Abstract # 356

CLDN18.2 Chimeric Antigen Receptor T Cell Therapy for Patients with Advanced Gastric and Pancreatic Adenocarcinoma: Results of ELIMYN18.2 Phase 1b Clinical Trial

Gregory P. Botta, MD, PhD[1]*; Ronan J. Kelly, MD[2]; Zhaohui Jin, MD[3]; Hong Ma, MD[8]; Geoffrey Y. Ku, MD[4]; Dan Zhao, MD, PhD[5]; Rutika Mehta, MD, MPH[6]; Julia Carnevale, MD[7]; Gloria Sierra, PhD[8]; Jie Jia, PhD[8]; Raffaele Baffa, MD[8]; Zonghai Li, MD, PhD[8]; Dae Won Kim, MD[6]; Harry H. Yoon, MD[3]

[1]University of California San Diego, Moores Cancer Center & CIRM Alpha Stem Cell Clinic, San Diego, CA; [2]Baylor University Medical Center, Charles A. Sammons Cancer Center, Dallas, TX; [3]Mayo Clinic, Rochester, MN; [4]Memorial Sloan Kettering Cancer Center, New York, NY; [5]The University of Texas MD Anderson Cancer Center, Houston, TX; [6]H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL; [7]University of California San Francisco, San Francisco, CA; [8]CARsgen Therapeutics Corporation, Houston, TX. *Corresponding author

Background

- Claudin18.2 (CLDN18.2) is a tight junction protein normally expressed in gastric mucosa and several types of cancer.[1] CLDN18.2 is considered a potential therapeutic target.[2]
- Autologous CLDN18.2 CAR T cell, satricabtagene autoleucel (satri-cel) was developed to treat solid tumors.
- Here, we report the dose escalation results of the Phase 1b ELIMYN18.2 study (Cohort A) in gastric/gastroesophageal (GC/GEJ) or pancreatic cancer (PC) in the US.

Methods

- The single-arm, open-label, Phase 1b/2 study (NCT04404595) evaluated the safety and efficacy of satri-cel in patients with CLDN18.2-positive histologically confirmed advanced GC/GEJ or PC who had progressed or were intolerant of at least 2 prior lines (GC/GEJ) or 1 prior line (PC) of systemic therapy.
- The Phase 1b study consisted of a modified 3+3 dose escalation/de-escalation with 5 dose levels (DLs) to be tested.
- Patients received a preconditioning regimen of fludarabine, cyclophosphamide, and nab-paclitaxel, followed by 1-3 cycles of satri-cel.
- **Primary Objectives:** Safety and determination of the Recommended Phase 2 Dose (RP2D).
- Adverse Events (AEs) were graded per CTCAE Version 5.0 and CRS and ICANS were graded by ASTCT 2019 consensus criteria.
- Objective Response Rate (ORR) and Clinical Benefit Rate (CBR), including Complete Response (CR), Partial Response (PR), and Stable Disease (SD) ≥ 180 days, were assessed per RECIST 1.1, tumor response (CR or PR) was confirmed by an imaging scan after the initial response assessment.
- **Data cutoff: 15-Sep-2023**

Conclusion

- **Satri-cel, the first autologous CLDN18.2 CAR T cell therapy safety profile was encouraging, with manageable treatment-related AEs.**
- **Initial efficacy was promising in heavily pre-treated CLDN18.2-positive advanced GC/GEJ and PC population and consistent with earlier reports.[3]**
- **DL3 (600×10^{6}cells) was selected as RP2D and enrollment in Phase 2 is currently ongoing.**

Results

Table 1. Patient Baseline Characteristics

Characteristic	Cancer Type: All DLs GC/GEJ (N=7)	All DLs PC (N=12)
Age (years) Median (min, max)	43.0 (33, 65)	63.5 (54, 77)
Male, n (%)	2 (28.6)	5 (41.7)
Race, n (%)		
Asian	3 (42.9)	1 (8.3)
White or Caucasian	4 (57.1)	10 (83.3)
Other	0	1 (8.3)
Months since diagnosis Median (min, max)	29.3 (13.7, 74.7)	20.6 (7.7, 97.7)
Number of prior systemic treatment lines		
Median (min, max)	4 (2, 10)	3 (1, 5)
≥3, n (%)	6 (85.7)	7 (58.3)
Prior anti-cancer treatment, n (%)		
Surgery	5 (71.4)	8 (66.7)
Systemic Therapy	7 (100)	12 (100)
Radiotherapy	3 (42.9)	5 (41.7)
Number of metastatic organs Median (min, max)	2.0 (1, 7)	2.0 (1, 4)
ECOG PS score		
0	1 (14.3)	9 (75.0)
1	6 (85.7)	3 (25.0)

Table 2. Drug Exposure and AE Summary

	DL3 (N=7) GC/GEJ (n=2) PC (n=5)	All DLs GC/GEJ (N=7)	All DLs PC (N=12)	Total (N=19)
Number of Infusions, median (min, max)	2 (1, 3)	2 (1, 3)	1.5 (1, 3)	2 (1, 3)
CT041-related TEAEs, n (%)	7 (100)	6 (85.7)	12 (100)	18 (94.7)
CT041-related serious TEAEs, n (%)	3 (42.9)	1 (14.3)	3 (25.0)	4 (21.1)
DLTs, n (%)	0	0	0	0
Gr ≥3 TEAEs, n (%)	7 (100)	7 (100)	12 (100)	19 (100)
Gr ≥3 CT041-related TEAEs, n (%)	5 (71.4)	5 (71.4)	4 (33.3)	9 (47.4)

Abbreviations: 600: 600×10^6 dose level; 375/400: 375/400×10^6 dose level; 250/300, 250/300×10^6 dose level; AE: adverse event; ALP: alkaline phosphatase; ALT: alanine aminotransferase; AST: aspartate aminotransferase; CRS: cytokine release syndrome; CR: complete response; DLTs: dose-limiting toxicities; Gr: grade; mPFS: median progression-free survival; mOS: median overall survival; PR: partial response; NE: not evaluable; SD: stable disease; mDOR: median duration of response (in months); TEAE: treatment-emergent adverse event.

Table 3. CT041-related TEAEs (All DLs, total incidence ≥15%)

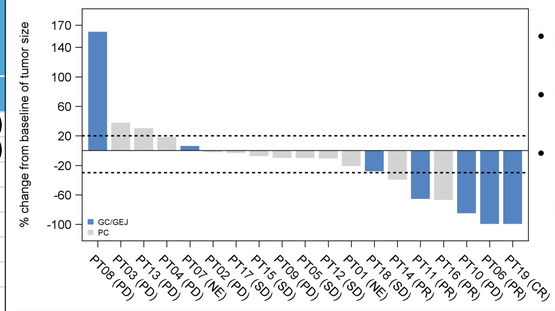
Preferred Term (PT)	All DLs GC/GEJ (N=7) n (%)		All DLs PC (N=12) n (%)		Total (N=19) n (%)	
	Gr ≥3	Any	Gr ≥3	Any	Gr ≥3	Any
CRS	0	6 (85.7)	2 (16.7)	11 (91.7)	2 (10.5)	17 (89.5)
Pyrexia	0	6 (85.7)	0	11 (91.7)	0	17 (89.5)
Fatigue	0	1 (14.3)	0	6 (50.0)	0	7 (36.8)
Rash	0	3 (42.9)	0	4 (33.3)	0	7 (36.8)
Chills	0	2 (28.6)	0	4 (33.3)	0	6 (31.6)
Headache	0	3 (42.9)	0	3 (25.0)	0	6 (31.6)
Hypotension	1 (14.3)	3 (42.9)	1 (8.3)	3 (25.0)	2 (10.5)	6 (31.6)
ALP increased	1 (14.3)	3 (42.9)	0	2 (16.7)	1 (5.3)	5 (26.3)
ALT increased	1 (14.3)	2 (28.6)	1 (8.3)	2 (16.7)	2 (10.5)	4 (21.1)
Tachycardia	0	1 (14.3)	0	3 (25.0)	0	4 (21.1)
Abdominal pain	0	2 (28.6)	0	1 (8.3)	0	3 (15.8)
AST increased	1 (14.3)	1 (14.3)	1 (8.3)	2 (16.7)	2 (10.5)	3 (15.8)
Hypoxia	0	1 (14.3)	1 (8.3)	2 (16.7)	1 (5.3)	3 (15.8)
Lipase increased	2 (28.6)	3 (42.9)	0	0	2 (10.5)	3 (15.8)
Vomiting	0	1 (14.3)	0	2 (16.7)	0	3 (15.8)

Table 4. Treatment Efficacy as Assessed by Investigator

	DL3 (N=7) GC/GEJ (n=2) PC (n=5)	All DLs GC/GEJ (N=7)	All DLs PC (N=12)
ORR, n (%)			
Confirmed ORR	3 (42.9)	3 (42.9)	2 (16.7)
95% CI	9.9, 81.6	9.9, 81.6	2.1, 48.4
Best overall response, n (%)			
CR	1 (14.3)	1 (14.3)	0
PR	2 (28.6)	2 (28.6)	2 (16.7)
SD	3 (42.9)	1 (14.3)	4 (33.3)
Progressive disease	1 (14.3)	2 (28.6)	5 (41.7)
Not evaluable (NE)	0	1 (14.3)	1 (8.3)
CBR, n (%)**	5 (71.4)	4 (57.1)	4 (33.3)
95% CI	29.0, 96.3	18.4, 90.1	9.9, 65.1
mPFS***, months (95% CI)	4.6 (1.0, NE)	5.7 (1.0, NE)	2.7 (1.0, 4.6)
mOS***, months (95% CI)	12.9 (8.9, NE)	8.9 (3.3, NE)	8.9 (2.5, 16.6)

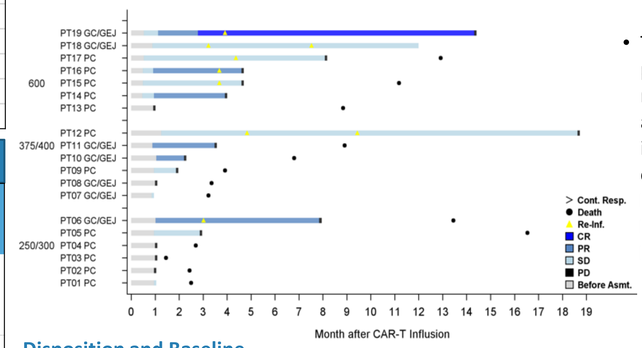
**CBR is defined as the incidence of a best overall response of CR, PR, or SD≥180 days
***from satri-cel infusion

Figure 1. Maximum Reduction of Target Lesions in Sum of Diameters



- 9 of 12 PC patients had tumor shrinkage.
- 5 of 7 GC/GEJ had tumor shrinkage.
- The parentheses in x-axis show confirmed best overall response.

Figure 2. Best Response and Duration of Response per Dose Level



- The following patients received additional infusions not captured in Figure 2: PT05, PT06, PT11, PT14.

Disposition and Baseline

- 24 eligible patients underwent leukapheresis and 19 patients were treated (7 GC/GEJ, 12 PC) across 3 dose levels ranging from 250-600×10^6 cells: DL1: 250-300×10^6 (n=6), DL2: 375-400×10^6 (n=6), DL3: 600×10^6 (n=7).
- All patients received prior systemic therapy, among which 6 GC/GEJ (85.7%) and 7 PC (58.3%) patients received ≥ 3 lines of prior systemic treatment (**Table 1**).
- **Median follow-up**: 8.9 months (range, 1.5, 18.7).
- **Treatment**: CT041 exposure is shown in **Table 2.**

Safety

- AEs, including TEAEs and DLTs are summarized in **Table 2 & Table 3.**
- The vast majority of CRS was Gr 1 with three Gr 2 events and two Gr 3 events, and one Gr 1 immune effector cell-associated neurotoxicity syndrome (ICANS). All events resolved.
- No hemophagocytic lymphohistiocytosis (HLH), DLTs, or treatment-related deaths were reported.

Efficacy

- GC/GEJ: ORR 42.9% (3/7), 1 CR & 2 PR, CBR of 57.1% (4/7), & mDOR 6.9 (2.6, NE);
- PC: ORR 16.7%(2/12), 2 PR, CBR of 33.3% (4/12), & mDOR 3.4 (3.0, NE);
- DL3 (600×10^6 cells): ORR 42.9%(3/7), CBR of 71.4% & mDOR 3.7 (3.0, NE); 50% ORR for GC/GEJ group (1/2) with 1 CR and 40% ORR for PC group (2/5); therefore, DL3 selected as RP2D.
- See details in **Table 4 & Figure 2**.

References

1. Sahin U, et al. *Clin Cancer Res.* 2008;14(23):7624–7634.
2. Cao W, et al. *Biomark Res*. 2022;10(1):38.
3. Qi C, et al. *Nature Med.* 2022;28:1189-1198.

Acknowledgment: We thank Nicole Law, PharmD, for writing and critical review and Zijing Zhang (Ph.D.) for statistical analysis support for this presentation.

***Email: gbotta@health.ucsd.edu**