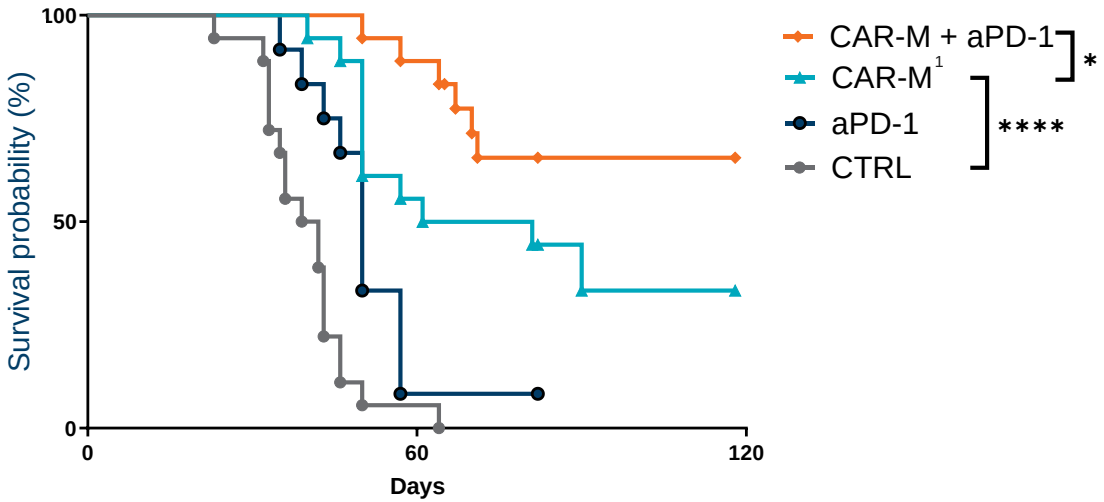


Based on single-cell RNAseq analysis of CD8 T cells within apheresis material.

CAR-M + Anti-PD1: Robust Synergy

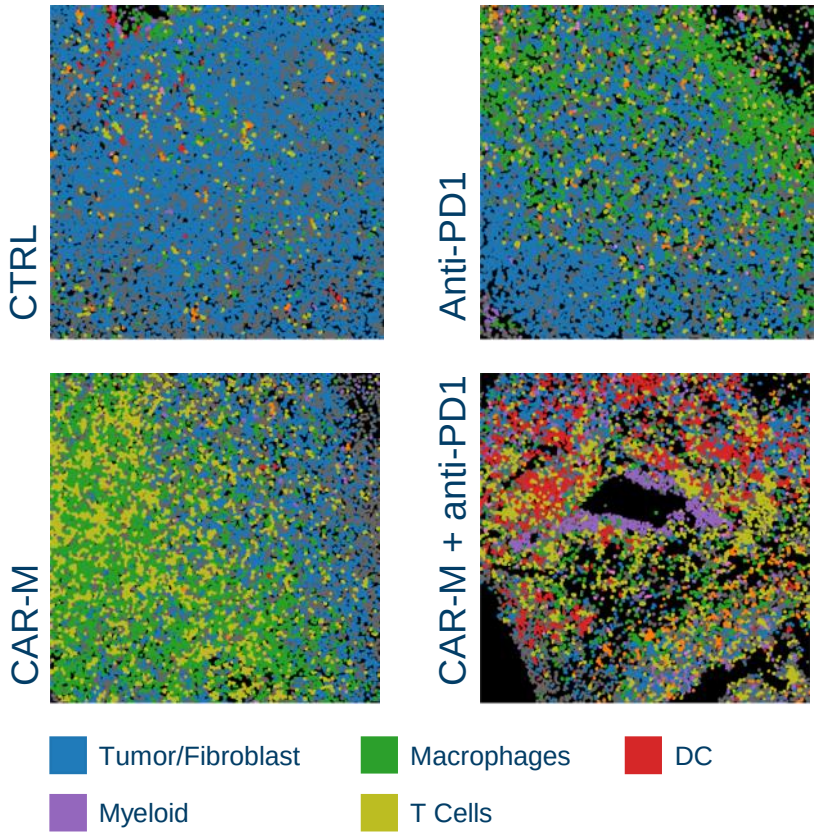
Synergy in a solid tumor model that is resistant to anti-PD1 monotherapy

Synergistic anti-tumor activity



Syngeneic CT26-HER2 solid tumor model.
Resistant to anti-PD1 monotherapy.

Synergistic TME modulation with combination

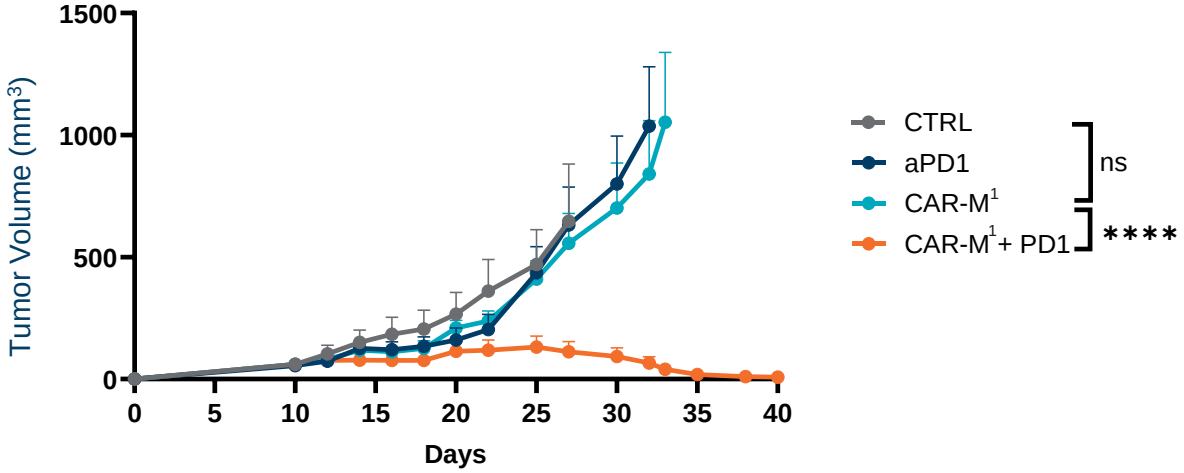


Data from preclinical models.
1: CAR-M: CAR-Macrophage
DC: Dendritic Cell; CTRL: Control

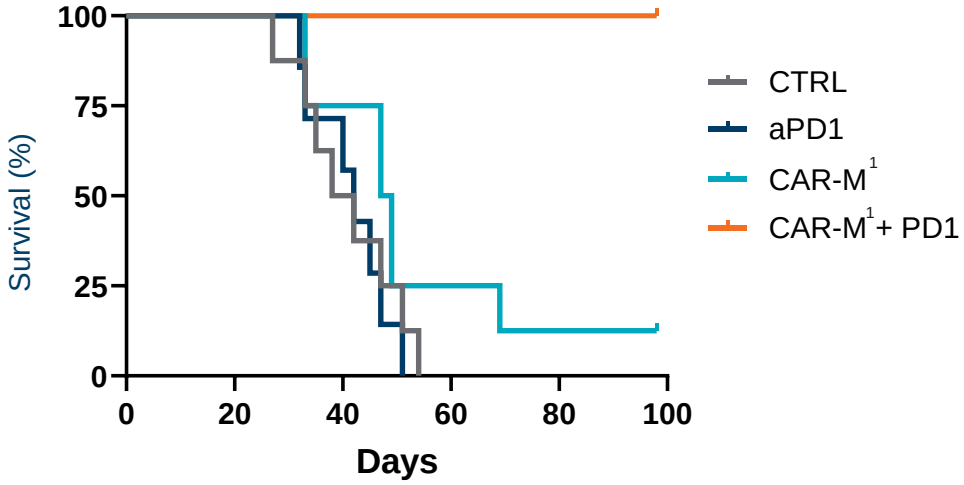
CAR-M + Anti-PD1: Synergistic tumor control and 100% survival

Synergy in CT26 solid tumor model that is resistant to both CAR-Macrophage *and* anti-PD1 monotherapy

I.V. CAR-M + anti-PD1 leads to synergistic tumor control



I.V. CAR-M + anti-PD1 leads to 100% survival



Syngeneic subcutaneous CT26-HER2 solid tumor model w/systemic CAR-M treatment.
Resistant to anti-PD1 monotherapy.

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CAR-M: murine surrogate version of CT-0508; IV (intravenous) CAR-M; CT26 HER2 model

CT-0508/Pembro Sub-study: Regimen Level 1 Demographics

Patient Demographics were consistent with Group 1 and Group 2

Summary of Participant and Tumor Characteristics			
Characteristic	**N = 3**	**Characteristic**	**N = 3**
Median age (range), years	62 (50, 73)	Tumor Type, n (%)	
Gender, n (%)		Breast Cancer	1 (33.3)
Male	1 (33.3)	Esophageal Cancer	1 (33.3)
Female	2 (66.7)	Ovarian Cancer	1 (33.3)
Race, n (%)		Median Number of Prior Cancer Therapies, n (range)	6 (5, 7)
White	3 (100.0)		
ECOG PS, n (%)		Median Number of Prior Anti-HER2 Therapies, n (range)	4 (0, 5)
0	0 (0.0)	Subjects with Prior Anti-HER2 Therapy	2 (66.7)
1	3 (100.0)		
HER2 Overexpression, n (%)		Prior Radiotherapy, n (%)	
IHC 3+	2 (66.7)	Yes	2 (66.7)
IHC 2+/FISH+	1 (33.3)		
Microsatellite Instability (MSI)*		Tumor Mutational Burden (TMB)*	
MSS/MSI-Low	3 (100.0)	Low (<10 mut/Mb)	2 (66.7)
MSI-High	0 (0)	High (≥10 mut/Mb)	1 (33.3)†

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* MSI-high and TMB high are known biomarkers associated with improved response to immune checkpoint
† patient has demonstrated HLA-A, HLA-B and HLA-C loss of Heterozygosity

CT-0508/Pembro Sub-study: Well Tolerated, No Dose Limiting Toxicities, Similar Safety Profile to CT-0508 Monotherapy

	CT-0508 Monotherapy Group 1: Fractionated Dosing	CT-0508 Monotherapy Group 2: Bolus Dosing	CT-0508 + Pembrolizumab Regimen 1
Patients Treated	**N=9 (%)**	**N=5 (%)**	**N=3 (%)**[1]
Any treatment-emergent AEs (TEAE)	**9** (100)	**5** (100)	**3** (100)
Grade 1-2	**4** (44)	**2** (40)	**1** (33)
Grade 3-4	**5** (56)	**3** (60)	**2** (66)
Any TEAEs related to CT-0508	**8** (89)	**4** (80%)	**3** (100)
Any TEAEs related to pembrolizumab	N/A	N/A	**1** (33%)
Any treatment-emergent SAEs (TESAE)	**4** (44)	**3** (60)	**3** (100)
Any TESAEs related to CT-0508[2]	**2** (22)	**2** (40)	**3** (100)
Any TESAEs related to pembrolizumab	N/A	N/A	**0** (0)
Cytokine release syndrome (CRS)	**6** (67)	**3** (60)	**2** (67)
Grade 1-2	**6** (67)	**3** (60)	**2** (67)
Grade 3-4	**0** (0)	**0** (0)	**0** (0)
Immune effector cell-associated neurotoxicity syndrome (ICANS)	**0** (0)	**0** (0)	**0** (0)

Similar safety profile between CT-0508 as monotherapy & in combination with pembrolizumab

No severe CRS or ICANS

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1. 2 of the 3 patients in the combination study were treated with corticosteroids post CT-0508, prior to pembrolizumab
2. All TESAEs related to CT-0508 were due to hospitalization for monitoring of either Grade 2 CRS or Grade 2 infusion reaction.

CT-0508/Pembro Sub-study: Regimen Level 1 (n=3) Summary

First two patients received corticosteroids prior to pembrolizumab

Patient	Steroids Given Prior to Pembro	Best Overall Response	Disease	HER2 Status	Additional Treatment Details
Patient 1	Yes	PD	Stage IV Breast Cancer	HER2 2+	• Treated with dexamethasone due to G2 CRS post CT-0508 infusion, prior to pembrolizumab administration
Patient 2	Yes	PD	Stage IV Ovarian Cancer	HER2 3+	• Treated with methylpredinosolone due to G3 Infusion reaction post CT-0508 infusion, prior to pembrolizumab administration • Triple HLA Class I loss of heterozygosity (HLA-A, B and C deletion in tumor genome).
Patient 3	No	SD (One out of two target lesions reduced by ~46%)	Stage IV Esophageal Cancer	HER2 3+	• Missed an early cycle (2nd infusion) of pembrolizumab due to medical issues unrelated to therapy • Patient had brain metastasis and progressed per RECIST 1.1 week 14 due to new brain met

Additional Information on Corticosteroids and CT-0508

- Systemic corticosteroids have the potential to reverse the activity of CT-0508.
- Based on *in vitro* studies, corticosteroids lead to CT-0508 cell death.
- Steroids were given post CT-0508, pre-pembrolizumab.

CT-0508/Pembro Sub-study: Patient Case Study

Patient #3: HER2+ Esophageal Adenocarcinoma w/ 6 prior lines of therapy and refractory to Enhertu

Cancer type: Stage IV Esophageal adenocarcinoma (EAC), HER2 3+

Prior history: 6 Prior lines of therapy; Most recent prior line: achieved BOR* of PD and DC'd Enhertu in 2 months

Pembrolizumab clinical studies in EAC:

- EAC is resistant to pembrolizumab monotherapy (KEYNOTE 180)
  - ORR 5%
  - PFS 1.5 months
- Pembrolizumab did not show a survival benefit over SOC chemotherapy in PDL1+ EAC (KEYNOTE 181)

Patient 3 - Prior Line	Prior Therapy	Start Time	End Time	Best Overall Response
1	Neoadjuvant carboplatin/paclitaxel	Feb 2019	April 2019	CR
2	Adjuvant Capacitabine, oxaliplatin, trastuzumab	Nov 2020	Nov 2020	Unknown
3	Fluorouracil, folinic acid, oxaliplatin, trastuzumab	Dec 2020	April 2021	PR
4	Fluorouracil, trastuzumab	May 2021	March 2022	SD
5	Paclitaxel, ramucirumab, trastuzumab, tucatinib	May 2022	Jan 2023	SD
6	Enhertu	Feb 2023	April 2023	PD

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* BOR: Best Overall Response
CR: Complete Response; PR: Partial Response; SD: Stable Disease; PD: Progressive disease

CT-0508/Pembro Sub-study: Patient Case Study

Patient #3: 46% reduction in 1 of 2 target lesions

Dosing

- Patient received 3.10E+09 cells
- Patient missed the 2nd cycle of pembrolizumab

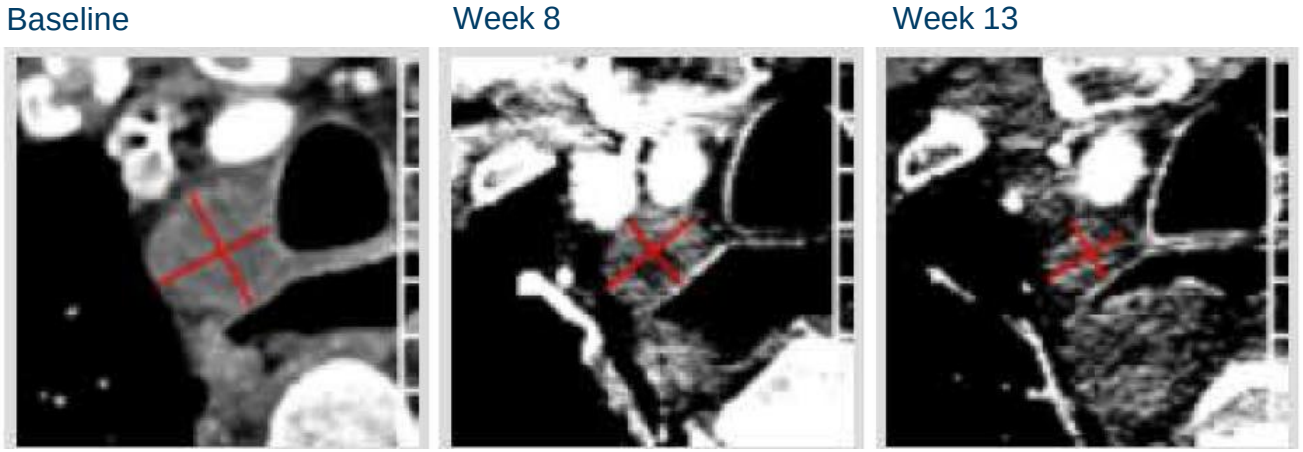
Tumor assessments

- Paratracheal target lesion reduction of 46% by week 13; 21.9mm to 11.8mm
- Mediastinal mass target lesion grew 31% by week 13; 26.9 to 35.3mm

Clinical assessments

- Achieved a BOR of SD per RECIST 1.1
- PD per RECIST at week 13 due to new CNS metastasis
- PFS of 3.25 months (13.3 weeks)

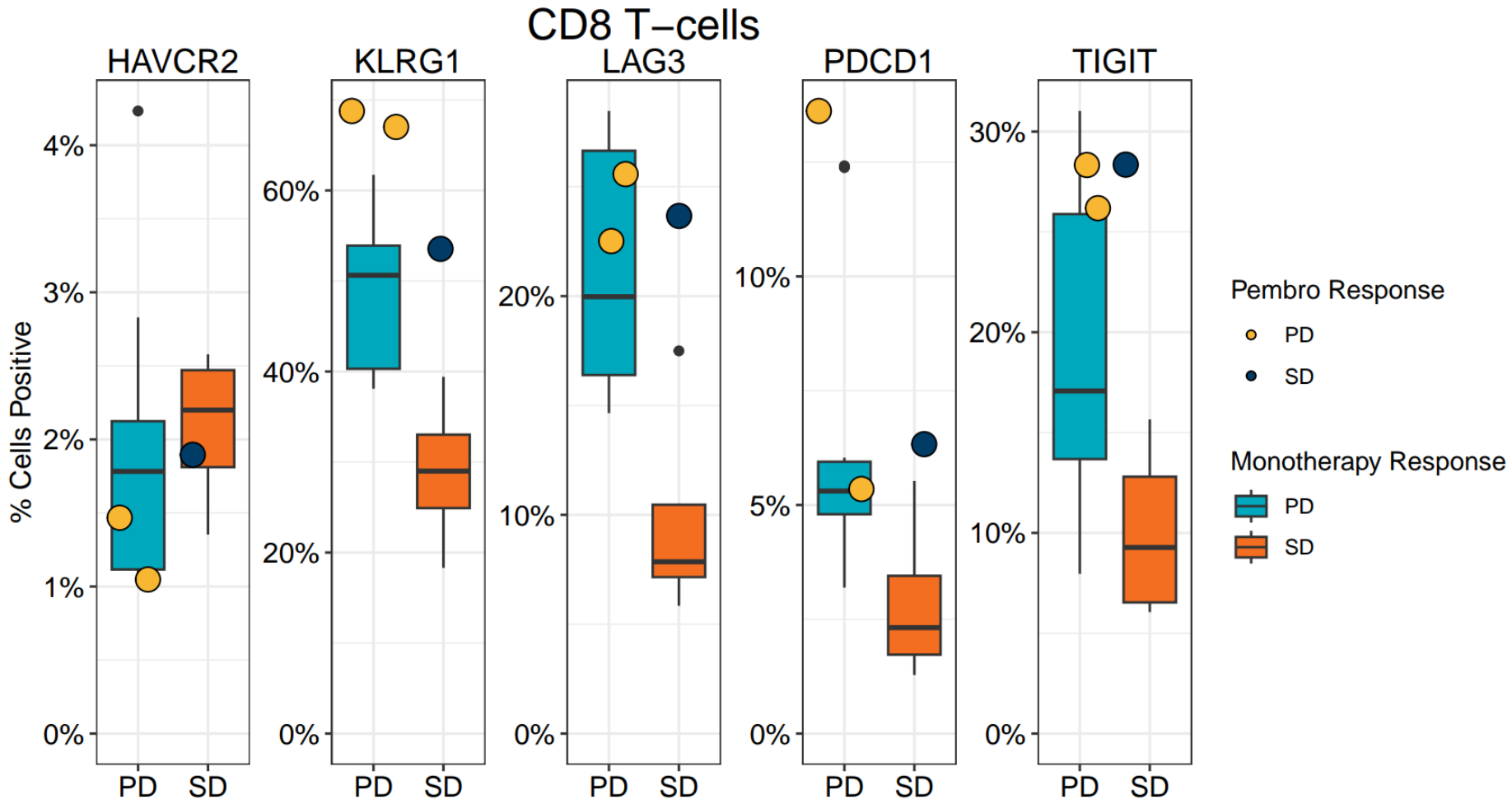
Paratracheal LN Target Lesion: 46% reduction by week 13



Outcome Comparators	PFS
Patient 3 – Regimen 1 CT-0508 / Pembro	3.25 months
Patient 3 – 6th Line of Therapy on Enhertu	2.0 months
Pembrolizumab monotherapy in KEYNOTE 180*	1.5 months

*KEYNOTE 180: Efficacy and Safety of Pembrolizumab for Heavily Pretreated Patients With Advanced, Metastatic Adenocarcinoma or Squamous Cell Carcinoma of the Esophagus. JAMA Oncology. 2019.

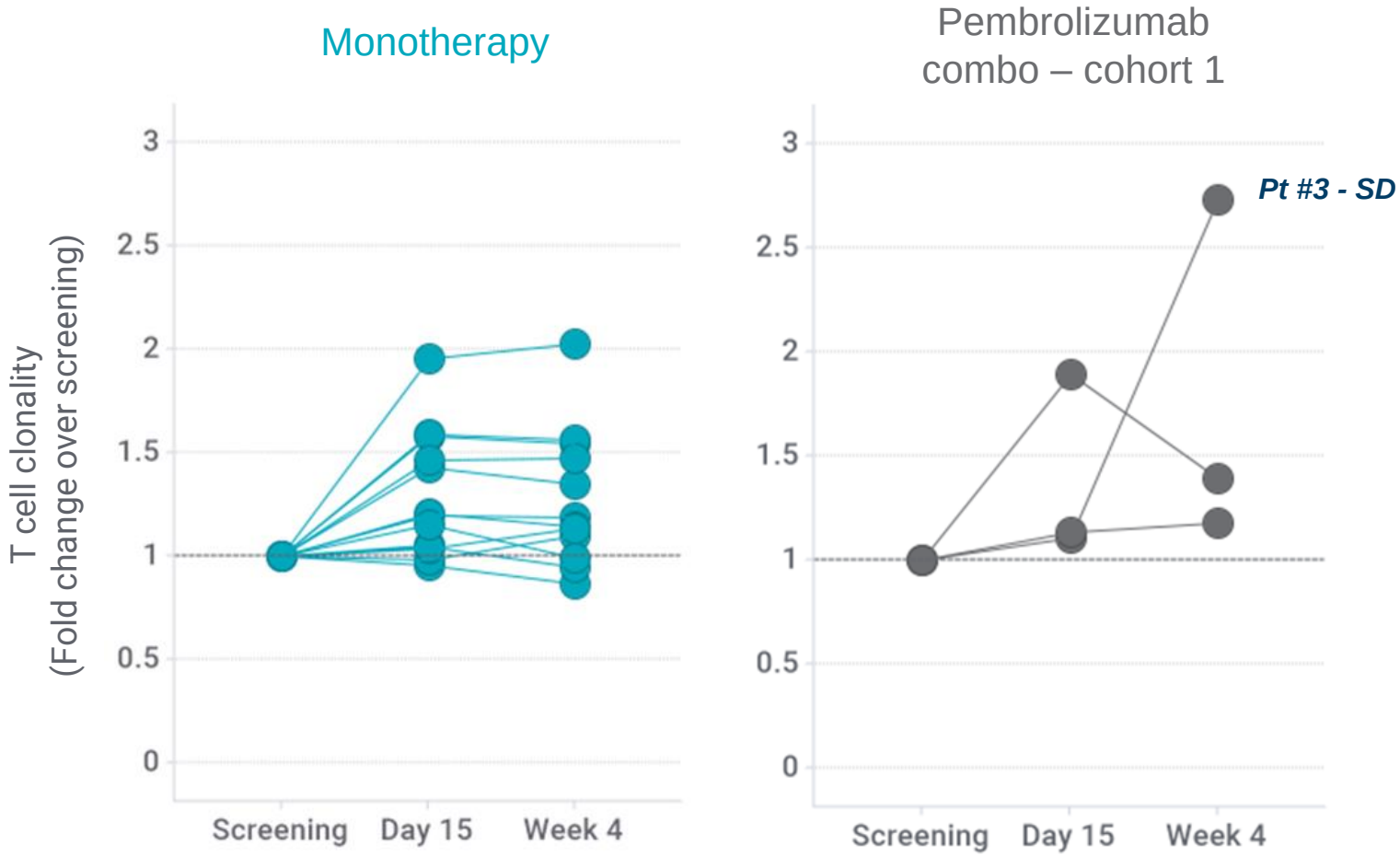
CT-0508/Pembro Sub-study: Pt 3 had high baseline peripheral CD8 T cell exhaustion



CT-0508/Pembro Sub-study: Individual Case Study

Patient 3: Greatest increase in peripheral blood T cell clonality seen to-date across all 17 patients treated with CT-0508

Increased T cell clonality in the peripheral blood



CT-0525 represents the next stage of CAR-M development

Demonstrate Safety, Tolerability, Feasibility & MOA:
CAR-Macrophage (CT-0508*)

Phase 1: No Further Data Expected

Increase Dose:
CAR-Monocyte (CT-0525)

Phase 1: Initial Data Expected 4Q'24

Overcome T Cell Exhaustion:
CAR-Macrophage (CT-0508) + Pembrolizumab

Phase 1: Data Expected 2Q'24

Potential Registrational Regimen:

Dose	Monotherapy vs. Combo Therapy	Line of Therapy	Tumor Type

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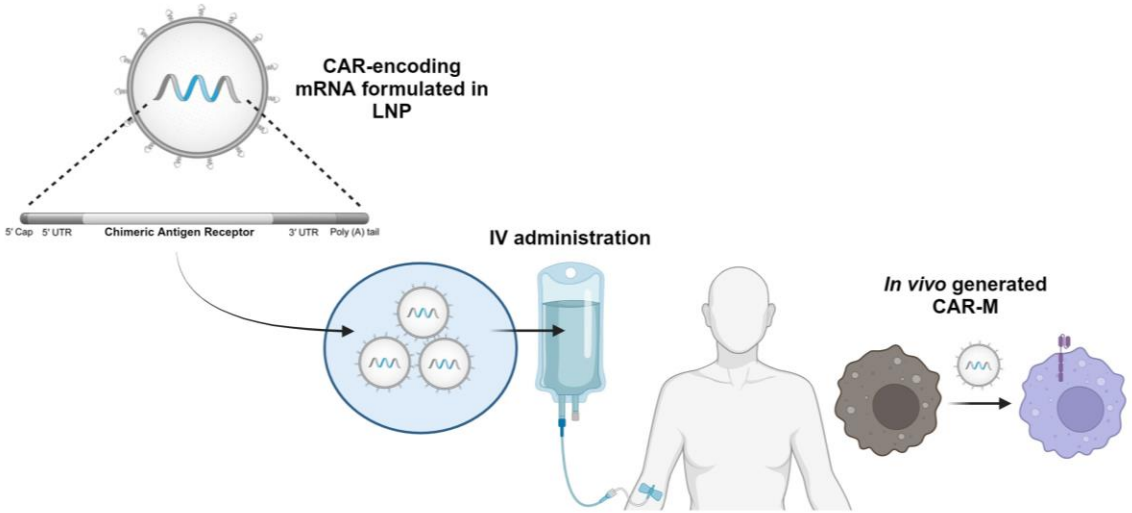
MOA: Mechanism of Action
* In late March 2024, Carisma made the decision to cease further development of CT-0508, including monotherapy and in combination with pembrolizumab

In Vivo CAR-M: Reprogramming myeloid cells within

Collaboration with Moderna to discover, develop and commercialize *in vivo* CAR-M in oncology

Redirecting endogenous myeloid cells with mRNA for cancer immunotherapy



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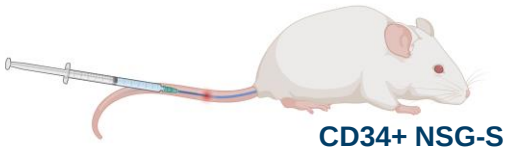
Key Advantages

- ✓ Off-the-shelf
- ✓ Full MHC matching (redirecting patient's own cells)
- ✓ Non-viral, mRNA-based platform
- ✓ Ability to re-dose to maintain pharmacologic pressure
- ✓ Robust platform that can be developed against diverse tumor antigens/indications

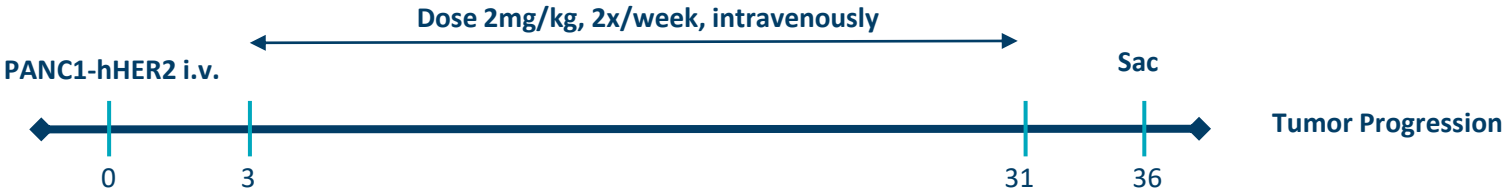
- ✓ **Benefits of CAR-M therapy:**
  - Targeted anti-tumor activity
  - Tumor infiltration
  - TME activation
  - T cell recruitment
  - Epitope spreading

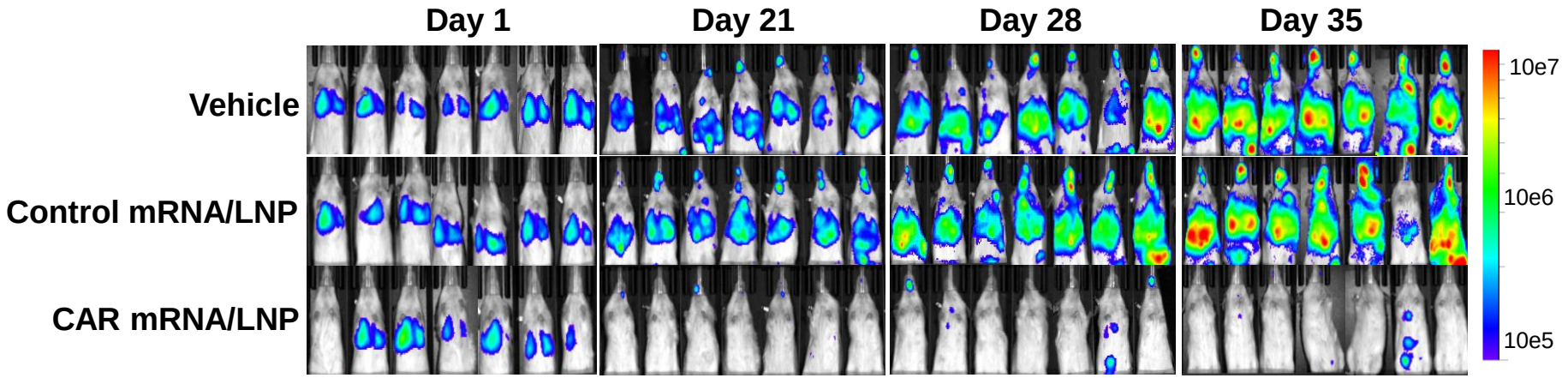
mRNA: Messenger RNA; LNP: Lipid Nanoparticle

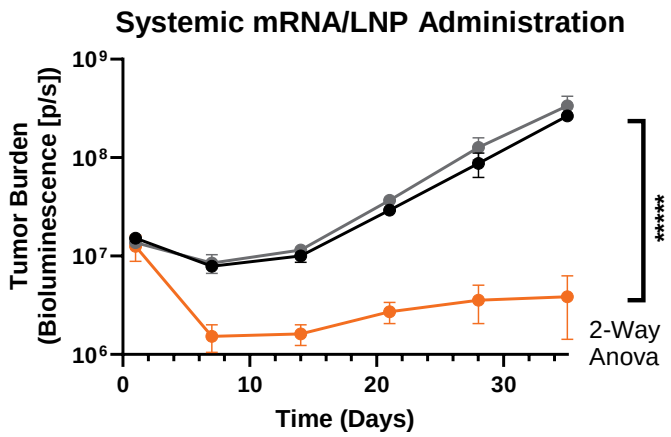
Intravenous administration of CAR mRNA/LNP leads to suppression of metastatic pancreatic tumor growth

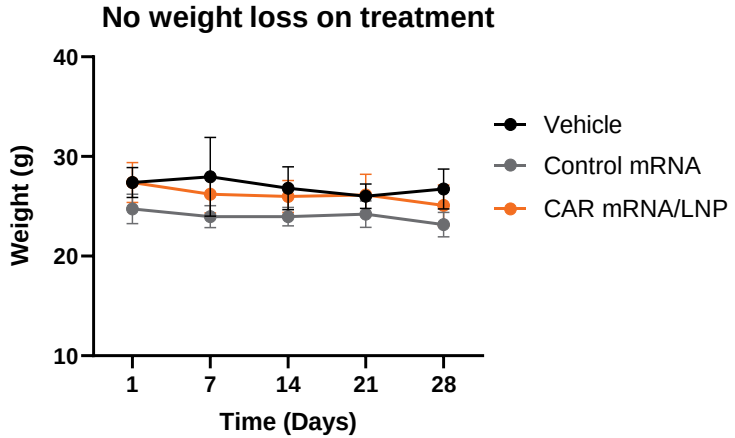


CD34+ NSG-S mice



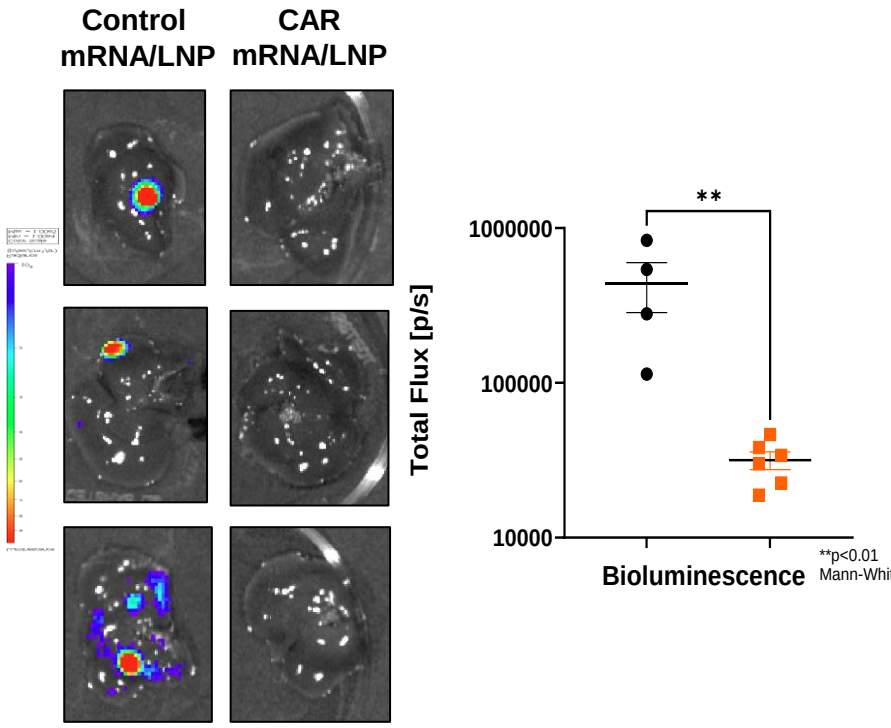




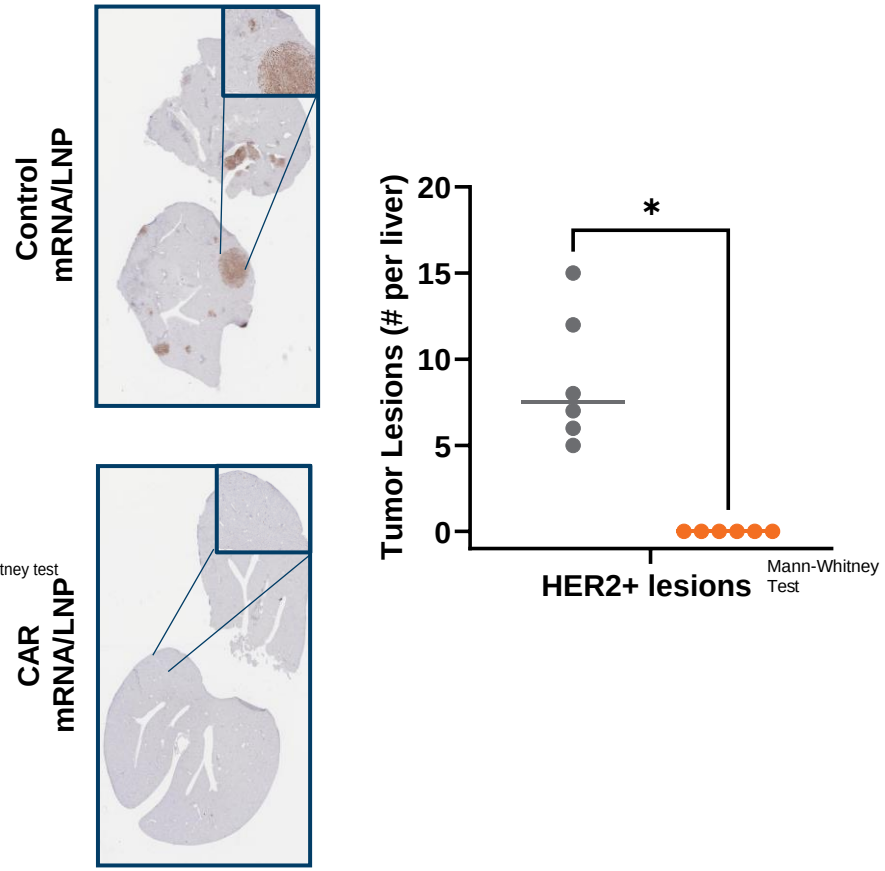


Intravenous delivery of CAR mRNA/LNP clears liver metastasis and reduces lung metastasis

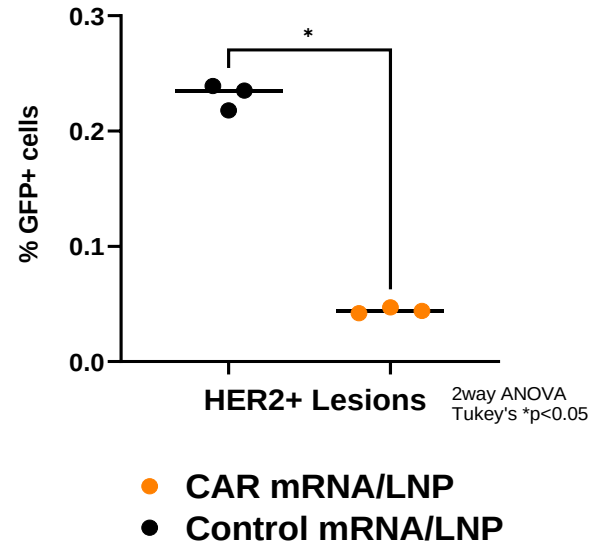
Tumor Lesions in Liver (BLI)



Tumor Lesions/Liver (IHC)



Tumor Lesions in Lung (IHC)



First-in-Class Pipeline

Multiple value inflection points across therapeutic areas and modalities

THERAPEUTIC AREA	PRODUCT CANDIDATE	PLATFORM	DISCOVERY / PRE-CLINICAL / PHASE 1 / PHASE 2 / PHASE 3	COLLABORATOR
***Ex Vivo* Oncology**				
HER2+ solid tumors	CT-0525	CAR-Monocyte *(1st Gen CAR)*	4Q 2024: Initial data[1]	
	CT-0508*	CAR-Macrophage *(1st Gen CAR)*	2Q 2024: Combination data[1]	
Mesothelin+ solid tumors	CT-1119**	CAR-Monocyte *(Next-Gen CAR[2])*		
***In Vivo* Oncology**				
Oncology	Solid Tumor Antigen[3]	CAR-Macrophage + mRNA/LNP		moderna
	4 Additional Targets[4]	CAR-Macrophage + mRNA/LNP		
Fibrosis and Immunology				
Liver Fibrosis	TBD	Engineered macrophage	2Q 2024: Preclinical proof of concept data[1]	

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* In late March 2024, Carisma made the decision to cease further development of CT-0508, including monotherapy and in combination with pembrolizumab
** In late March 2024, Carisma made the decision to pause further development of CT-1119, pending additional financing
1. Anticipated milestones; 2. Includes SIRPα knockdown technology; 3. Target undisclosed
4. Moderna collaboration has identified 5 total oncology targets, with the option to identify an additional 7 oncology targets; First lead candidate was nominated in 4Q 2023

Q&A

carismatx.com