Novità dal Meeting della Società Americana di Ematologia

Torino
Centro Congressi Lingotto
19-21 febbraio 2026

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Anticorpi monoclonali e CAR-T

*Dipartimento di Oncologia-Ematologia Università degli Studi di Milano
e Azienda Socio Sanitaria Territoriale Papa Giovanni XXIII, Bergamo*

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DICHIARAZIONE Federico Lussana

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
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Agenda

- **Acute lymphoblastic leukemia**
  - Abstract N 443: CAR-T in Ph- ALL in CR1: phase 1 study. *Aldoss I et al.*
  - Abstract N 442: Single CAR-T in Ph+ALL as first consolidation: phase 2 study. *Runxia G et al.*
  - Abstract N 732: Role of alloHSCT pre or post CAR-T brexucel in the real world. *Logan A et al.*

- **Acute myeloblastic leukemia**
  - Abstract N 1044: CAR-NK SENTI-202 in relapsed/refractory AML. *Farhadfar N. et al.*
  - Abstract 816: CD7-targeted universal CAR T cells in R/R CD7$^+$ AML *Yong-Xian H et al.*

Dismal Outcomes Among Older Adults With Ph- ALL Receiving Chemotherapy-Based Therapy

Study	No. of Patients	TKI	Median Age (years; range)	CR Rate (%)	IM Rate (%)	OS	Response, EFS, or DFS
Studies including both Ph-positive and Ph-negative ALL							
HyperCVAD[2]	122	NR	≥ 60	84	10	20% at 5 years	NR
MRC UKALL XII/ECOG E2993[3]	100	None	56 (55-65)	73	18	21% at 5 years	5-year EFS, 19%
Modified DFCI[19]	30	Imatinib	58 (51-72)	67	13	52% at 2 years	2-year DFS, 52%
Ph-negative ALL studies							
CALGB 9111[4]	41	None	≥ 60	77	17	17% at 3 years	3-year DFS, 19%
GMALL[6]	268	NA	67 (55-85)	76	18	23% at 5 years	5-year CCR, 32%
EWALL[7]	59	NA	65 (61-83)	76	7	24% at 3 years	3-year DFS, 19%
PETHEMA ALL-96[17]	33	NA	65 (56-77)	58	36	39% at 2 years	2-year DFS, 46%
GRAALL-SA1[34]	60	NA	66 (55-80)	82	8	24% and 35% at 2 years	2-year EFS, 24% and 35%
PETHEMA ALL-OLD07[20]	56	NA	66 (56-79)	74	11	Median, 12.4 months	Median DFS, 8 months

- Poor tolerability
- Disease biology
- Co-morbidities, poly-pharmacy, & psychosocial support

Aldoss et al. J Oncol Pract. 2019

City of Hope.

CD19 CAR T Cells as Definitive Consolidation Therapy in Older Adult
NCT05707273
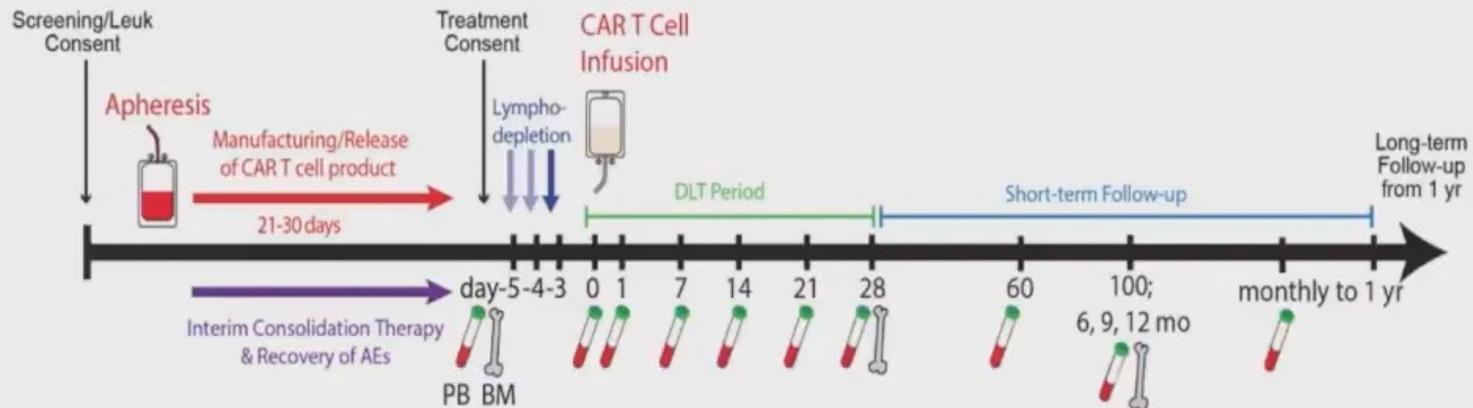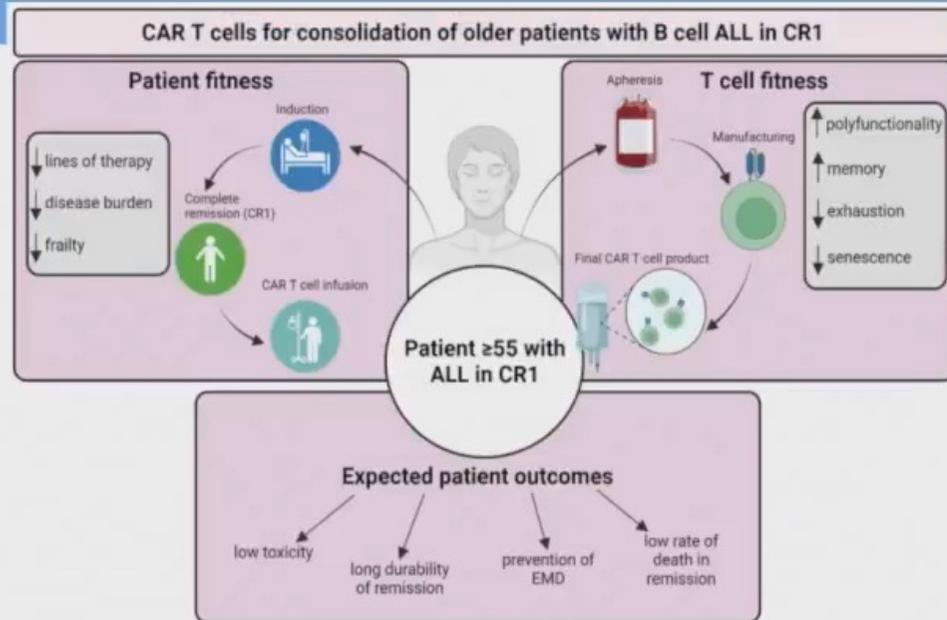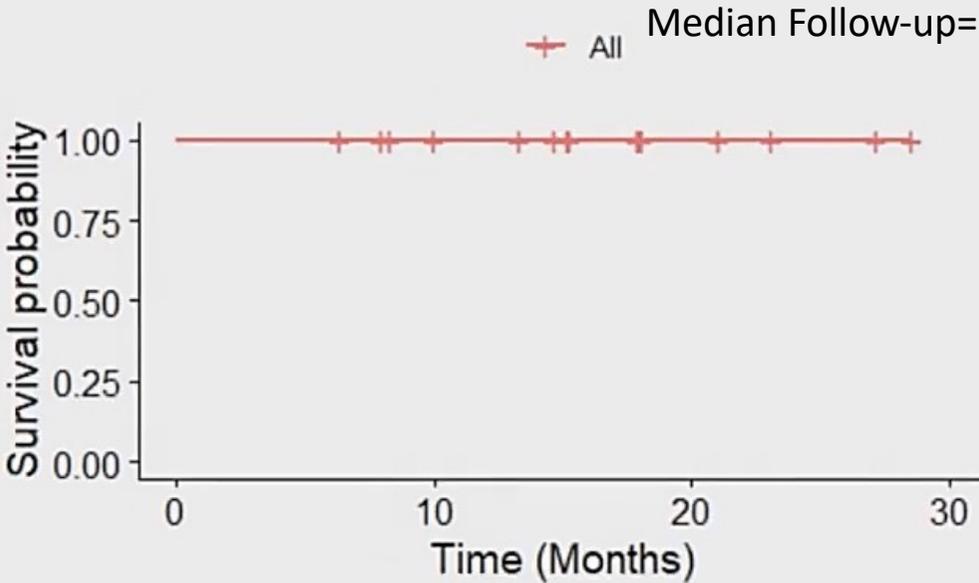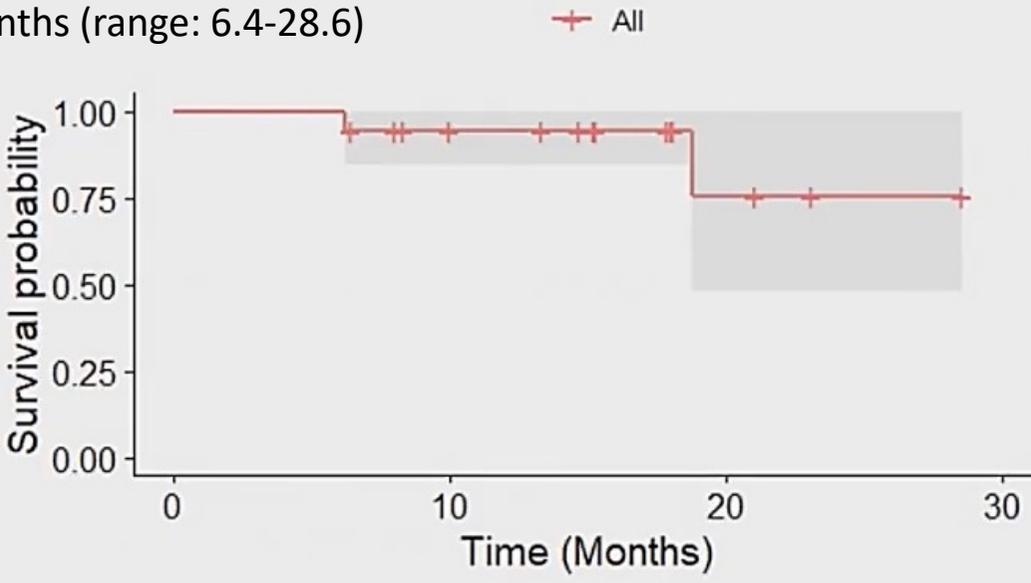
CAR T Cells Demonstrate Sufficient Expansion in the Low-Antigen Setting (MRD-)
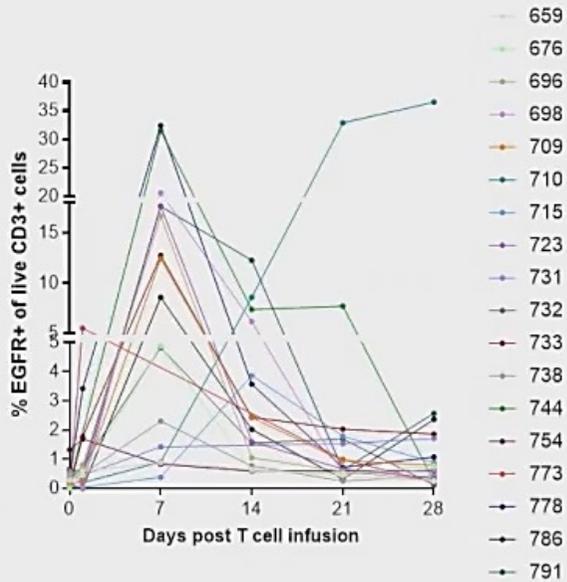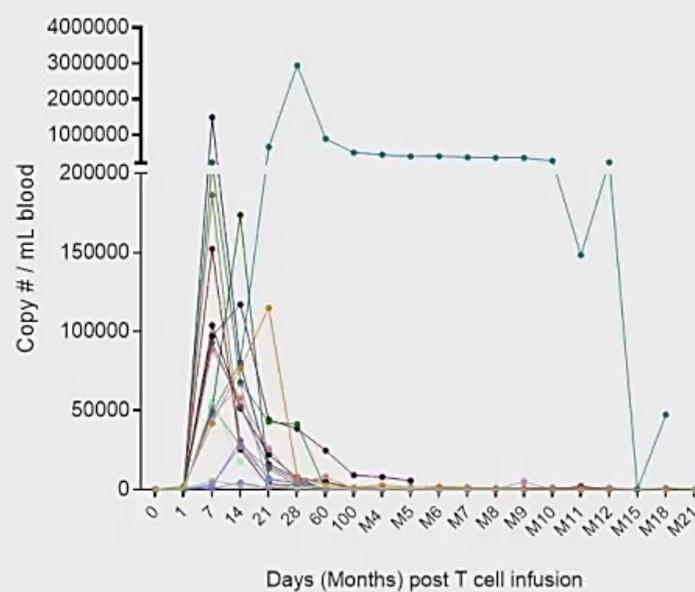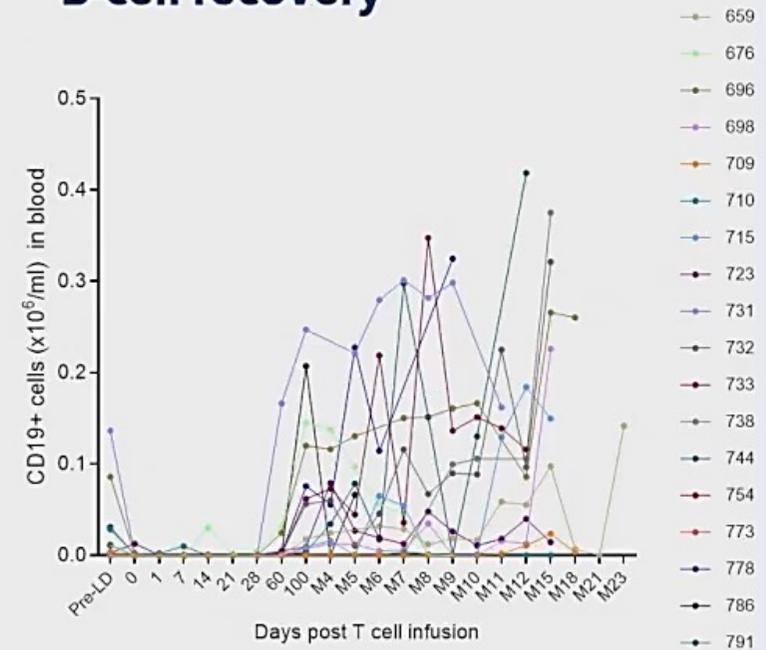
No ICANS or grade ≥2 CRS
A confirmatory multicenter study with Obe-Cel is planned in patients > 40 years

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Single CAR-T infusion during frontline consolidation in Ph+ ALL: a prospective phase 2 study

- Frontline treatment with immunotherapy and TKIs has proven highly effective

- Relapse remains a persistent clinical challenge, especially in patients with IKFZ1 plus genotype or high WBC counts

- More than half of these relapses occur at extramedullary sites

Treatment Schema

Institute of Hematology & Blood Diseases Hospital
Chinese Academy of Medical Sciences
Peking Union Medical College

Induction → Consolidation → Maintenance

VOVP | VOVP/OVP | CAR-T | Maintenance

Venetoclax 100 mg D1, 200mg D2, 400mg D3-28
Olverembatinib 40 mg QOD D1-28
VCR | VCR | VCR | VCR
Prednisone 60 mg/m² D1-14; 40 mg/m² D15-28

CAR-T Infusion :
A single infusion of murine-derived 2nd CD19-directed CAR T-cells (with a 4-1BB co-stimulatory domain, dose : 1-2 × 10^6 cells/Kg) during first CR

Maintenance therapy:
olverembatinib at a dose of 30 mg on alternate days, in combination with the MM regimen on a monthly basis, alternating with the VPV regimen

Prophylactic triple intrathecal injections were performed 11 times to patients who maintained a consistent CR

Runxia G et al . ASH Annual Meeting (67th) • Oral Session 613 • Abstract #442

Baseline Characteristics of patients received CAR-T infusion

Consort Diagram

Assessed for eligiblility (n=47)

3 exclued
- with active cardiovasculer condition (n=2)
- with poorly controlled diabetes (n=1)

Started induction (n=44)

All patients achieved CR, 9 withdrew consent opted for alternative treatment
- Blinatumomab+TKI (n=4)
- allo-transplantation (n=2)
- Chemotherapy (n=3)

Received CAR-T therapy (n=35)
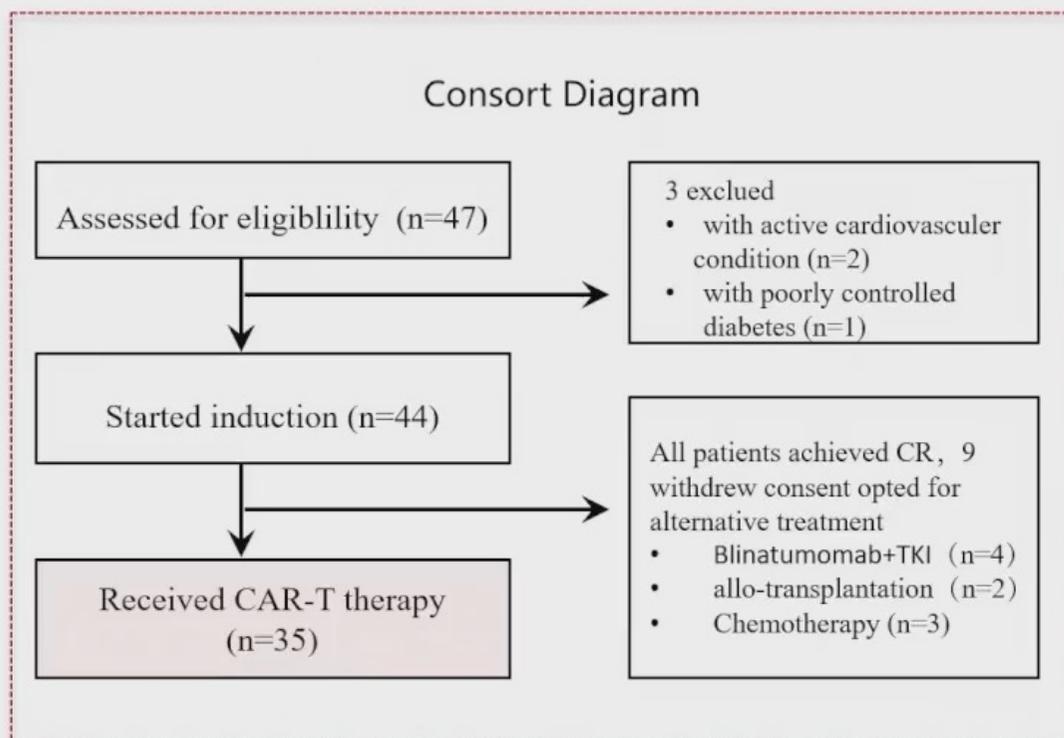
	N(%)/Median[range]
Age (median, range)	39(20-60)
Male	18 (51.4%)
Female	17 (48.6%)
WBC (median, range)	$30\ (1.54\text{-}257)\times 10\ ^9/L$
WBC $> 70\times 10\ ^9/L$	9(25.7%)
BCR-ABL transcript	
P190	31(88.6%)
P210	3(8.6%)
P230	1(2.9%)
IZKF1 plus	8(22.8%)

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Survival rate

- After a median follow-up of 10.9 months, the 1-year estimate LFS rate was 100%

- No severe CRS ≥2 was observed, non ICANS was observed
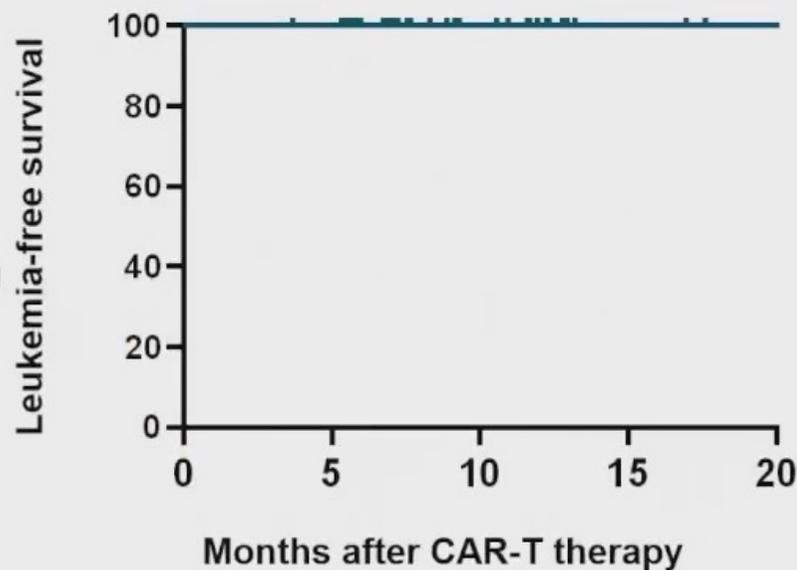
- No patients experienced bone marrow or extramedullary relapse

- Three patients underwent hematopoietic stem cell transplantation during CR1 by personal choice

Runxia G et al . ASH Annual Meeting (67th) • Oral Session 613 • Abstract #442

Role of Allogeneic HCT After Brexu-cel in R/R Ph– B-ALL

Background: The role for consolidative allogeneic HCT remains one of the most important unresolved questions in the use of CAR-T therapy for r/r B-ALL

- Multicenter cohort: 41 US centers (standard-of-care brexu-cel)

- Included: MRD-negative CR after brexu-cel (flow or NGS)

- Groups 165 pts: Never HCT (n=69) | Pre-CAR HCT (n=49) Post-CAR-T HCT (n=47)

- Landmark analysis at day 73 (median time to consolidative HCT)

- Similarly, baseline patient characteristics

ROCCA Real-World

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Key Outcomes: RFS and OS

- Median RFS: 260 days (Never HCT) vs Not reached (Pre-/Post-CAR-T HCT)

- 1-year RFS: 38% (Never) vs 64% (Pre-CAR-T) vs 67% (Post-CAR-T); p=0.002

- Median OS: Not reached in all groups, 1-year OS: 68–79% across groups; p=0.13

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Conclusions

- There is a benefit for relapse-free survival in pts receiving an allogeneic HCT at some point in the course of treatment for R/R Ph neg B-ALL:
    - before CAR-T (donor-derived product context) or after CAR-T (consolidation) may be associated with improved durability/reduced relapse compared with never transplanting

- With the current follow-up, OS was not significantly different

- Supports considering HCT consolidation in appropriate candidates but:
    - the decision should remain individualized, because OS is still immature and transplant eligibility is constrained by patient fitness, comorbidities, and post-CAR-T complications.

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Acute myeloblastic leukemia

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CAR-NK SENTI-202 in relapsed/refractory AML

- SENTI-202 is an on-demand, off-the-shelf allogeneic CAR-NK approach designed to:
  - selectively kill both AML blasts and LSCs
  - protect healthy HSC/HSPCs

OR gate: recognize CD33 and/or FLT3 → intended AML blast/LSC killing

NOT gate: recognize EMCN (healthy-cell antigen) → intended sparing of HSPCs

SENTI-202 Gene Circuit Design
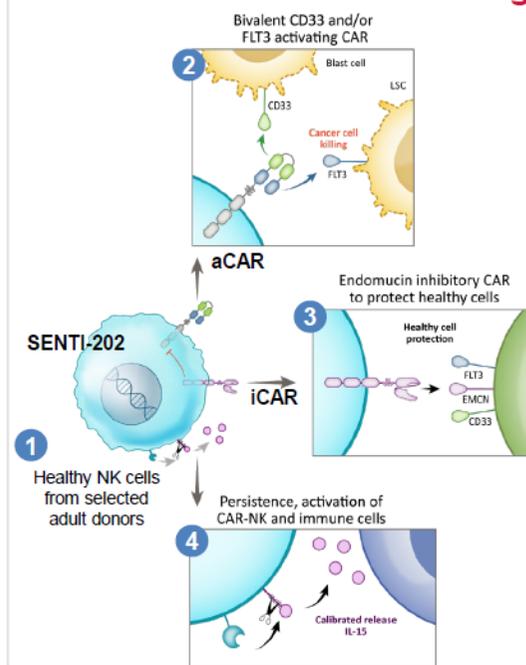
1. NK cells have inherent clinical anti-AML activity
2. CD33/FLT3 OR Gated activating CAR _kills_ AML blasts and LSCs
3. EMCN NOT Gated inhibitory CAR _protects_ healthy HSC/HSPCs
4. crIL15 _enhances_ both SENTI-202 and local immune cell activation and expansion

Farhadfar N. et al ASH Annual Meeting (67th) • Oral Session 704 • Abstract #1044

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Study Design
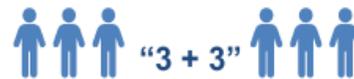

Key Eligibility Criteria

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

- 20 R/R AML treated (6 DL1 (1.0×10^9 CAR+ NK cells); 14 at RP2D (1.5×10^9 CAR+ NK cells)
- Schedule: 3 weekly doses (28-day cycle)

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Results

Safety & tolerability

- G1–2 pyrexia (CRS) on day of cell administration

- IL-6 generally not elevated

- Early toxicity profile appears manageable

Efficacy

- Overall: 9/20 responded (ORR 50%)

- CR/CRh: 7/20 (39%); MLFS 2/20 (10%)

- MRD: 5/5 CR MRD-negative; 6/7 CR/CRh MRD-negative

- Median time to response ~1.2 months

- Median DoR not reached at data cut; some bridged to HSCT

Potential to easily combine this treatment with standard-of-care agents in earlier stages of therapy
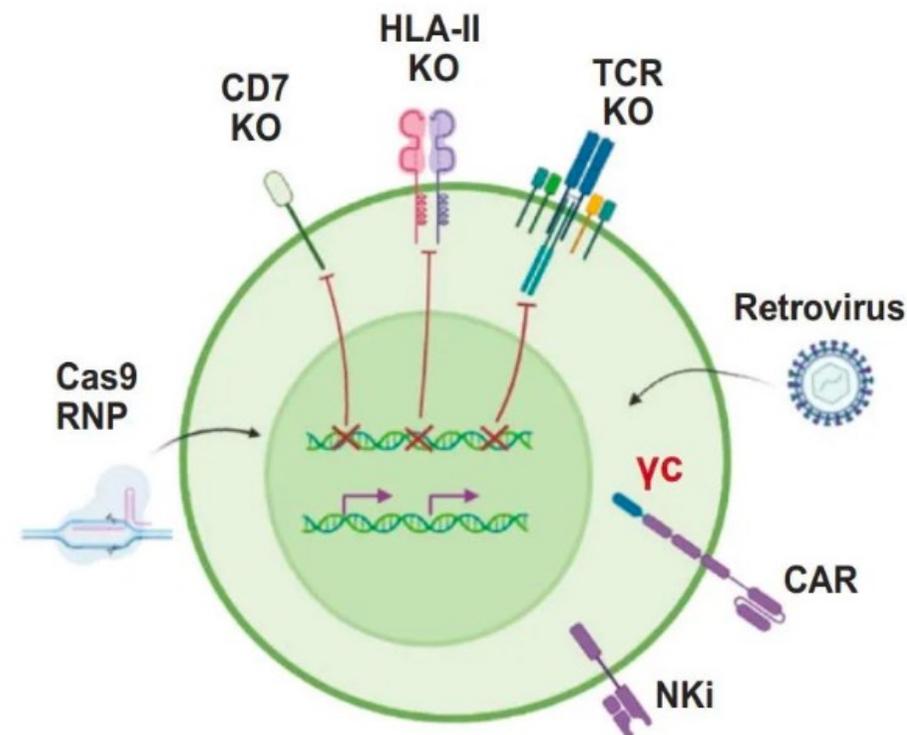
Farhadfar N. et al ASH Annual Meeting (67th) • Oral Session 704 • Abstract #1044

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CD7-targeted universal CAR T cells in R/R CD7+ AML

CD7 biology: aberrant expression on blast/progenitor cells in ~30% of AML; minimal expression on normal myeloid/erythroid lineages → potential therapeutic window.

Therapy concept: "universal" (allogeneic) CD7 CAR-T products CTD401 → optimized CTD402.

Program context: CTD402 described as a multiplex-edited allogeneic anti-CD7 CAR-T designed to reduce fratricide, GvHD, and host rejection.

Yong-Xian Hu et al. ASH Annual Meeting (67th) • Oral Session 704 • Abstract #816

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Study design and patient characteristics

Treatment workflow (single infusion)

| Screen CD7 by flow | → | Lymphodepletion Flu/Cy 3–5d ± etoposide | → | Infuse CAR⁺ T cells 2×10⁸ to 1×10⁹ cells | → | Assess response CR/CRi + MRD |

Baseline characteristics (n=10)

Characteristic	Value
Median age (range)	34.5 y (3.5–67)
Prior therapy lines, median (range)	3 (1–7)
Prior HSCT	2 patients
Median marrow blasts (range)	39% (0.35–83)
Baseline CD7 on blasts	High ≥80%: 8 pts Partial <80%: 2 pts

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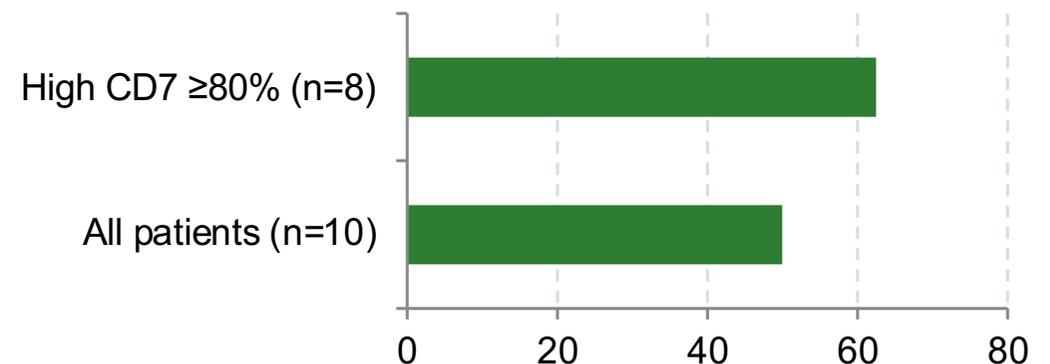Torino, 19-21 Febbraio 2026

Immune effector toxicities
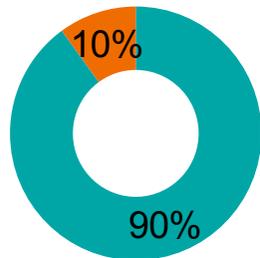
CRS: 100% mild
(G1: 90%, G2: 10%)

Neurotoxicity:

- 1 Grade 2 ICANS

- No dose-limiting toxicities (DLTs)
- No treatment-related deaths
- Most common ≥Grade 3 AEs: cytopenias
  - Thrombocytopenia 40%
  - Neutropenia 30%
  - Leukopenia 30%

Best overall response: CR/CRi

- Best ORR was 50%, increasing to 62.5% (5/8) among high CD7 expression patients
- All responders achieved MRD negativity
- Median duration of response: 10.1 months (0.7–53.6)
- Consolidation after CR/CRi:
  - HSCT in 2 patients
  - Hematopoietic stem cell boost in 3 patients (no preconditioning)

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Abstract on anti-CD7 CAR-T in AML

• **Abstract 816 (Oral, China) CD7-targeted universal CAR T-cell therapy in relapsed or refractory (R/R) acute myeloid leukemia (AML): Clinical results from CTD401/402 studies**

• Abstract 1040 (Oral, China) Interim Phase 1 study of sequential CD7 CAR T-cell therapy and haploidentical HSCT without GVHD prophylaxis in patients with Relapsed/Refractory CD7-positive hematologic malignancies

• Abstract 4161 (Poster, China) Anti-CD7 CAR-T cells in patients with relapsed or refractory CD7+ Acute Myeloid Leukemia: First-in-human phase I study

• Abstract 2540 (Poster, China) CD7 CAR-T cell therapy based on "Natural Selection" for the treatment of Relapsed or Refractory CD7-positive Hematologic Malignancies: A large cohort Study

• Abstract 6946 (Poster, Rome) Fratricide-resistant anti-CD7 CAR-T cells for relapsed/refractory Acute Myeloid Leukemia

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Thank you for your attention