UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): September 1, 2023

Carisma Therapeutics Inc.
(Exact Name of Registrant as Specified in its Charter)

Delaware	**001-36296**	**26-2025616**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**
3675 Market Street, Suite 200 Philadelphia, PA		**19104**
(Address of Principal Executive Offices)		**(Zip Code)**

Registrant's telephone number, including area code: (267) 491-6422

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (*see* General Instruction A.2 below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of exchange on which registered**
Common Stock, $0.001 par value	**CARM**	**The Nasdaq Stock Market LLC**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01. Other Events.

On September 1, 2023, Carisma Therapeutics Inc. (the "Company") issued a press release announcing preliminary findings from the first five patients enrolled in group 2 of the Company's Phase 1 clinical trial of its lead product candidate, CT-0508, a human epidermal growth factor receptor 2 ("HER2") targeted chimeric antigen receptor macrophage for the treatment of HER2 overexpressing cancers. The Company will provide an overview of the group 2 data during a presentation at the 8th Annual CAR-TCR Summit on September 1, 2023. A copy of the press release and an excerpt from the presentation are attached hereto as Exhibits 99.1 and 99.2 and are incorporated herein by reference.

The Company is providing the following supportive data for the Phase 1 clinical trial:

The Company initiated a second group to evaluate the safety of bolus dosing of patients, and five patients have been successfully dosed to date with a single-day bolus infusion. Consistent with results from group 1 of the trial, based on preliminary results assessed to date from these five patients enrolled in group 2, CT-0508 has been generally well-tolerated after infusion with no dose-limiting toxicities, was successfully manufactured using macrophages obtained from heavily pre-treated, advanced solid tumor patients, and has shown high CAR expression, viability, and purity. While the results from this early clinical trial data are both preliminary and limited, the Company believes the combined group 1 and group 2 results support the previously presented preliminary results from this trial indicating that CT-0508 can potentially lead to remodeling and activation of the tumor microenvironment ("TME") and induce anti-tumor adaptive immunity. In group 1, a best overall response ("BOR") of stable disease was seen in 4 out of 9 patients, and in group 2, the best overall response was progressive disease. Translational analyses combining group 1 and group 2 demonstrated a correlation between TME activation, T cell activation, and HER2 status with BOR of stable disease.

The single-agent arm of the study remains open and up to four additional patients may be enrolled. However, given the clinical findings observing T cell exhaustion as a potential limiting factor, and pre-clinical data demonstrating robust synergy upon combining CT-0508 with T cell checkpoint inhibition, the Company expects to focus its ongoing efforts primarily on enrolling patients in its sub-study administering CT-0508 in combination with pembrolizumab.

Item 9.01. Financial Statements and Exhibits.

Exhibit Number	Description
99.1	Press Release issued by Carisma Therapeutics Inc. on September 1, 2023.
99.2	Excerpt from Company Presentation, dated September 2023.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

CARISMA THERAPEUTICS INC.

By: /s/ Steven Kelly
Steven Kelly
President and Chief Executive Officer

Date: September 1, 2023

Exhibit 99.1

Carisma Announces Latest Data from Phase 1 Clinical Trial of CT-0508 at 8th Annual CAR-TCR Summit

Group 2 data available to date support primary safety and feasibility endpoints of single-day bolus dosing of CT-0508

New translational analyses combining group 1 & group 2 continue to support CAR-M mechanism of action, demonstrating a correlation between biomarkers and best overall response

PHILADELPHIA, PA – September 1, 2023 – Carisma Therapeutics Inc. (Nasdaq: CARM) ("Carisma" or the "Company"), a clinical stage biopharmaceutical company focused on discovering and developing innovative immunotherapies, will present findings today at the 8th Annual CAR-TCR Summit from its Phase 1 clinical trial of the Company's lead product candidate, CT-0508, a human epidermal growth factor receptor 2 ("HER2") targeted chimeric antigen receptor macrophage ("CAR-M") for the treatment of advanced/metastatic HER2 overexpressing cancers.

The presentation includes data from group 1 (n=9) and group 2 (n=5). Patients in both groups received the same total dose (up to $5x10^9$ CT-0508) either via a fractionated, multi-day infusion regimen (group 1) or via a single-day bolus infusion (group 2). The data are drawn from the ongoing clinical trial led by Kim A. Reiss, MD, principal investigator of the Phase 1 clinical trial and an associate professor of Hematology-Oncology in the Perelman School of Medicine at the University of Pennsylvania.

In the presentation, Michael Klichinsky, PharmD, PhD, Co-Founder and Chief Scientific Officer at Carisma, will present data demonstrating that, in both groups, CT-0508 was successfully manufactured for patients and that the administration of CT-0508 was well-tolerated after infusion with no dose-limiting toxicities reported to date.

"As the CT-0508 trial progresses, it is promising to see consistent results supporting the safety profile, feasibility, and mechanism of action of this first-in-class CAR-M investigational therapy," commented Dr. Klichinsky. "We look forward to results from the CT-0508 combination sub-study with pembrolizumab and continued development of CAR-M and CAR-Monocyte therapies."

Previously, Carisma presented findings from group 1 showing that CT-0508 remodeled and activated the tumor microenvironment ("TME") and initiated anti-tumor T cell immunity. Translational analyses combining group 1 and group 2 show that various biomarkers including metrics of TME activation, T cell activation, and HER2 status correlate with best overall response ("BOR") of stable disease, providing further evidence of the CT-0508 mechanism of action.

The Phase 1 study translational analyses further demonstrate an increase in exhausted CD8 T cells on treatment, supporting the ongoing combination sub-study with Merck's anti-PD1 therapy KEYTRUDA® (pembrolizumab). This latest data readout follows the dosing of the first patient in the ongoing sub-study of the Phase 1 clinical trial of CT-0508 in combination with pembrolizumab for the treatment of HER2 overexpressing cancers.

The Company is filing a Current Report on Form 8-K today with the U.S. Securities and Exchange Commission disclosing the new data from its Phase 1 clinical trial of CT-0508, including an excerpt of the presentation being made at the 8th Annual CAR-TCR Summit.

Editor's Note: Carisma has licensed certain Penn-owned intellectual property from the University of Pennsylvania, and Penn's Perelman School of Medicine receives sponsored research and clinical trial funding from the company. Penn may be entitled to receive additional financial benefits from technologies licensed and optioned to Carisma. In addition, Penn is a co-founder of the company and holds equity in Carisma.

About CT-0508

CT-0508 is a human epidermal growth factor receptor 2 (HER2) targeted chimeric antigen receptor macrophage (CAR-M). It is being evaluated in a landmark Phase 1 multi-center clinical trial that focuses on patients with recurrent or metastatic HER2-overexpressing solid tumors whose cancers do not have approved HER2-targeted therapies or who do not respond to treatment. Carisma is selecting participants who have tumors of any anatomical origin, but with the commonality of overexpressing the HER2 receptor on the cell surface, which is the target for our CAR-M. The Phase 1 clinical trial marks the first time that engineered macrophages are being studied in humans. The trial continues to enroll patients at seven clinical sites in the U.S., including (i) Penn Medicine's Abramson Cancer Center, (ii) the University of North Carolina Lineberger Comprehensive Cancer Center, (iii) the City of Hope National Medical Center, (iv) the MD Anderson Cancer Center, (v) the Sarah Cannon Cancer Research Institute, (vi) Oregon Health & Science University and (vii) Fred Hutchinson Cancer Center.

About Carisma

Carisma Therapeutics Inc. is a clinical stage biopharmaceutical company focused on utilizing our proprietary macrophage and monocyte cell engineering platform to develop transformative immunotherapies to treat cancer and other serious diseases. We have created a comprehensive, differentiated proprietary cell therapy platform focused on engineered macrophages and monocytes, cells that play a crucial role in both the innate and adaptive immune response. Carisma is headquartered in Philadelphia, PA. For more information, please visit www.carismatx.com.

Cautionary Note on Forward-Looking Statements

Statements in this press release about future expectations, plans and prospects, as well as any other statements regarding matters that are not historical facts, may constitute "forward-looking statements" within the meaning of The Private Securities Litigation Reform Act of 1995. These statements include, but are not limited to, statements relating to Carisma's business, strategy, future operations, cash runway, the advancement of Carisma's product candidates and product pipeline, and clinical development of Carisma's product candidates, including expectations regarding timing of initiation and results of clinical trials and ability to replicate in later clinical trials positive results found in preclinical studies and early-stage clinical trials of its product candidates. The words "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "goals," "intend," "may," "might," "outlook," "plan," "project," "potential," "predict," "target," "possible," "will," "would," "could," "should," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Any forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in, or implied by, such forward-looking statements. For a discussion of these risks and uncertainties, and other important factors, any of which could cause Carisma's actual results to differ from those contained in the forward-looking statements, see the "Risk Factors" set forth in the Company's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on August 10, 2023, as well as discussions of potential risks, uncertainties, and other important factors in Carisma's other recent filings with the Securities and Exchange Commission. Any forward-looking statements that are made in this press release speak as of the date of this press release. Carisma undertakes no obligation to revise the forward-looking statements or to update them to reflect events or circumstances occurring after the date of this press release, whether as a result of new information, future developments or otherwise, except as required by the federal securities laws.

Media Contact:

Julia Stern
(763) 350-5223
jstern@realchemistry.com

Investor Contact:

investors@carismatx.com

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Exhibit 99.2

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HARNESSING THE POWER OF ENGINEERED MACROPHAGES

Michael Klichinsky, PharmD PhD
Co-Founder & Chief Scientific Officer

CAR-TCR
September 2023

Cautionary Note Regarding Forward-Looking Statements Regarding Carisma

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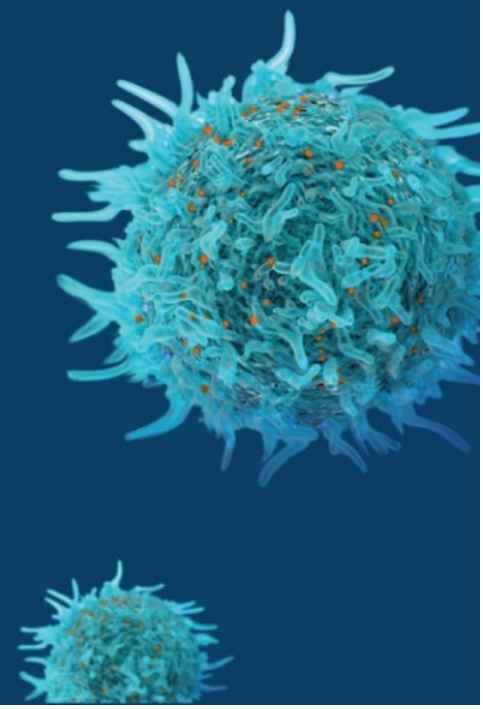
Lead Program CT-0508

Anti-HER2 CAR-M Phase I Trial

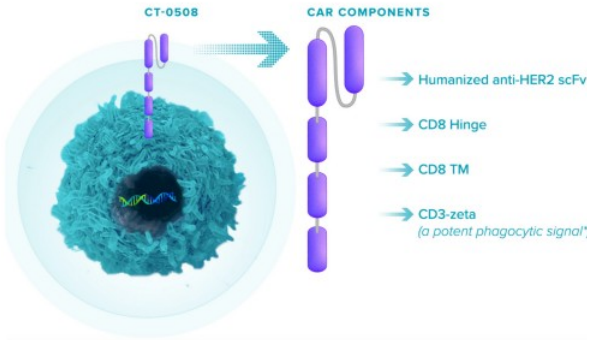


CT-0508: HER2 Targeted CAR-Macrophage

First-in-class & first-in-human engineered macrophage

Program Overview

- HER2 2+/3+ metastatic solid tumor basket trial
- Phase I multi-center, open-label study open at 7 US sites
- Cohorts:
  - **Group 1** (Fractionated dosing): Complete – *data presented at '22 SITC*
  - **Group 2** (Bolus dosing): Enrolling – Early data included today
  - **CT-0508** + pembrolizumab: Enrolling



Cells: Autologous monocyte derived macrophages
Vector: Ad5f35
Phenotype: M1
Target: HER2
CAR: 1st Generation

Study Summary

- Pts pre-mobilized with G-CSF
- Dose: 1 to 5 x 10^9 cells
- No pre-conditioning
- Endpoints
  - Feasibility
  - Safety
  - PK and MOA

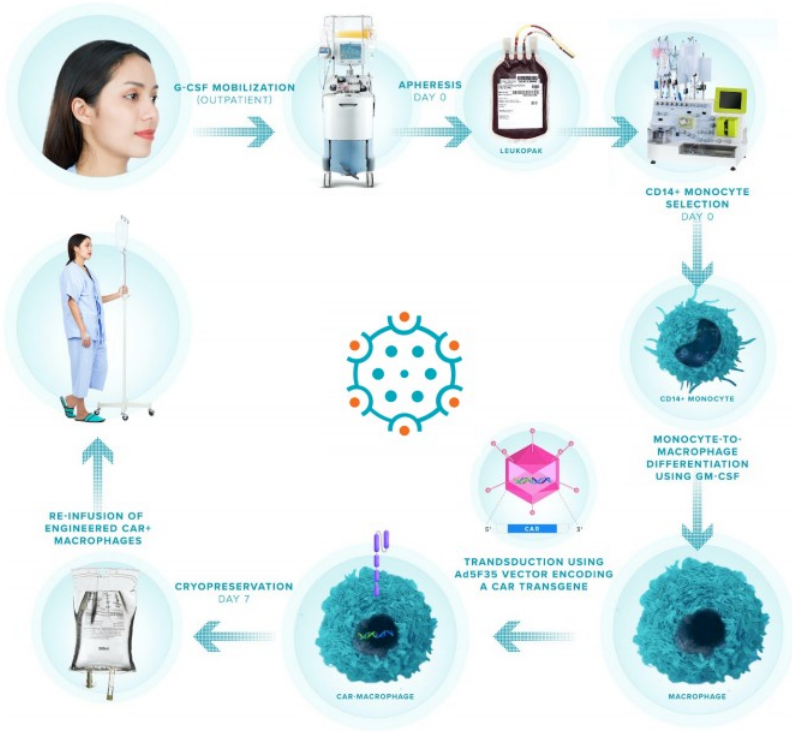
Cohorts

- Single Agent Days 1 / 3 / 5 Dosing (*n=9*)
- Single Agent Day 1 Bolus Dosing (*n=up to 9*)
- CT-0508 + Pembro Combination (*n=9*)

CAR-M Manufacturing Process

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

Viability mean %	86%
Purity mean %	89%
CAR+ mean %	79%
Total cells based on label (cells)	2.06E+09



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Manufacturing Partners: NOVARTIS Miltenyi Biotec

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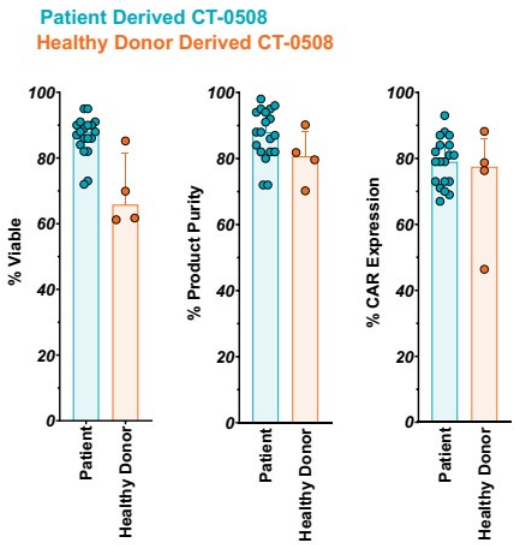
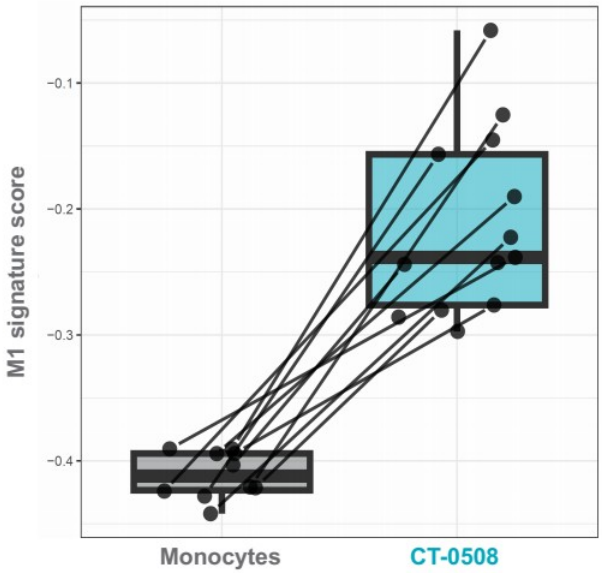
Successful CT-0508 Manufacturing:

Functional M1 Polarized CAR-M Generated

High viability, purity, and CAR expression



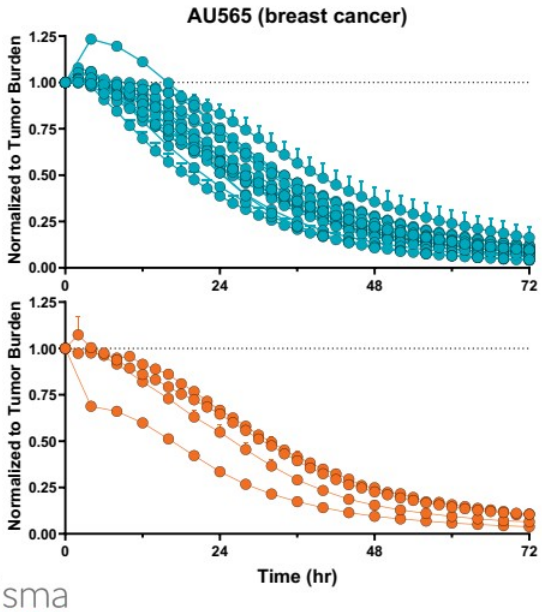
All patient CT-0508 batches show M1 polarizatior



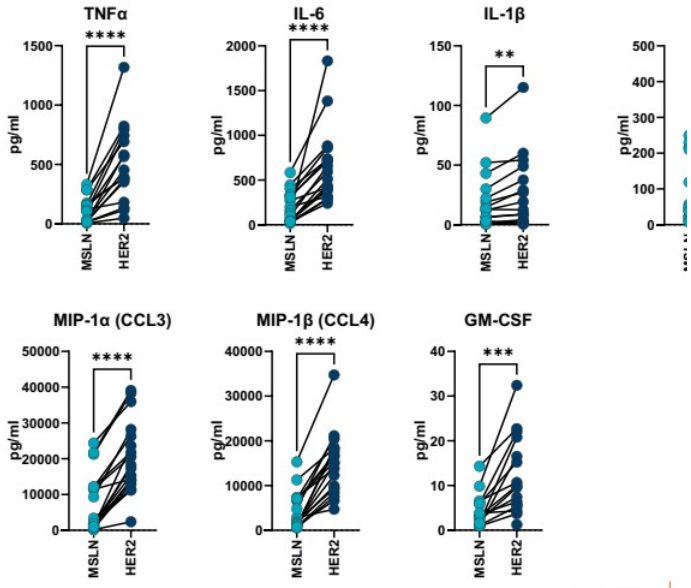
Patient CT-0508 are functional *in vitro*:

Each batch demonstrated target killing, phagocytosis, M1 polarization, and cytokine release

All CT-0508 batches kill HER2+ tumor cells



Patient CT-0508 CAR-dependent cytokine secreti



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

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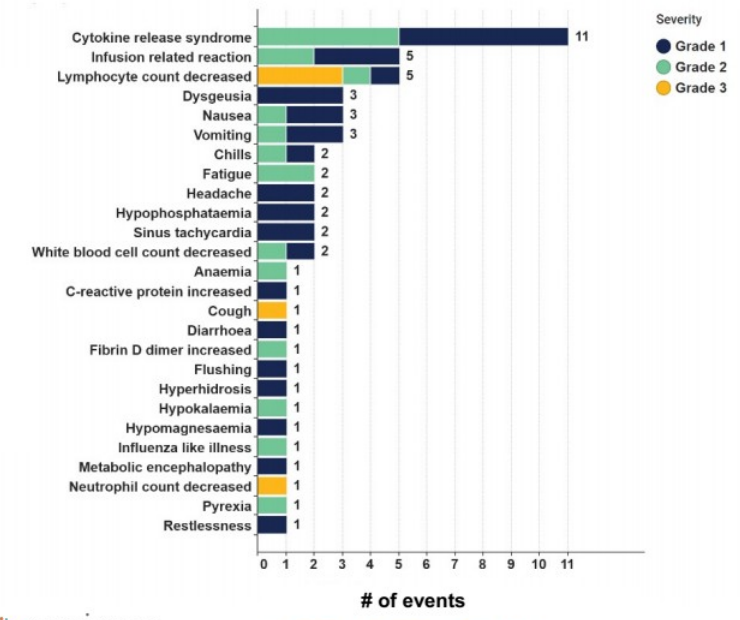
** MSI-high and TMB high are known biomarkers associated with improved response to immune checkpoint*

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

CT-0508 is Well Tolerated with No Dose Limiting Toxicities

Similar safety profile between Group 1 and Group 2

Majority of Adverse Events were Grade 1-2



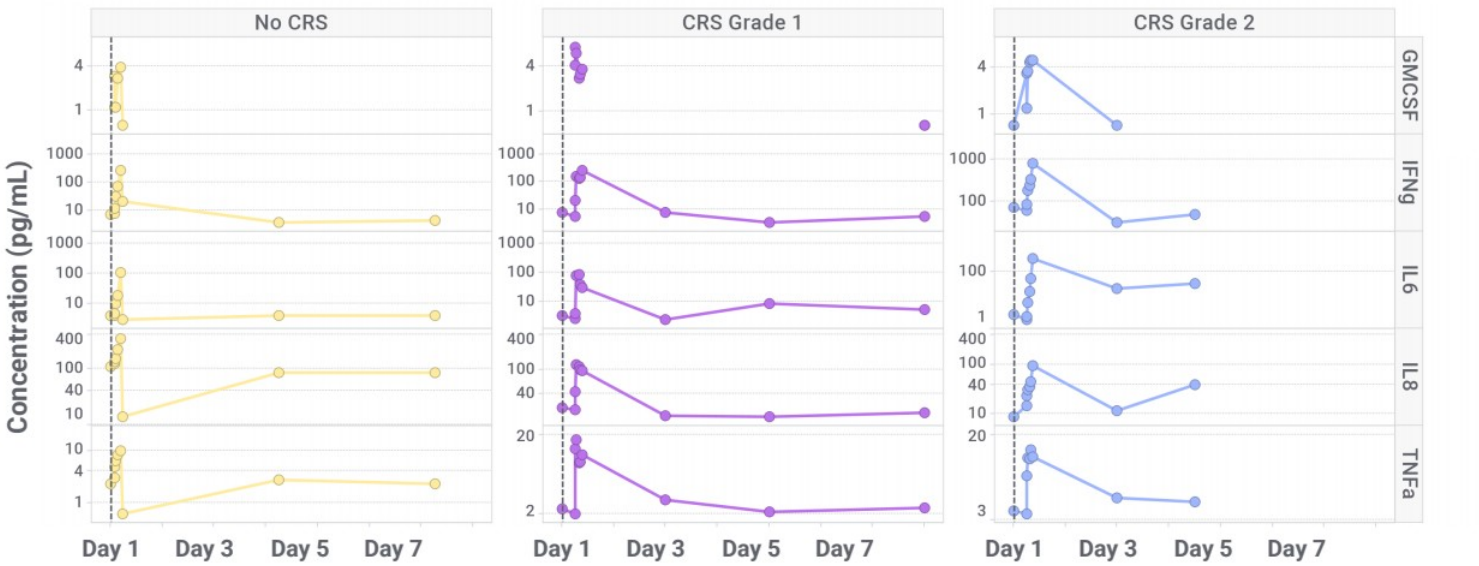
Group 1 & Group 2 Combined

Similar safety profile between Group 1 and Group 2

	Group 1	Group 2	Comb
Patients Treated	N=9 (%)	N=5 (%)	N=14 (%
Infusion Reaction	2 (22.2%)	1 (20.0%)	3 (21.4%
Grade 1	1 (11.1%)	0 (0.0%)	1 (7.1%
Grade 2	1 (11.1%)	1 (20.0%)	2 (14.2%
CRS (cytokine release syndrome)	6 (66.7%)	3 (60.0%)	9 (64.2%
Grade 1	4 (44.4%)	1 (20.0%)	5 (35.7%
Grade 2	2 (22.2%)	2 (40.0%)	4 (28.6%
Grade 3-4 (Severe)	0 (0.0%)	0 (0.0%)	0 (0.0%
ICANS	0 (0.0%)	0 (0.0%)	0 (0.0%
SAEs Related To Treatment	2 (22.2%)	3 (60.0%)	5 (35.7%

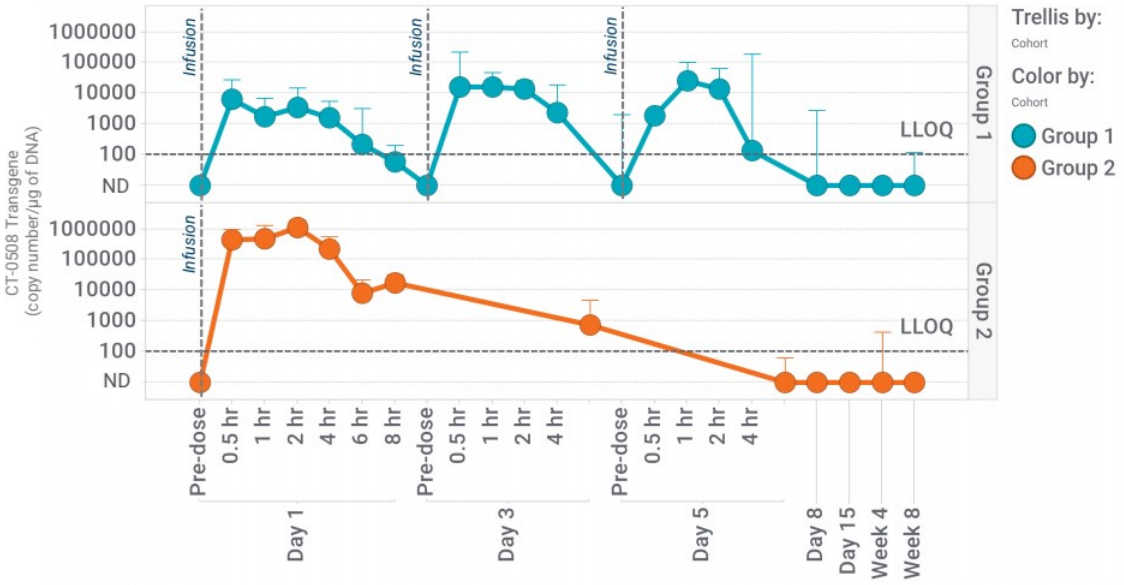
- No dose limiting toxicities.
- No severe CRS or ICANS.
- All SAEs related to treatment were due to hospitalization f monitoring of either Grade 2 CRS or Grade 2 infusion reaction.

Transient Elevations of Pro-Inflammatory Cytokines



CT-0508 rapidly extravasates from peripheral blood and were detected in the tumor of 8/9 patients

CT-0508 peripheral blood pharmacokinetics:
Rapid egress out of peripheral blood following each dose.

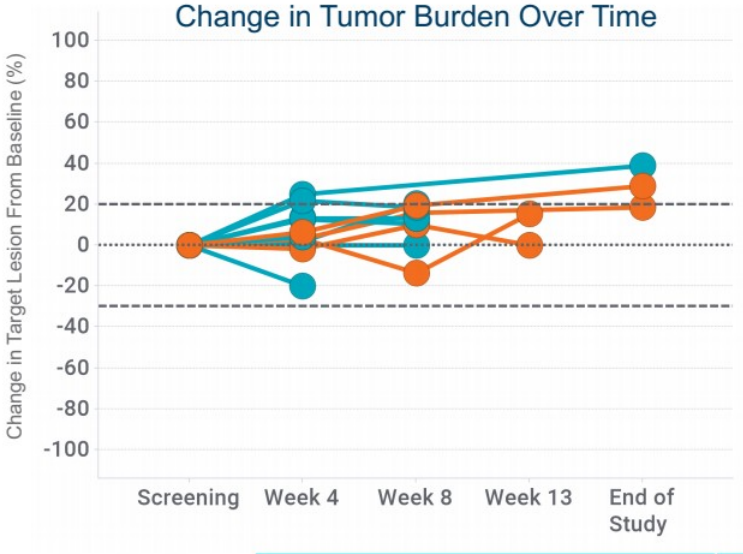


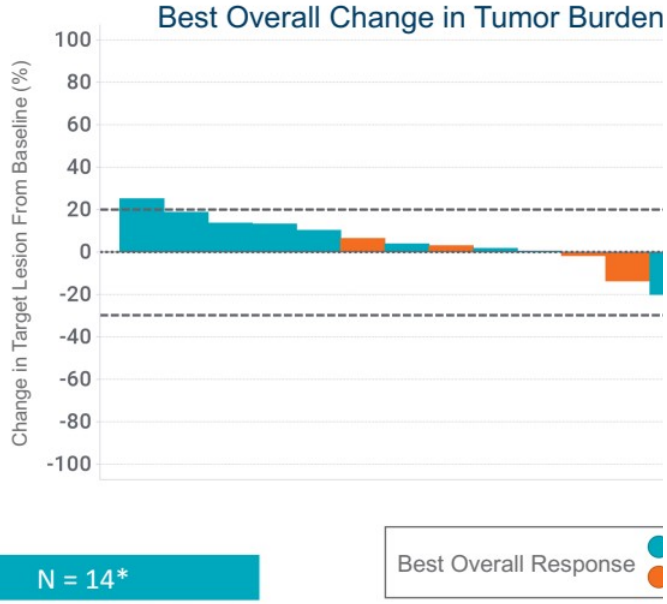
CT-0508 detection in the TME:

Pt	Day 8	Week
1	-	+
2	+	+
3	+	-
4	-	+
5	+	N/A
6	+	-
7	+	-
8	+	-
9	-	-

CT-0508 was detected in
TME of 8/9 pts.

Best Overall Response of Stable Disease

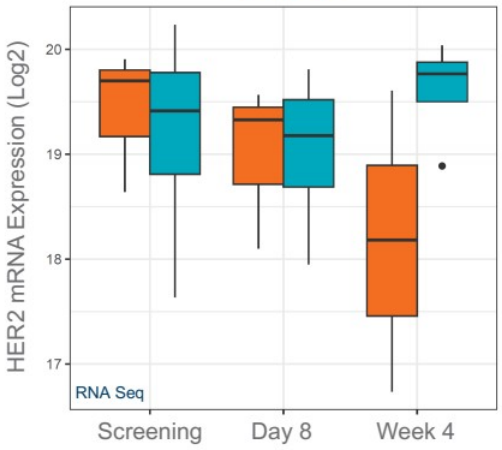




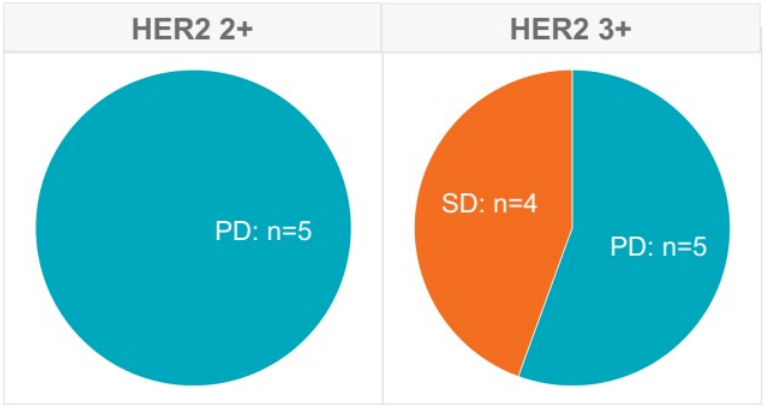
Evaluated Participants	N = 14*
Best Overall Response (RECIST 1.1)	Stable Disease: 4 (28.6%)

HER2 expression (3+) correlated with Best Overall Response*

Trend toward decrease in HER2+ tumor cells in pts with SD



Correlation between HER2 status and Best Overall Response



Evaluated Participants	N = 14*
HER2 2+	SD: 0/5 (0.00%)
HER2 3+	SD: 4/9 (44.4%)

Best Overall Response

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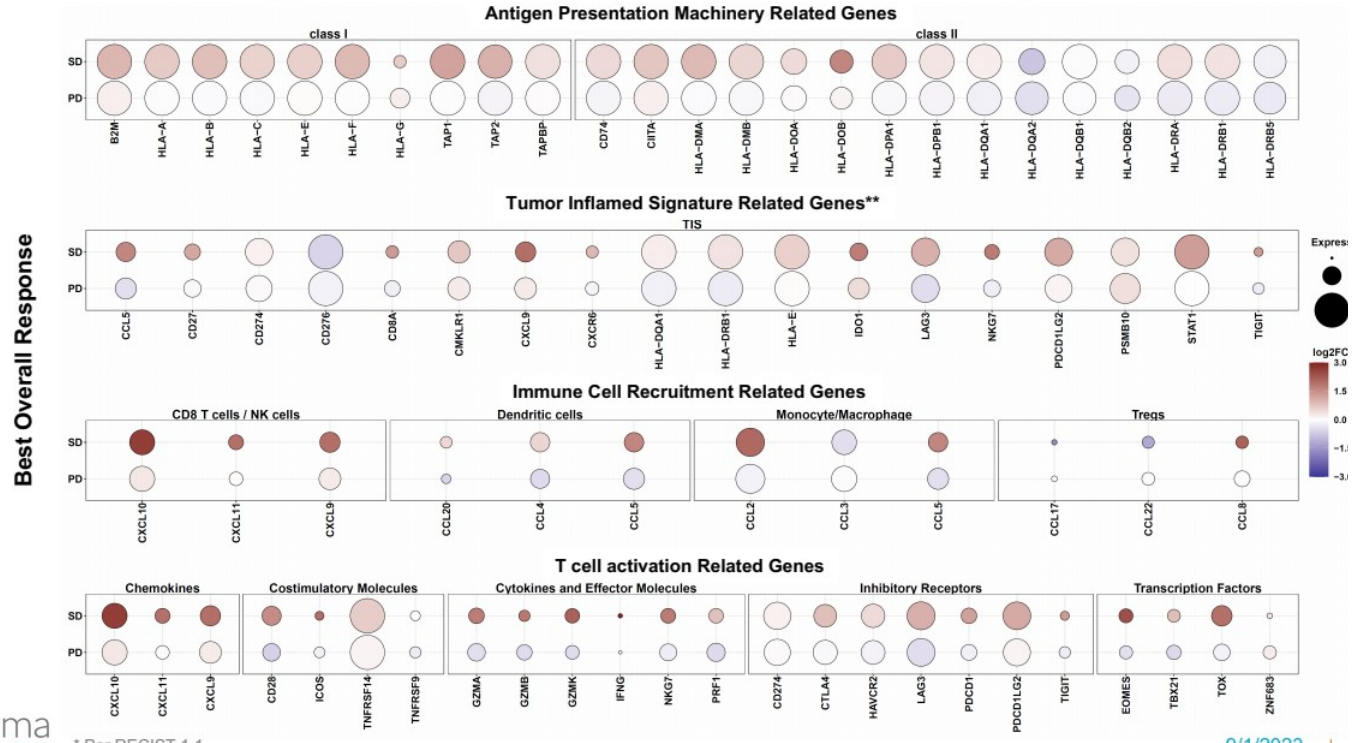
TME remodeling correlated with Best Overall Response*



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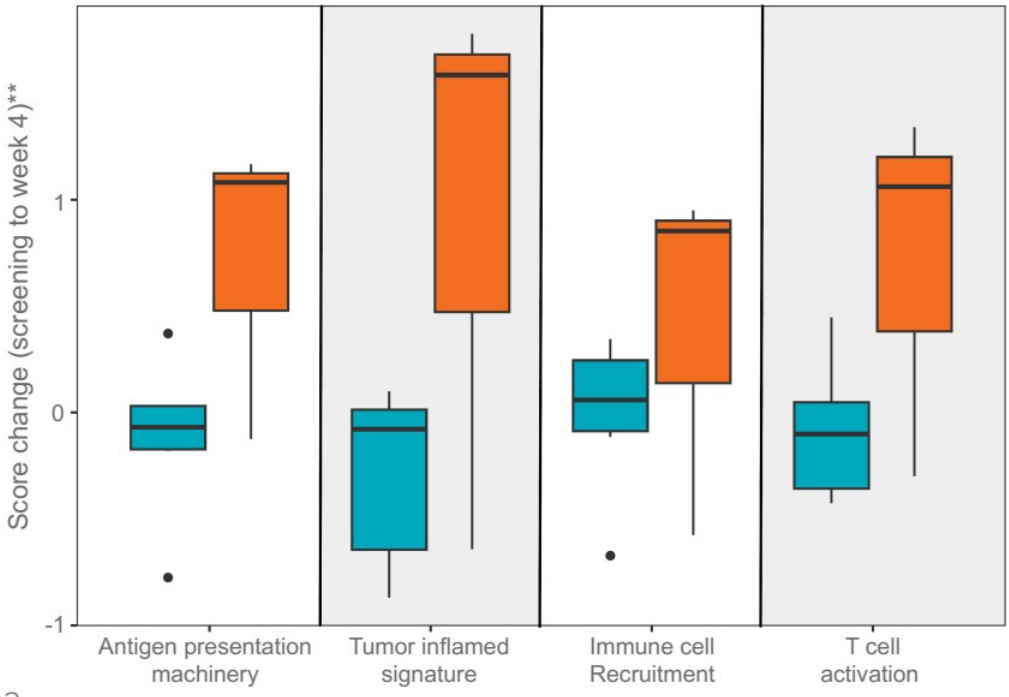
* Per RECIST 1.1

**18 gene Tumor Inflammation Signature developed by Nanostring

TME remodeling correlated with Best Overall Response*



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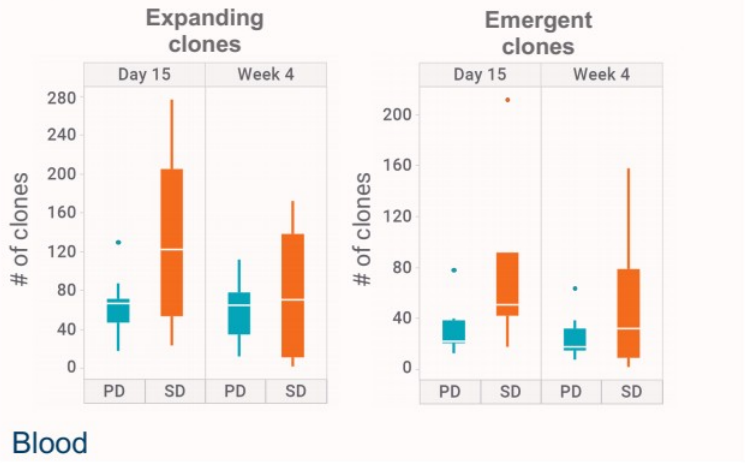
* Per RECIST 1.1

**Calculated using gene set variation analysis (GSVA) using the gene sets presented on the previous slide

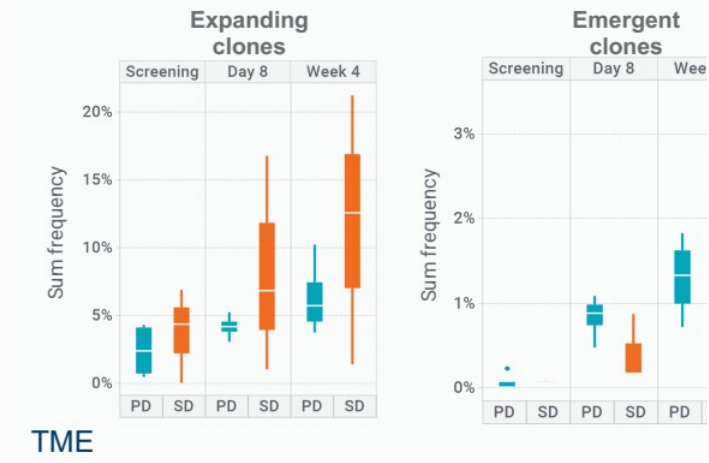
T cell expansion in the blood & TME correlated with Best Overall Response*

Expansion of T cell clones in blood correlates w/ BOR



Blood

Accumulation of peripherally expanded clones in the



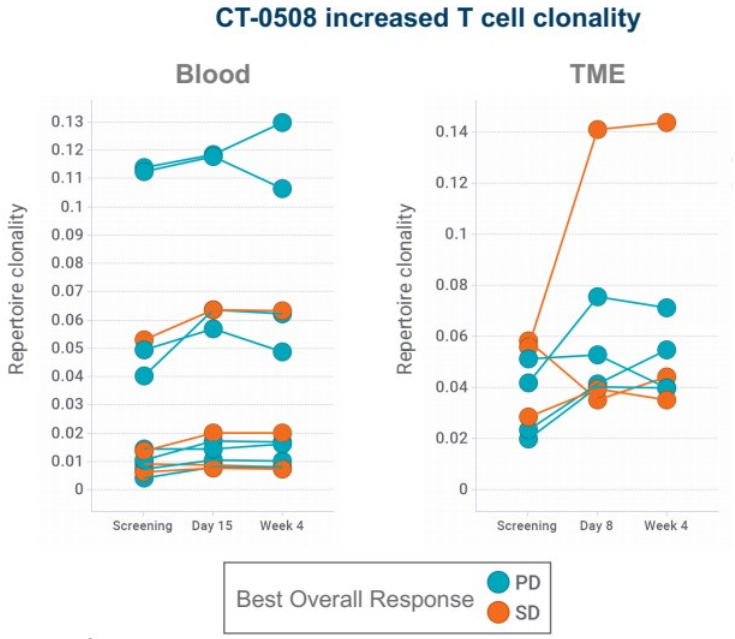
TME

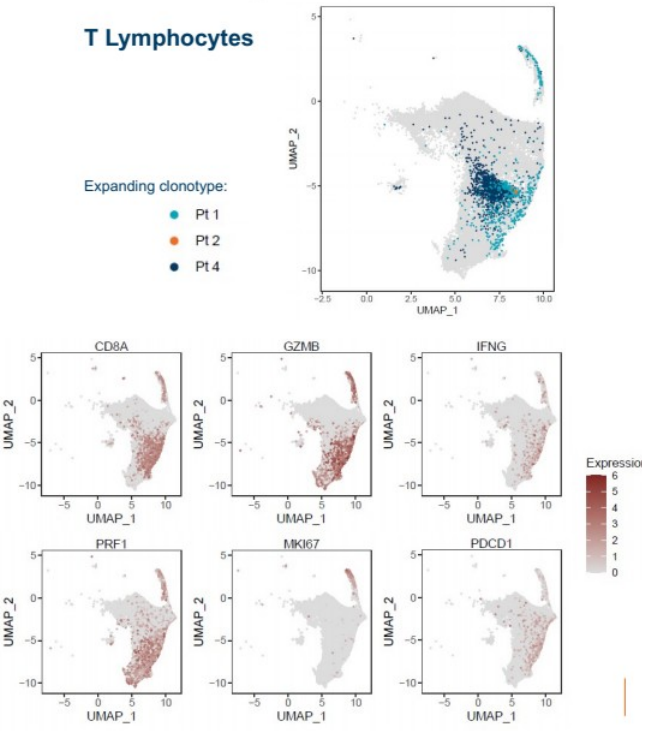
carisma THERAPEUTICS * Per RECIST 1.1

Best overall response PD SD

9/1/2023

CT-0508 increased T cell clonality in TME and activated dominant clones suggesting epitope spreading





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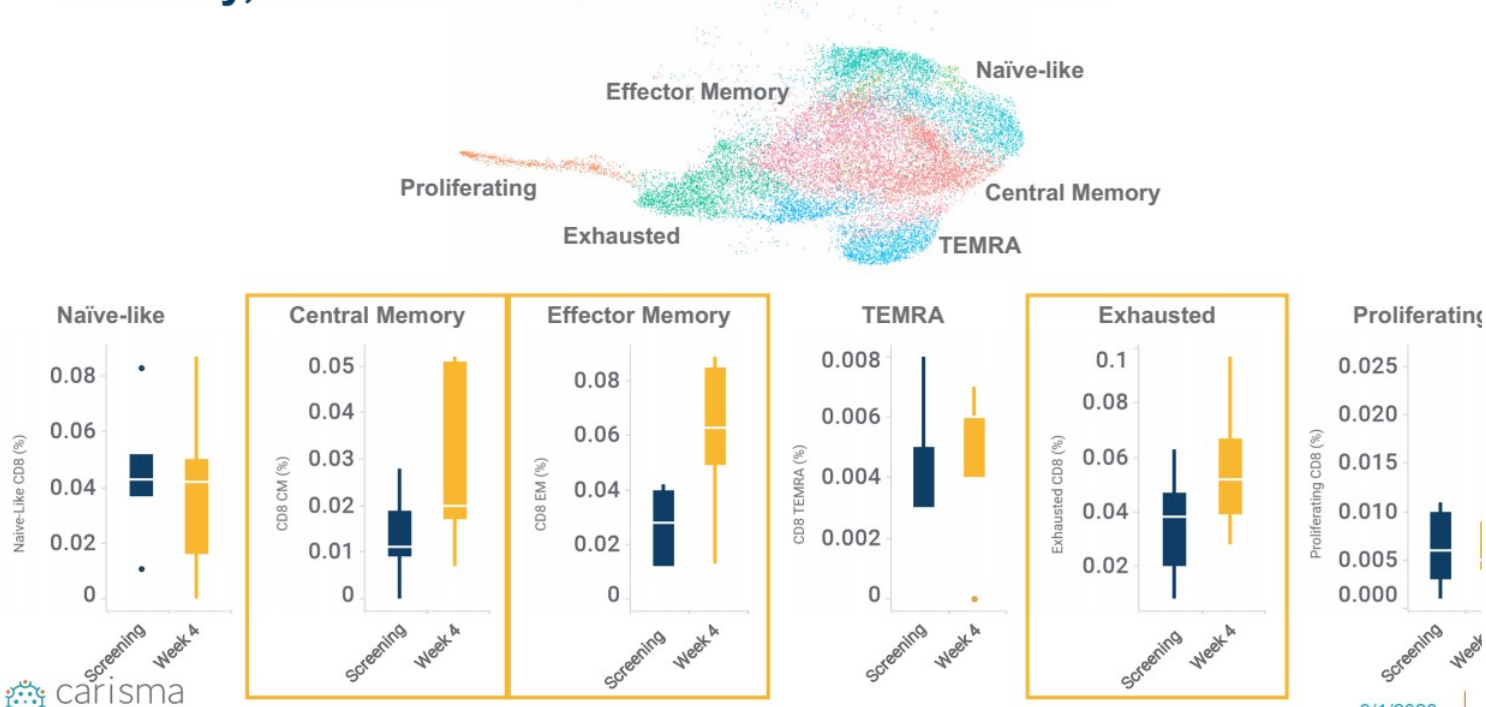
CT-0508 increased the frequency of central memory, effector memory, and exhausted CD8 T cells in the TME



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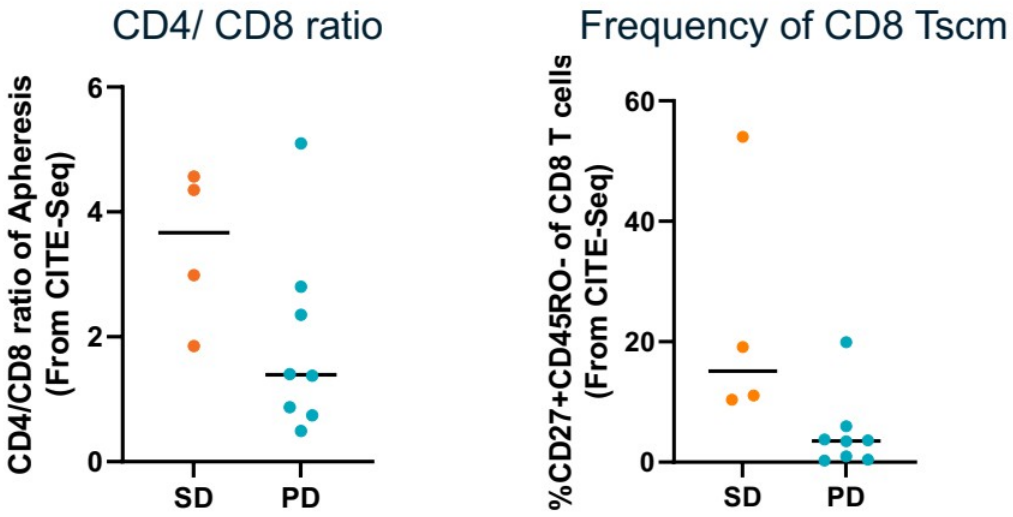
Early trends suggest improved baseline T cell fitness* correlates with Best Overall Response



Higher CD4/CD8 ratio and % of CD8 Tscm associated with improved T cell fitness

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* Based on peripheral blood T cell CD4/CD8 ratio and frequency of CD8+ T stem central memory in apheresis material

CT-0508 Study 101 Interim Data Supports CAR-M Hypothesis and Combination with Pembrolizumab

FEASIBILITY

- CT-0508 was successfully manufactured from autologous mobilized monocytes
- Patient product demonstrated high CAR expression, purity, viability, M1 polarization and confirmed functionality
- No lymphodepletion

PRELIMINARY CLINICAL PROFILE

- No dose limiting toxicities
- No severe CRS, no ICANS, and no major organ system toxicity observed
- Best overall response of SD
- SD in HER2 3+ population 44.4% (n=4/9); SD in HER2 2+ population 0% (n=0/5)
- Group 2 enrolling

MECHANISM OF ACTION

- CT-0508 tumor infiltration detected
- TME remodeling correlates with clinical outcome
- T cell expansion and fitness correlates with clinical outcome
- Exhausted T cells increase on treatment