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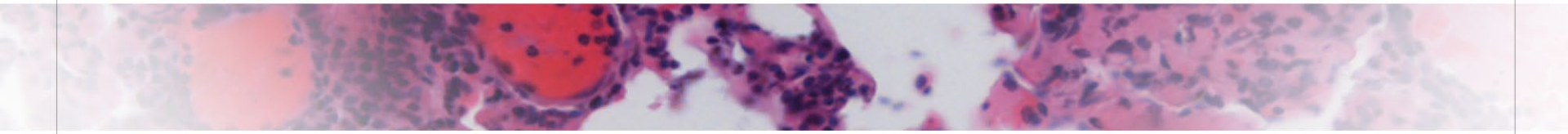

Promising Results from an Ongoing Phase I Multicenter Study of SENTI-202, a First-In-Class, CD33 AND/OR FLT3 & NOT endomucin (EMCN), Selective Off-the-Shelf Logic Gated CAR NK Cell Therapy in Adults with Relapsed/Refractory Acute Myeloid Leukemia (R/R AML)

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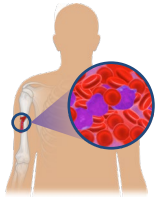
Publication Number: 1044

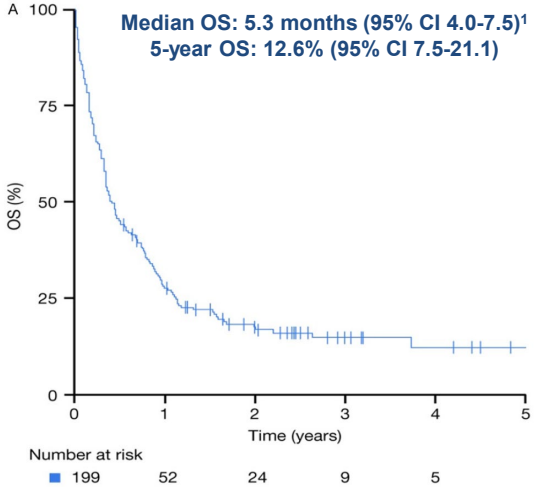
High Unmet Need in Patients with R/R AML even with Recently Approved Therapies

R/R AML Patients have Poor Prognosis



~28k R/R AML patients in US/EU

Current Standard of Care Responses[2,3]:
- CR ~12-25%
- CR/CRh ~20-35%



Effective Anti-AML Therapies Need To

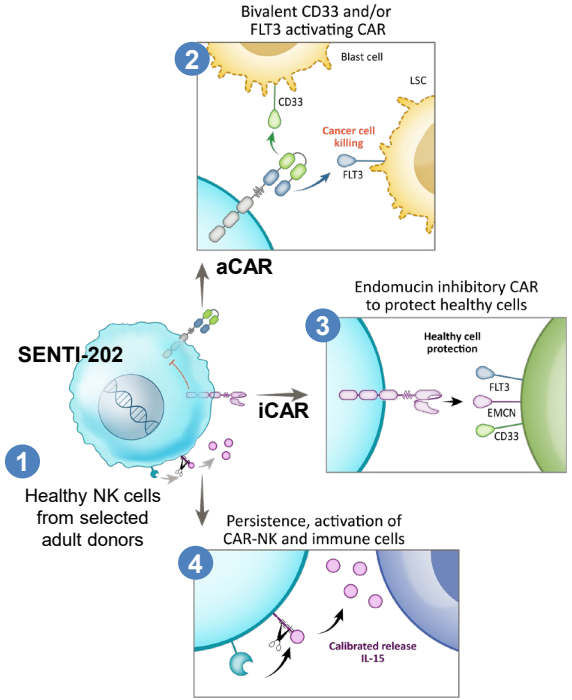
- Target heterogenous clones / LSCs[4]
  - To achieve deep / MRD negative CR
  - Leading to durable remissions / longer survival[3,4]
- Selectively kill AML blasts & LSCs, and spare HSCs
  - To support normal blood cell count recovery
  - Leading to improved prognosis / longer survival[5]

Novel Effective Therapies with Limited On-Target Off-Tumor Toxicities are Urgently Needed

CR: complete remission; CRh: complete remission with partial hematologic recovery; OS: overall survival; MRD: measurable residual disease; HSCs: hematopoietic stem cells; [1]Brandwein AJBR 2020; [2]Dohner Blood 2022; [3]USPI Idhifa, Rezlidhia, Xospata, Tibsovo, Revuforj, Mylotarg; [4]Zeijlemaker Leukemia 2019; [5]Innes Blood 2018

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



1. NK cells have inherent clinical anti-AML activity
2. CD33/FLT3 OR Gated activating CAR ***kills*** AML blasts and LSCs
3. EMCN NOT Gated inhibitory CAR ***protects*** healthy HSC/HSPCs
4. crIL15 ***enhances*** both SENTI-202 and local immune cell activation and expansion

SENTI-202 is designed to:

a) selectively kill both AML blasts and LSCs, and
b) protect healthy HSC/HSPCs;

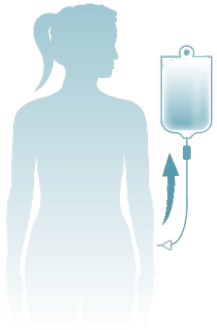
using its novel CD33 OR FLT3 NOT EMCN logic gated gene circuit

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

SENTI-202 is an Off-the-Shelf Allogeneic CAR-NK Cell Therapy Available On Demand

Scalable ~14 Day Manufacturing Process

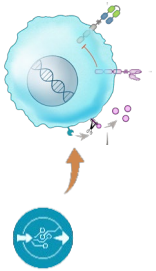
1 **Isolate from selected donors**



Selected Donor

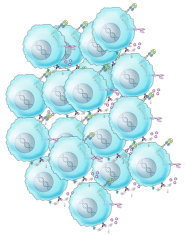
NK Cells

2 **Engineer**



Single transduction step delivers the full Gene Circuit

3 **Expand**



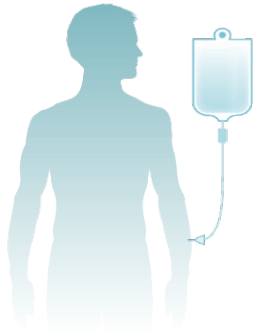
SENTI-202

4 **Cryopreserve**

Final product harvested and cryopreserved

SENTI-202

1 **Thaw and infuse**



Patient

NK cells isolated from peripheral blood of selected adult donors

NK cells efficiently engineered with Gene Circuit

High post-thaw potency

Easy to thaw vials

Outpatient use potential

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

"3 + 3"

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

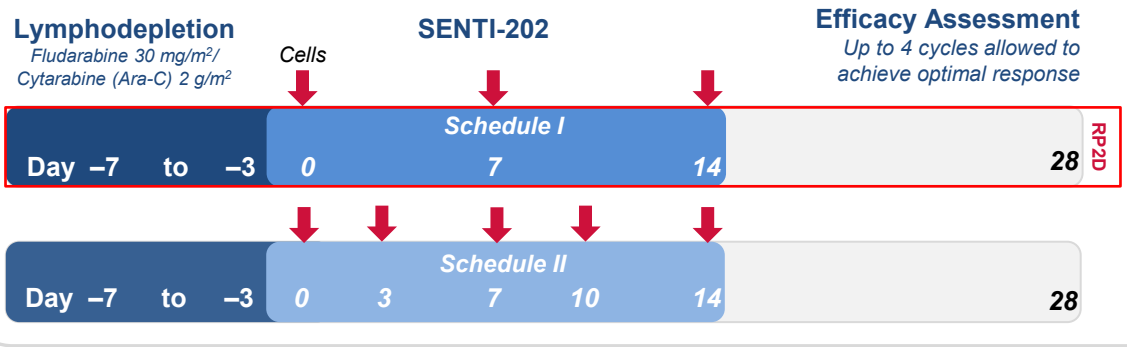
- Measurable residual disease assessed locally
- Pharmacokinetics
- Pharmacodynamics using CyTOF on serial BM samples

*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

Study Treatment Dosing and SENTI-202 RP2D Selection

Study Treatment



Dose Finding

Dose Level	1	2 (RP2D)
CAR+ NK Cells/Dose	1×10^9	**1.5×10^9**

9 R/R AML patients (pts) initially enrolled in dose finding

6 pts in Dose Level 1
(3 each in Schedule I and II)

3 pts in Dose Level 2
(all 3 in Schedule I)

Preliminary RP2D determined to be Dose Level 2, Schedule I based on:

- No DLTs/ SENTI-202 related SAEs in any patient/ any dose level
- Numeric increase in efficacy with
  - Dose Level 2 compared to Dose Level 1 with ORR of 67% (2/3) vs 50% (3/6)
  - Schedule I compared to Schedule II with ORR of 67% (4/6) vs 33% (1/3)

R/R AML expansion cohort opened after:

- RP2D confirmed as Dose Level 2, Schedule 1 with 3 additional R/R AML patients with no DLTs and continued efficacy

Here we present clinical data from 20 R/R AML patients, including 14 at RP2D and 6 at Dose Level 1

RP2D: recommended Phase 2 dose ; DLTs: dose limiting toxicities; ORR: overall response rate; SAEs: treatment emergent serious adverse events

Study Enrolled R/R AML Patients with Multiple Baseline Adverse-risk Characteristics and Poor Prognosis

	Dose Level 1	Dose Level 2/ RP2D	
Baseline Characteristics	**1 x 10^9 CAR+ NK cells/ dose N=6**	**1.5 x 10^9 CAR+ NK cells/ dose N=14**	**All Patients N=20**
Age, yr, median (range)	52.5 (26, 72)	**49 (19, 69)**	49 (19, 72)
Male, n (%)	3 (50)	**7 (50)**	10 (50)
Race, White/ Other, n (%)	5 (83) / 1 (17)	**11 (79) / 3 (21)**	16 (80) / 4 (20)
ECOG PS 0-1, n (%)	5 (83)	**13 (93)**	18 (90)
Adverse risk by ELN 2022 at diagnosis, n (%)	5 (83)	**8 (57)**	13 (65)
Baseline bone marrow blasts, %, median (range)	21.5 (15.1, 69)	**45.2 (6, 92.5)**	35 (6, 93)
Mutational Status at baseline			
FLT3: ITD/ TKD/ Type Unk mutated, n (%)	0 / 0 / 1 (17)	**3 (21) / 0 / 0**	3 (15) / 0 / 1 (5)
IDH1/ IDH2 mutated, n (%)	0 / 0	**0 / 1 (7)**	0 / 1 (5)
Baseline absolute neutrophil count < 1 x 10^9/L, n(%)	1 (17)	**12 (86)**	13 (65)
Baseline platelet count < 50 x 10^9/L, n(%)	2 (33)	**11 (79)**	13 (65)

- Majority of patients had AML with adverse risk genetics by ELN 2022 criteria
- RP2D cohort enrolled patients with increased baseline blasts and more patients with baseline thrombocytopenia/ neutropenia

ECOG PS: European Cooperative Oncology Group performance status; ELN: European LeukemiaNet; Dose Level 1 patients include 3 each dosed in Schedule I and Schedule II, Dose Level 2 patients were all dosed in Schedule I. Data from an open clinical database of an ongoing study as of 17-Oct-2025

Heavily Pretreated R/R AML Population Including Many Primary Refractory & Refractory to Most Recent Line of Therapy before Study Entry

	Dose Level 1	Dose Level 2/ RP2D	
Prior AML Treatments	**1 x 10^9 CAR+ NK cells/ dose N=6**	**1.5 x 10^9 CAR+ NK cells/ dose N=14**	**All Patients N=20**
Years from AML diagnosis to study entry, median (range)	0.6 (0.3, 6.1)	**0.85 (0.2, 8.6)**	0.75 (0.2, 8.6)
Number of prior lines, median (range)	1 (1,2)	**2 (1,3)**	2 (1, 3)
Chemotherapy, n (%)	6 (100)	**14 (100)**	20 (100)
Fludarabine and/or Cytarabine, n (%)	6 (100)	**14 (100)**	20 (100)
Cytarabine (Ara-C), n (%)	6 (100)	**14 (100)**	20 (100)
Fludarabine (Flu) , n (%)	2 (33)	**5 (36)**	7 (35)
Anthracycline, n (%)	5 (83)	**11 (79)**	16 (80)
Venetoclax, n (%)	4 (67)	**13 (93)**	17 (85)
Hypomethylating Agents, n (%)	4 (67)	**11 (79)**	15 (75)
FLT3/IDH targeted therapy, n (%)	2 (33)/ 0	**3 (21)/ 1 (7)**	5 (25)/1 (5)
Prior HCT, n (%)	1 (17)	**6 (43)**	7 (35)
Refractory to most recent regimen, n (%)	1 (17)	**11 (79)**	12 (60)
Primary refractory*, n (%)	3 (50)	**8 (57)**	11 (55)
Refractory to Flu and/or Ara-C containing regimen, n (%)	3 (50)	**8 (57)**	11 (55)

- All patients were exposed to chemotherapy
- Most patients were exposed to anthracycline, venetoclax & hypomethylating agents
- RP2D cohort enrolled patients who were more heavily pre-treated, more prior HCT and more patients refractory to most recent regimen before SENTI-202 compared to Dose Level 1

*Primary refractory defined as failure to achieve complete remission +/- count recovery lasting <3 mo with front-line therapy. Dose Level 1 patients include 3 each dosed in Schedule I and Schedule II, Dose Level 2 patients were all dosed in Schedule I. Data from an open clinical database of an ongoing study as of 17-Oct-2025

Patients Received a Median of 1 Cycle on Treatment Overall and None Discontinued due to an Adverse Event

	Dose Level 1	Dose Level 2/ RP2D	
Exposure	**1 x 10^9 CAR+ NK cells/ dose N=6**	**1.5 x 10^9 CAR+ NK cells/ dose N=14**	**All Patients N=20**
Number of SENTI-202 treatment cycles, n (%)			
1 Cycle	2 (33)	**12 (86)**	14 (70)
2 Cycles	4 (67)	**2 (14)**	6 (30)
Number of SENTI-202 Cycles, median (range)	2 (1,2)	**1 (1,2)**	1 (1, 2)
Subjects continuing treatment as of data-cut, n (%)	0	**4 (29)**	4 (20)
Subjects discontinuing treatment, n (%)	6 (100)	**10 (71)**	16 (80)
Adverse Event	0	**0**	0

- In general, RP2D patients achieved a response with 1 Cycle and received a median of 1 Cycle of SENTI-202 compared to Dose Level 1 patients who received a median of 2 Cycles

CR: complete remission, CRh :CR with partial hematologic recovery; MLFS: morphologic leukemia- free state. Dose Level 1 patients include 3 each dosed in Schedule I and Schedule II, Dose Level 2 patients were all dosed in Schedule I. Data from an open clinical database of an ongoing study as of 17-Oct-2025

Any Grade 3+ Treatment Emergent Adverse Events (AE) or Serious Adverse Events (SAE) On Study, Regardless of Relationship to SENTI-202

Event Term	Dose Level 1: 1×10^9 CAR+ NK cells/ dose N=6	Dose Level 2/ RP2D: 1.5×10^9 CAR+ NK cells/ dose N=14	All Patients N=20
Any ≥ Grade 3 AE, n (%) *regardless of relationship**	6 (100)	**12 (86)**	18 (90)
Febrile Neutropenia	2 (33)	**7 (50)**	9 (45)
Platelet Count Decreased	2 (33)	**2 (14)**	4 (20)
Anemia	2 (33)	**1 (7)**	3 (15)
Thrombocytopenia	1 (17)	**2 (14)**	3 (15)
Pneumonia	0	**3 (21)**	3 (15)
Abdominal Pain	3 (50)	**0**	3 (15)
Hypokalemia	0	**2 (14)**	2 (10)
Hypoxia	1 (17)	**1 (7)**	2 (10)
Sepsis	0	**2 (14)**	2 (10)

**All events are unrelated to SENTI-202 as assessed by the Investigator except for 1 patient with events of both Grade 3 febrile neutropenia and Grade 4 platelet count decreased*

Event Term	Dose Level 1: 1×10^9 CAR+ NK cells/ dose N=6	Dose Level 2/ RP2D: 1.5×10^9 CAR+ NK cells/ dose N=14	All Patients N=20
Any Grade SAE, n (%) *regardless of relationship**	2 (33)	**5 (36)**	7 (35)
Pneumonia	0	**2 (14)**	2^ (10)
Sepsis	0	**2 (14)**	2^ (10)

**All events are unrelated to SENTI-202 as assessed by the Investigator, ^1 patient experienced both events*

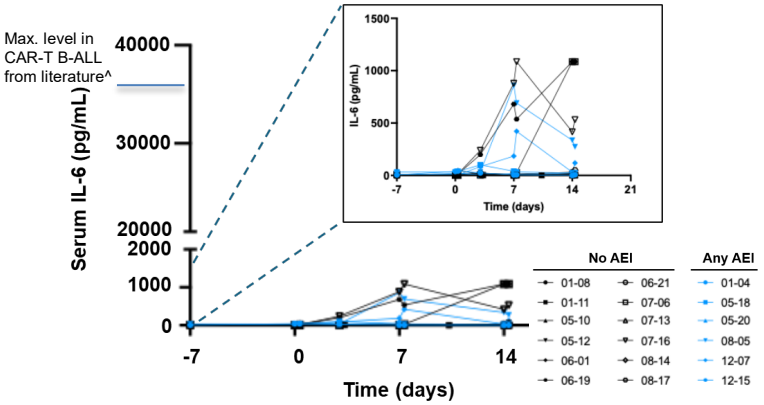
- Grade 3+ AEs or SAEs of any Grade in ≥10% of patients are predominantly hematologic events or pneumonia/sepsis in the setting of neutropenia and consistent with effects of LD chemotherapy in patients with R/R AML
- Hematologic events generally resolved rapidly in patients achieving CR/CRh with SENTI-202

Treatment emergent adverse events includes events with onset after SENTI-202 dosing and within 30 days of last dose of study treatment regardless of relationship, and events that are at least possibly related to SENTI-202 with onset date > 30 days after last dose of study treatment. Grading per CTCAE v5.0. Dose Level 1 patients include 3 each dosed in Schedule I and Schedule II, Dose Level 2 patients were all dosed in Schedule I. Data from an open clinical database of an ongoing study as of 17-Oct-2025

SENTI-202 Related AEIs are Predominantly Grade 1/2 Pyrexia Events that are Readily Managed with Standard of Care

Dose	Pt	Event Term	Grade	Onset Day from Most Recent Dose of SENTI-202	Duration of Event	AEI Term	Serious? / Resolution
Dose Level 1 (1×10^9 CAR+ NK cells/ dose)	01-04	Pyrexia Chills	2 1	0	<24 hours	CRS	No / Resolved with Standard of Care
	08-05	Pyrexia Hypotension	1 1	0 3	5 days < 24 hours		
Dose Level 2 /RP2D (1.5×10^9 CAR+ NK cells/ dose)	12-07	Pyrexia Hypoxia	1 2	1	< 24 hours		
	05-18	Pyrexia Pyrexia Hypotension	1 2 2	2 7 7			
	05-20	Pyrexia	2	1			
	12-15	Pyrexia	1	0	< 24 hours	IRR	
	12-22	IRR	1				

AEI: Treatment Emergent Adverse Event of Interest, Pt: Patient ID, CRS: Cytokine Release Syndrome, IRR: Infusion Related Reaction



SENTI-202 related AEIs reported in 7/20 (35%) of patients:

- Grade 1/2 pyrexia +/- chills, hypotension and/or hypoxia
- Majority on day of dosing and resolved rapidly with standard of care
- Reported as CRS or IRR and all events non-serious
- Consistent with delayed infusion related reactions reported with NK cell therapies
- Cytokines, including IL-6, generally not elevated on trial including in patients experiencing any AEI

Grading per ASTCT criteria where applicable; Dose Level 1 patients include 3 each dosed in Schedule I and Schedule II, Dose Level 2 patients were all dosed in Schedule I. * Sample values ULOQ for 2 patients; ^ IL-6 levels referenced from Teachey et al (2016), maximum level observed from adult cohort treated with anti-CD19 CAR-T; Data from an open clinical database of an ongoing study as of 17-Oct-2025

50% of Patients Achieved a Response with SENTI-202 Treatment

Response	Dose Level 1: 1 x 10^9 CAR+ NK cells/ dose N=6	Dose Level 2/ RP2D: 1.5 x 10^9 CAR+ NK cells/ dose N=12	All Patients N=18^
Overall Response Rate (ORR), n (%)	3 (50)	**6 (50)**	9 (50)
CR/CRh rate, n (%)	2 (33)	**5 (42)**	7 (39)
Response Category, n(%)			
CR	2 (33)	**3 (25)**	5 (28)
CRh	0	**2 (17)**	2 (11)
MLFS	1 (17)	**1 (8)**	2 (11)
Negative MRD* Status, n/n (%)			
in CR patients	2/2 (100)	**3/3 (100)**	5/5 (100)
in CR/CRh patients	2/2 (100)	**4/5 (80)**	6/7 (86)
in CR/CRh/MLFS patients	2/3 (67)	**5/6 (83)**	7/9 (78)
Median Time to Response (min, max), mo	1.2 (1.1,1.2)	**1.2 (1.0,1.3)**	1.2 (1.0, 1.3)
Median Duration of Follow-Up (min, max) mo	8.0 (3.6, 17.5)	**3.1 (0.9, 9.1)**	4.8 (0.9, 17.5)

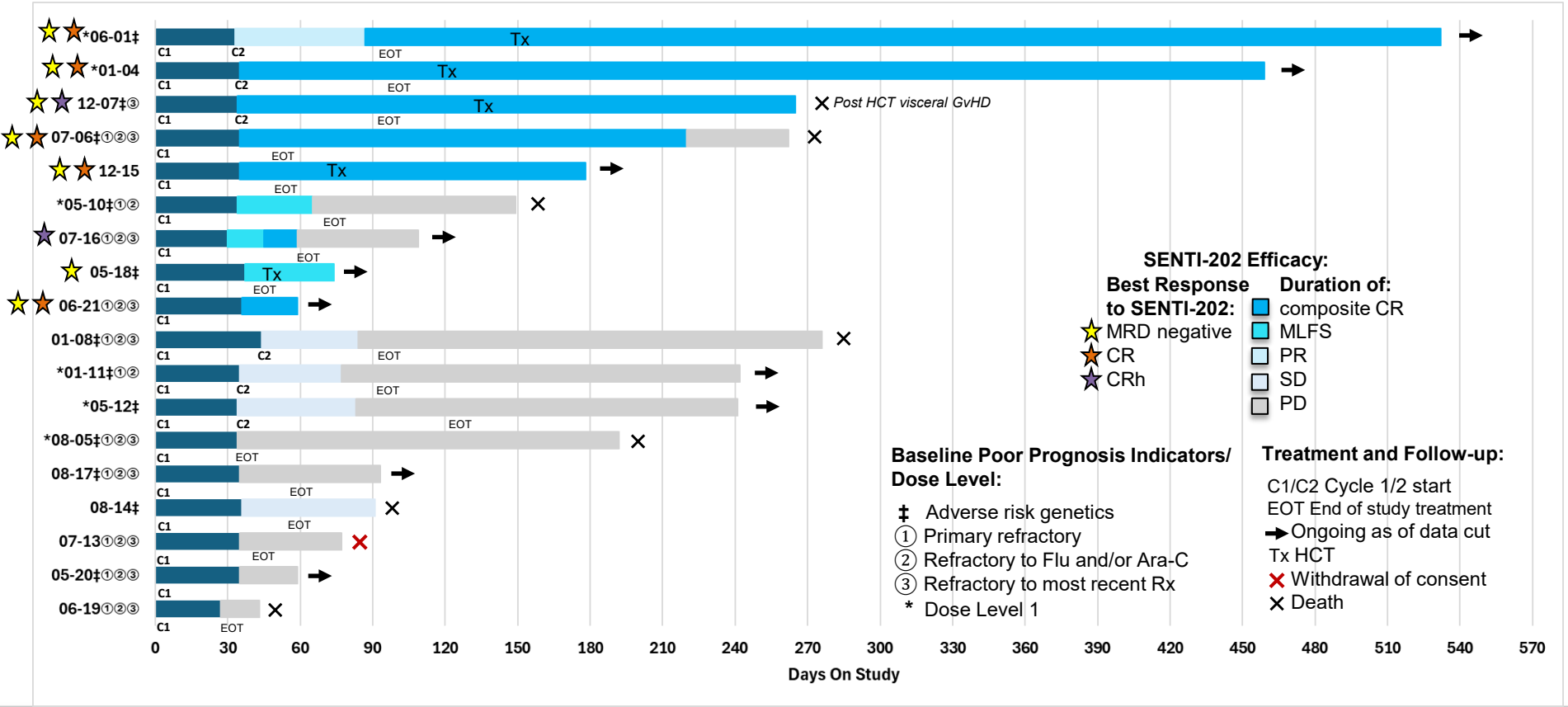
^2 patients early in Cycle 1 and too early to evaluate response as of data cut-off date; *MRD assessed by multi-parametric flow (sensitivity ≤10^{-4}) in all patients except one (assessed by NGS, sensitivity ≤10^{-2})

50% of patients at RP2D and overall achieved a response

- 42% of patients at RP2D and 39% overall achieved a CR/CRh
- All CRs and ~80+% of all responses are MRD negative
- With limited follow up in RP2D cohort, current Kaplan-Meier estimate of median duration of composite CR across all patients:
  - 7.6 months (25th and 75th percentile being 6.1, NE)

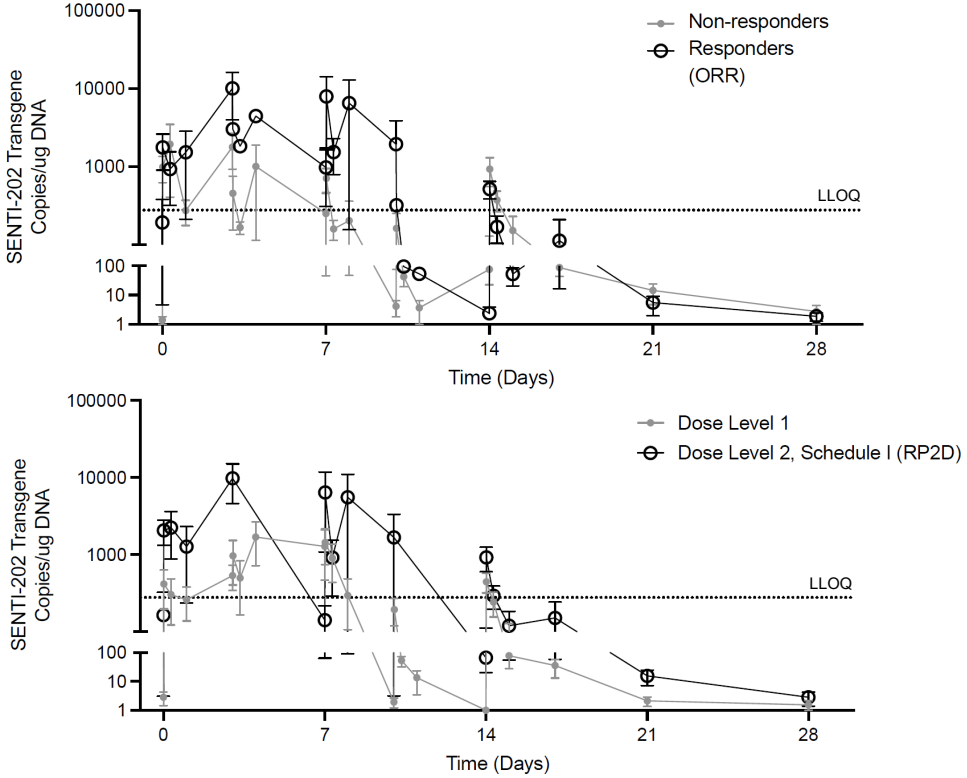
CR: complete remission, CRh :CR with partial hematologic recovery; MLFS: morphologic leukemia- free state; MRD: measurable residual disease; NGS; next-generation sequencing; composite CR includes CR/ CRh and CR with incomplete hematologic recovery; NE: not estimated. Dose Level 1 patients include 3 each dosed in Schedule I and Schedule II, Dose Level 2 patients were all dosed in Schedule I. Data from an open clinical database of an ongoing study as of 17-Oct-2025

SENTI-202 Responses are Durable with Longest Durability > 1 year



CR: complete remission, CRh :CR with partial hematologic recovery; MLFS: morphologic leukemia- free state; PR: partial remission; SD: stable disease; PD; progressive disease. MRD: measurable residual disease assessed by multi-parametric flow (sensitivity $\leq 10^{-4}$) in all patients except one (assessed by NGS, sensitivity $\leq 10^{-2}$); composite CR includes CR/ CRh and CR with incomplete hematologic recovery; HCT: hematopoietic stem cell transplant; GvHD: graft versus host disease. Pt 07-06 had detectable IDH2 mutation by NGS ~3.5 months prior to morphologic relapse and started on venetoclax/enasidenib. Data from an open clinical database of an ongoing study as of 17-Oct-2025

SENTI-202 Peripheral Blood Exposure is Generally Consistent Across All Dosed Patients



- SENTI-202 is detected in periphery of treated subjects, with PK profile consistent with allogeneic NK cell therapies
  - Peripheral expansion in the first 14 days
  - Clearance from periphery after the first two weeks
- Patients who responded (ORR) had a preliminary trend* to increased SENTI-202 exposure compared to non-responders
- Preliminary trend* to dose dependent increased SENTI-202 exposure with increased dose level

**statistically not-significant*

PK: pharmacokinetics; ORR: overall response. Value of 1 assigned for timepoints with non-measurable transgene, LLOQ estimated using equivalent DNA loading and is the lower limit of quantitation; Note: Subject 1 Cycle 1 samples were processed out of stability window and are excluded from analysis of PK parameters Dose Level 1 patients include 3 each dosed in Schedule I and Schedule II, Dose Level 2 patients were all dosed in Schedule I. Interim PK data as of 17-Oct-2025

SENTI-202 is Well-Tolerated in a Heavily Pretreated R/R AML Population, with Future Out-Patient Dosing Potential

- SENTI-202 is a First-In-Class Off-the-Shelf Logic Gated selective CD33 OR FLT3 NOT EMCN CAR NK cell therapy
  - Designed to selectively kill both AML blasts and LSCs while protecting healthy HSPCs with a novel OR/NOT logic gated gene circuit
  - Potential to readily combine with standard of care agents in earlier lines of treatment based on novel mechanism of action and differentiated safety profile
- SENTI-202-101 trial has enrolled heavily pretreated R/R AML patients with poor prognosis
  - Dose finding is complete with no DLTs/ MTD and RP2D confirmed
  - Dose expansion is ongoing at RP2D of 1.5 x 10^9 CAR+ NK cells/ dose X 3 weekly doses/ 28 days
- SENTI-202 is well tolerated with out-patient dosing potential
  - Most frequent Grade 3+ AEs were predominantly hematologic, unrelated to SENTI-202 and consistent with events observed in R/R AML patients receiving LD
  - No SENTI-202 related SAEs/ Dose Limiting Toxicities/ AEs resulting in discontinuation
  - Most frequent SENTI-202 related AEIs: Grade 1/2 pyrexia that resolves rapidly with standard of care

SENTI-202 Achieved a High Rate of Deep, Durable, MRD-Negative Responses

- SENTI-202 demonstrates promising preliminary efficacy
  - 50% of patients at RP2D and 50% of patients overall achieved an ORR
  - 42% of patients at RP2D and 39% of patients overall achieved CR/CRh
  - Estimated median duration of composite complete remission across all patients of 7.6 months (6.1, NE)
  - 100% CR and ~80+% of all responses are MRD negative
- SENTI-202 peripheral PK consistent with allogeneic CAR NK cell therapy profiles
  - Preliminary trend to dose dependent increased exposure observed at RP2D and in patients achieving an ORR

SENTI-202 dose expansion is ongoing to further evaluate efficacy and safety in patients with R/R AML

Also at ASH…

Correlative Data from an Ongoing Phase 1, Multicenter Study of SENTI-202, a First-in-Class, CD33 OR FLT3 & NOT Endomucin (EMCN), Selective Off-the-Shelf CAR NK Cell Therapy for Acute Myeloid Leukemia (AML) is Consistent with SENTI-202's Clinical Activity and Unique Logic Gated Mechanism of Action

- Session Name: 704. Cellular Immunotherapies: Early Phase Clinical Trials and Toxicities: Poster III
  Session Date: **Today, December 8, 2025**
  Session Time: **6:00 PM - 8:00 PM**
  Presentation Time: 6:00 PM - 8:00 PM
  Room: OCCC - West Halls B3-B4

Acknowledgements

- **We deeply appreciate our Patients and their caregivers**
- **Clinical and research staff at all participating Institutions**
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    - Colorado Blood Cancer Institute, Denver CO
    - Methodist Physician Practices, PLLC, San Antonio
    - The University of Texas M.D. Anderson Cancer Center, Houston, TX
    - UCLA Department of Medicine, Los Angeles, CA
  - **Australia:**
    - Peter MacCallum Cancer Center, Melbourne, Australia
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