Correlative data from an ongoing Phase 1, multicenter study of SENTI-202, a first-in-class, CD33 and/or FLT3 & not endomucin (EMCN), selective off-the-shelf CAR NK cell therapy for Acute Myeloid Leukemia (AML), is consistent with its clinical activity and unique logic gated mechanism of action

Muharrem Muftuoglu[1]*, Enping Hong[2]*, Nosha Farhadfar[3], Stephen A. Strickland[4], Ashish R. Bajel[5], Alireza Eghtedar[6], Gary Schiller[7], Mahesh Basyal[1], Li Li[1], Lawrence Naitmazi[2], Rochelle Emery[2], Timothy Lu[2], Brian S. Garrison[2], Kanya Rajangam[2], Farhad Ravandi[1], Michael Andreeff[1]

* Denotes co-authorship. [1]The University of Texas M.D. Anderson Cancer Center, Houston, TX, [2]Senti Biosciences, Inc, South San Francisco, CA, [3]Sarah Cannon Transplant and Cellular Therapy Program at Methodist Hospital San Antonio, TX, [4]SCRI at TriStar Centennial, Nashville, TN, [5]Peter MacCallum Cancer Centre, Melbourne, Australia, [6]Colorado Blood Cancer Institute, Denver, CO, [7]David Geffen School of Medicine at UCLA, Los Angeles, CA

ABSTRACT 5921

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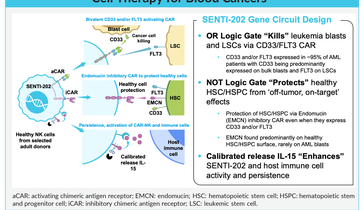
BACKGROUND

SENTI-202 is being evaluated after lymphodepletion in patients with relapsed/refractory (R/R) acute myeloid leukemia (AML) in an ongoing Phase I clinical trial, SENTI-202-101 (NCT06325748). SENTI-202 is a Logic Gated CAR NK cell therapy designed to target CD33 and/or FLT3 positive hematologic malignancies, including AML. To achieve deeper & longer remissions, SENTI-202 is designed to target both bulk AML blasts and leukemic stem cells (LSCs), which are often FLT3$^+$ (+/-CD33$^+$), while enabling long-term multilineage hematopoiesis by maintaining a healthy HSPC population. The SENTI-202 Logic Gated Gene Circuit therefore includes an inhibitory CAR recognizing EMCN (expressed by healthy HSPCs, but rarely by AML) to protect HSPCs from potential SENTI-202-mediated off-tumor on-target toxicity even if they express CD33 and/or FLT3 and enable post-treatment hematopoietic recovery. Here, we report preliminary correlative data evaluating hematopoietic cell fractions in bone marrow (BM) and peripheral blood (PB) from 18 treated R/R AML patients with available data from the ongoing study (October 17th, 2025). **Efficacy and clinical results are discussed in our clinical oral presentation (abstract# 1044).**

SENTI-202 is a First-in-Class Off-the-Shelf Logic-Gated Selective CD33 OR FLT3 NOT EMCN CAR NK Cell Therapy for Blood Cancers



SENTI-202 Gene Circuit Design

- **OR Logic Gate "Kills"** leukemia blasts and LSCs via CD33/FLT3 CAR
  - CD33 and/or FLT3 expressed in ~95% of AML patients with CD33 being predominantly expressed on bulk blasts and FLT3 on LSCs
- **NOT Logic Gate "Protects"** healthy HSC/HSPC from 'off-tumor, on-target' effects
  - Protection of HSC/HSPC via Endomucin (EMCN) inhibitory CAR even when they express CD33 and/or FLT3
  - EMCN found predominantly on healthy HSC/HSPC surface, rarely on AML blasts
- **Calibrated release IL-15 "Enhances"** SENTI-202 and host immune cell activity and persistence

aCAR: activating chimeric antigen receptor; EMCN: endomucin; HSC: hematopoietic stem cell; HSPC: hematopoietic stem and progenitor cell; iCAR: inhibitory chimeric antigen receptor; LSC: leukemic stem cell.

SENTI-202-101 Study Design

RP2D identified as **Schedule I, Dose Level 2**

SENTI-202-101 is a Multicenter, Multinational, Open-label Phase 1 Trial in Patients with R/R Hematologic Malignancies*

Key Eligibility Criteria

- Adult patients: ≥18 & <75 years
- ECOG PS 0-1
- R/R CD33 and/or FLT3 expressing hematologic malignancies
- CD33+ by local assessment
  - R/R AML (1-3 prior therapies)
  - R/R MDS with increased blasts^1 (1-2 prior therapies)
- **Must have** received targeted agents if applicable mutations

Study Design

Dose finding followed by AML, MDS and other disease specific expansion cohorts at RP2D

Study Dosing

2 DOSE LEVELS and **2 SCHEDULES**

Starting dose level anticipated to be biologically active

Key Objectives

Primary objective
- Safety and determination of MTD/RP2D
- Efficacy (expansion cohorts) based on ELN2022 criteria for AML

Other key objectives
- Measurable residual disease assessed locally
- Pharmacokinetics
- Pharmacodynamics using CyTOF on serial BM samples

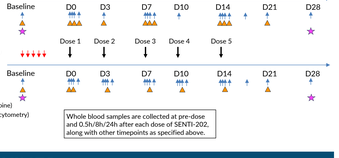
NCT06325748

ECOG PS: European Cooperative Oncology Group performance status; MTD: maximum tolerated dose; RP2D: recommended phase 2 dose; ELN: European LeukemiaNet; CyTOF: Cytometry by Time-of-Flight; BM: bone marrow; [1]Per WHO 2022 Classification

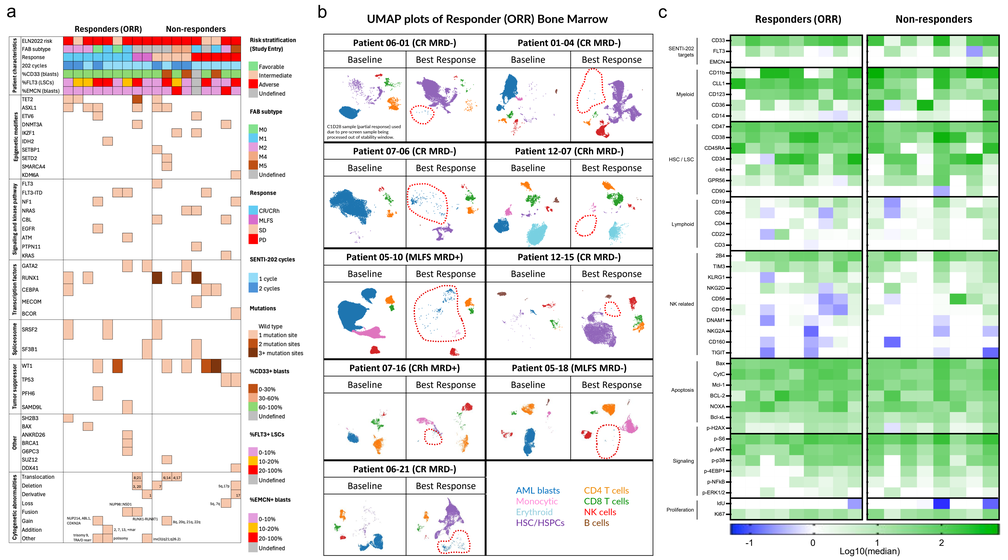
SENTI-202-101 Dosing and Correlative Sampling Timepoints

Methods

- Whole blood and BM aspirate are collected into sodium heparin tubes, then processed to cryopreserved PBMC/BMMC by Ficoll separation.
- Pharmacokinetics was determined by detection of the SENTI-202 transgene in PBMC samples by ddPCR.
- BMMC samples were analyzed by a 49-marker mass cytometry (CyTOF) panel.
- Serum samples were collected for cytokine analysis by MSD.
- Additional whole blood samples collected in Cyto-Chex BCT tubes were analyzed by flow cytometry.

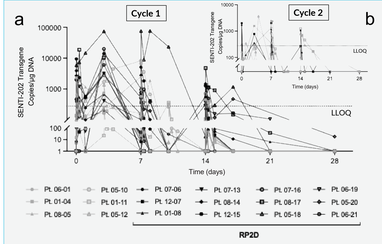


PATIENT CHARACTERISTICS AND CLINICAL RESPONSES



Patient characteristics and responses in the SENTI-202-101 clinical trial at study entry. (a) Representation of the ELN risk classification, FAB subtype, response, number of SENTI-202 cycles given, SENTI-202 target expression, and mutational profiles of the 18 patients with relapsed/refractory AML in the SENTI-202-101 clinical trial. Data from an open clinical database as of October 17th, 2025. (b) UMAP plots of responder (ORR) patients at baseline and best response, showing the disappearance of AML cells in patient bone marrow during response. Cell populations are marked with different colors, and the AML population (dark blue) is further circled in red. (c) Heat map analysis of CyTOF markers expressed by AML populations in bone marrow samples show the prevalence of AML-associated markers and their heterogeneity of expression across all patients. The log(median intensity) of all channels were grouped by function and ranked by average intensity across all patients.

SENTI-202 PHARMACOKINETICS

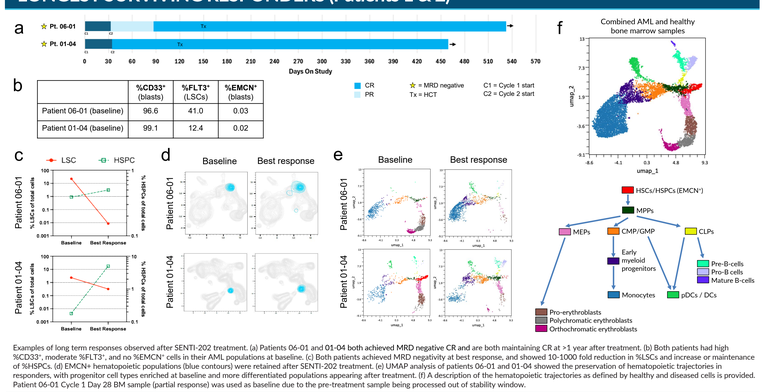


b

PK Parameters Median (range) given for all		C_{max} (Copies/µg DNA)	AUC_{last} (Days*Copies/µg DNA)	T_{max} (Days)	Peripheral clearance (Days)
Dose Level 1 (1x10⁹ CAR⁺ NK/dose)	Schedule I, 3 doses (N=3)	2392 (1567 - 2496)	6873 (3160 - 11074)	5 (0 - 7)	15 (14 - 26)
	Schedule II, 5 doses (N=3)	1358 (380 - 8212)	2842 (720 - 29067)	7 (3 - 14)	15 (14 - 17)
Dose Level 2 (1.5x10⁹ CAR⁺ NK/dose)	**Schedule I, 3 doses (N=12) (RP2D)**	**3275 (412 - 76600)**	**13494 (1752 - 434178)**	**3 (0 - 8)**	**15 (14 - 23)**
RP2D	Non-responders (N=6)	3163 (412 - 18750)	12395 (1752 - 37852)	3 (0 - 3)	17 (15 - 23)
	Responders (ORR) (N=6)	**6021 (676 - 76600)**	**19634 (2777 - 434178)**	**3 (2 - 8)**	**14 (14 - 17)**
All patients	Non-responders (N=9)	2655 (380 - 18750)	5743 (720 - 37852)	3 (0 - 14)	15 (14 - 23)
	Responders (ORR) (N=9)	**2472 (676 - 76600)**	**8030 (2777 - 434178)**	**3 (0 - 8)**	**15 (14 - 26)**
	All (N=18)	2496 (380 - 76600)	8030 (720 - 434178)	3 (0 - 14)	15 (14 - 26)

Pharmacokinetic (PK) analysis of SENTI-202 in patients. SENTI-202 was detected in all treated patients, (a) with data shown from Cycle 1 and (inset) Cycle 2. SENTI-202 PK profile was consistent with allogeneic NK cell therapy with cells detected in the first 2 weeks in periphery followed by clearance thereafter. (b) A preliminary signal of higher SENTI-202 exposure (C_{max} and AUC_{last}) was observed for the RP2D cohort compared to dose level 1. Similarly, responders (ORR: CR/CRh and MLFS) also showed a preliminary signal of higher exposure compared to non-responders when assessed in all patients (higher AUC_{last}) and in the RP2D cohort only (higher C_{max} and AUC_{last}). The PK trends noted above were not statistically significant. Peripheral clearance was defined as the last time point where a non-zero SENTI-202 signal was noted; 3 patients with ongoing PK collections were excluded from this analysis. Estimated LLOQ assumes equivalent DNA loading for each reaction. Note: Patient 06-01 Cycle 1 samples were processed out of stability window and are excluded from analysis of PK parameters.

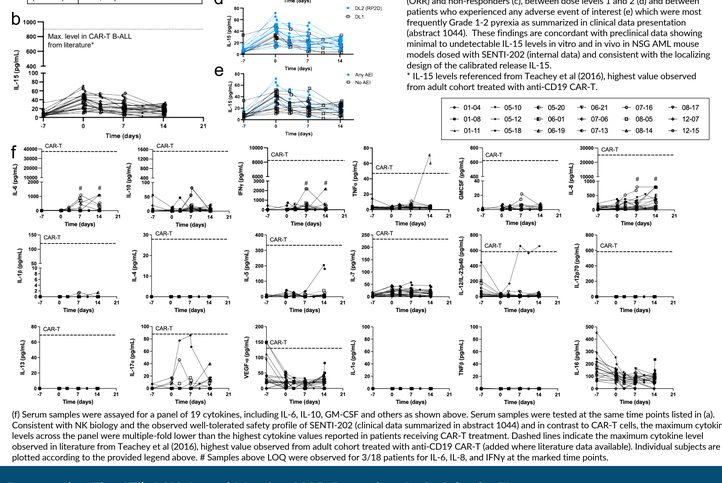
LONGEST SURVIVING RESPONDERS (Patients 1 & 2)



Examples of long term responses observed after SENTI-202 treatment. (a) Patients 06-01 and 01-04 both achieved MRD negative CR and are both maintaining CR at >1 year after treatment. (b) Both patients had high %CD33$^+$, moderate %FLT3$^+$, and no %EMCN$^+$ cells in their AML populations at baseline. (c) Both patients achieved MRD negativity at best response, and showed 10-1000 fold reduction in %LSCs and increase or maintenance of %HSPCs. (d) EMCN+ hematopoietic populations (blue contours) were retained after SENTI-202 treatment. (e) UMAP analysis of patients 06-01 and 01-04 showed the preservation of hematopoietic trajectories in responders, with progenitor cell types enriched at baseline and more differentiated populations appearing after treatment. (f) A description of the hematopoietic trajectories as defined by healthy and diseased cells is provided. Patient 06-01 Cycle 1 Day 28 BM sample (partial response) was used as baseline due to the pre-treatment sample being processed out of stability window.

SENTI-202 PHARMACODYNAMICS: CYTOKINES

Dosing schedule	Time points tested
Schedule I (3 doses)	Day -7 (baseline), pre-dose and 8h post each dose, Day 3
Schedule II (5 doses)	Day -7 (baseline), Day 0 pre-dose, 8h post each dose

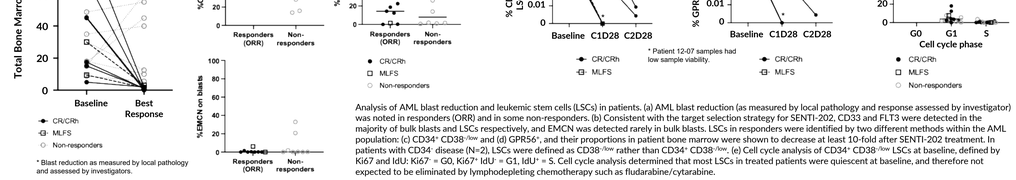


Interim analysis of patient serum samples was performed at selected time points (a). Serum IL-15 levels were modestly elevated (maximum values >10-fold lower than that reported for CAR-T cells) prior to SENTI-202 dosing (Day 0 pre-dose) and following LD, as expected from removal of cytokine sinks such as Treg cells. Overall, IL-15 levels were not elevated beyond 80 pg/mL across all patients. There was no trend to differences in IL-15 levels between responders (ORR) and non-responders (c), between dose levels 1 and 2 (d) and between patients who experienced any adverse event of interest (e) which were most frequently Grade 1-2 pyrexia as summarized in clinical data presentation (abstract 1044). These findings are concordant with preclinical data showing minimal to undetectable IL-15 levels in vitro and in vivo in NSG AML mouse models dosed with SENTI-202 (internal data) and consistent with the localizing design of the calibrated release IL-15.

* IL-15 levels referenced from Teachey et al (2016), highest value observed from adult cohort treated with anti-CD19 CAR-T.

(f) Serum samples were assayed for a panel of 19 cytokines, including IL-6, IL-10, GM-CSF and others as shown above. Serum samples were tested at the same time points listed in (a). Consistent with NK biology and the observed well-tolerated safety profile of SENTI-202 (clinical data summarized in abstract 1044) and in contrast to CAR-T cells, the maximum cytokine levels across the panel were multiple-fold lower than the highest cytokine values reported in patients receiving CAR-T treatment. Dashed lines indicate the maximum cytokine level observed in literature from Teachey et al (2016), highest value observed from adult cohort treated with anti-CD19 CAR-T (added where literature data available). Individual subjects are plotted according to the provided legend above. # Samples above LOQ were observed for 3/18 patients for IL-6, IL-8, and IFNγ at the marked time points.

SENTI-202 MOA: AML BLAST & LSC ANALYSIS

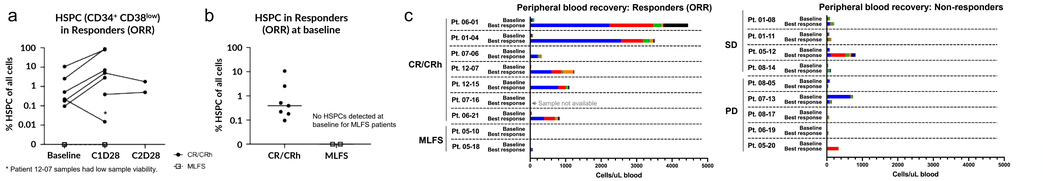


* Blast reduction as measured by local pathology and assessed by investigators.

* Patient 12-07 samples had low sample viability.

Analysis of AML blast reduction and leukemic stem cells (LSCs) in patients. (a) AML blast reduction (as measured by local pathology and response assessed by investigator) was noted in responders (ORR) and in some non-responders. (b) Consistent with the target selection strategy for SENTI-202, CD33 and FLT3 were detected in the majority of bulk blasts and LSCs respectively, and EMCN was detected rarely in bulk blasts. LSCs in responders were identified by two different methods within the AML population: (c) CD34$^+$ CD38$^{-/low}$ and (d) GPR56$^+$, and their proportions in patient bone marrow were shown to decrease at least 10-fold after SENTI-202 treatment. In patients with CD34$^+$ disease (N=2), LSCs were defined as CD38$^{-/low}$ rather than CD34$^+$ CD38$^{-/low}$. (e) Cell cycle analysis of CD34$^+$ CD38$^{-/low}$ LSCs at baseline, defined by Ki67 and IdU: Ki67$^-$ = G0, Ki67$^+$ IdU$^-$ = G1, IdU$^+$ = S. Cell cycle analysis determined that most LSCs in treated patients were quiescent at baseline, and therefore not expected to be eliminated by lymphodepleting chemotherapy such as fludarabine/cytarabine.

SENTI-202 MOA: HSPC ANALYSIS



* Patient 12-07 samples had low sample viability.

(a) HSPCs were identified as CD34$^+$CD38$^{-/low}$ cells within the healthy hematopoietic cell population, which clusters distinctly from AML cells in UMAP analysis of CyTOF data. Of note, amongst all responders (ORR), patients with detectable HSPC at baseline achieved CR/CRh with SENTI-202, and the proportion of HSPCs in bone marrow was either increased or maintained during SENTI-202 treatment consistent with SENTI-202's unique logic-gated NOT gate mechanism of action designed to selectively kill AML blasts and LSCs while sparing HSPCs. (b) Patients with no detectable HSPC at baseline achieved an MLFS without accompanying blood count recovery. (c) Similarly, flow cytometry analysis of peripheral blood cells showed that most responders achieving CR/CRh had robust immune recovery by the end of each cycle, consistent with normal hematopoiesis, while patients with MLFS, SD, or PD did not.

SUMMARY

- **Substantial AML blast reduction was observed in 50% of patients.** 9/18 patients evaluable for best overall response had blast reduction by CyTOF consistent with clinical response of CR/CRh (7) or MLFS (2). All CR patients were MRD- as assessed locally. **Longest surviving responders are currently >450 and >525 days post-initiation of SENTI-202 treatment.**
- **AML disease characterization revealed unique mutational and proteomic signatures between patients.** Of note, all patient AMLs expressed CD33 (range 14-99% CD33$^+$), and 5/7 CR/CRh patients expressed FLT3 on LSCs (range 12-41% FLT3$^+$).
- **Responder AML leukemic stem cell (LSC) numbers decreased at least 10X after treatment**. Most LSCs were in G0/G1 at baseline and would not be expected to be eliminated by traditional chemotherapy approaches.
- **Responder hematopoietic stem and progenitor cell (HSPC) numbers were increased (or maintained) during SENTI-202 treatment.** While MLFS patients showed responses against AML disease, they showed no detectable HSPCs at baseline or response.
- Consistent with NK biology and the observed well-tolerated safety profile of SENTI-202 (clinical data summarized in abstract 1044) and in contrast to CAR-T cells, **serum cytokine levels from a 19-cytokine panel were multiple-fold lower than the highest cytokine values reported in patients receiving CAR-T treatment.**
- **SENTI-202 was detected in all treated patients**, with comparable PK to other CAR NK cell therapies. Preliminary findings show that RP2D and responders had higher SENTI-202 exposure (AUC_{for}, C_{max}) compared to dose level 1 or non-responders, respectively.
- **Patients responding to SENTI-202 treatment had pharmacodynamics consistent with the designed SENTI-202 MOA.** Consistent with the **OR Logic Gate mechanism of action** and SENTI-202 target selection strategy, CR/CRh/MLFS responders showed AML blast and LSC reduction. Consistent with the **NOT Logic Gate mechanism of action**, CR/CRh responder baseline HSPCs were increased (or maintained) during SENTI-202 treatment, and experienced peripheral blood cell count recovery. Responding patients with no detectable HSPC at baseline achieved MLFS and no peripheral immune cell recovery. Consistent with design of the calibrated release IL15 that localizes IL15, there was no marked elevation in peripheral IL15 levels beyond that observed due to lymphodepletion. The observed effects are consistent with the pharmacodynamic action of the Logic Gate in SENTI-202 in sparing EMCN$^+$ HSPCs while selectively killing CD33$^+$ and/or FLT3$^+$ AML tumor cells. **Additional dose expansion is on-going.**

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SENTI BIOSCIENCES, CONTACT
email: kanya.rajangam@sentibio.com