(LB5007) First-in-class Switchable Allogeneic CAR-T therapy for CD123+ AML – Results from the Phase Ia RevSTAR-123 (AVC-201-01) Study

Topic: 26. Gene therapy, cellular immunotherapy and vaccination - Clinical

Martin Wermke*[1], Mojca Jongen-Lavrencic[2], Stephan Metzelder[3], Jörg Westermann[4], Elisa Sala[5], Marion Subklewe[6], Sabrina Kraus[7], Felicitas Thol[8], Arjan Van de Loosdrecht[9], Veit Bücklein[6], Remco Molenaar[9], Jingting Luan[1], Jonas Schäfer[3], Manfred Klevesath[10], Marc Cartellieri[10], Reynald Lescarbeau[11], Johannes Spehr[10], Michael Kramer[10], Matti Vänskä[10]

[1]University Hospital Carl Gustav Carus, Division of Hematology, Oncology and Stem Cell Transplantation, Dresden, Germany; [2]Erasmus University Medical Center, Erasmus MC Cancer Institute, Department of Hematology, Rotterdam, The Netherlands; [3]Philipps University Marburg and University Hospital Giessen and Marburg, Marburg, Germany; [4]Charité University Medicine Berlin, Department of Hematology, Oncology and Tumor Immunology, Berlin, Germany; [5]University Hospital of Ulm, Department of Internal Medicine III, Ulm, Germany; [6]University Hospital, LMU Munich, Medicine III (Hematology / Oncology), München, Germany; [7]University Hospital Würzburg, Department of Internal Medicine II, Würzburg, Germany; [8]Hannover Medical School, Department of Hematology, Hemostasis, Oncology, and Stem Cell Transplantation, Hannover, Germany; [9]Amsterdam UMC, Department of Hematology, Amsterdam, The Netherlands; [10]Avencell Europe GmbH, Dresden, Germany; [11]AvenCell Inc, Boston, United States of America;

Background

Developing CAR-T therapies for AML has been challenging, and presumed T cell dysfunction of heavily pre-treated patients suggests that autologous approaches may not be feasible. CD123 is a potential therapeutic target, overexpressed on leukemic blasts and leukemic stem cells in most AML patients. A key limitation of CD123 targeting is expression on e.g. hematopoietic progenitors. To address on-target/off-tumor toxicities and to eliminate reliance on patient T cells, a switchable CD123-directed allogeneic CAR-T technology was developed, with off-the-shelf availability. We report results from the completed RevSTAR-123 Phase Ia dose escalation.

Aims

To assess safety, incidence of DLTs, and biological and clinical activity.

Methods

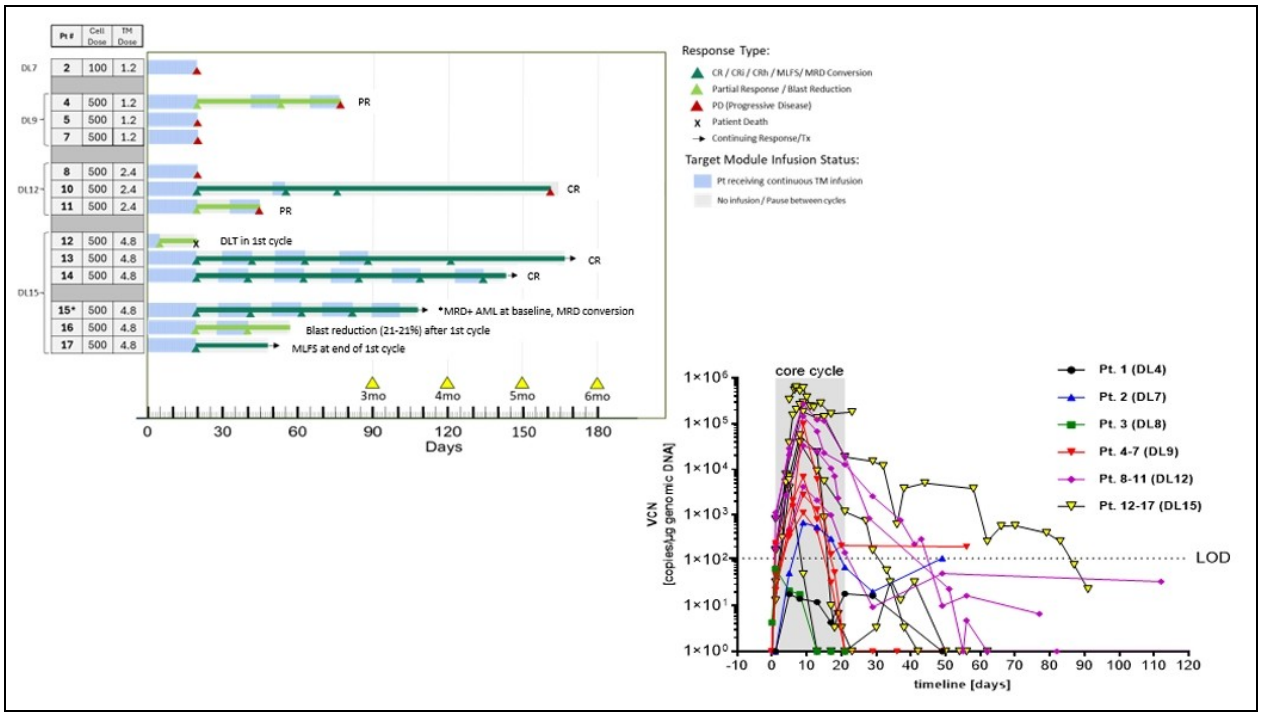
Adults with RR or MRD-positive AML were eligible if they had a CD123 expression on ≥20% of leukemic blasts, no available SoC treatment options, and HLA-B and -C compatibility with the allogeneic CAR-T cell product. *R-TM123* (TM), a bispecific adapter enabling activation against CD123, was delivered as a continuous IV infusion during a 20-day induction cycle and subsequent 12-day consolidation cycles, with 7–14 days between cycles. The initial dose escalation followed a BOIN Comb design (3 *Allo-RevCAR01-T* cell doses; 100, 250, and 500 × 10^6, single infusion) combined with 3 doses of the TM (up to 9 combinations). A second escalation phase explored additional TM doses using a 3+3 design in combination with the 500M cell dose. Lymphodepletion (LD) consisted of Fludarabine (Flu) and Cyclophosphamide (Cy) administered over 3 days.

Results

Phase Ia was completed in April 2026 with 17 pts treated with the induction cycle and 7 completing at least one consolidation cycle. The first 4 pts received LD with Cy 300 mg/m²/day and Flu 30 mg/m²/day; the last 13 received an intensified regimen with Cy 600 mg/m²/day and Flu 30 mg/m²/day. Median age was 63 years (range 41–74, 10 male/7 female), the cohort was heavily pretreated (median 4 prior lines of therapy). One DLT was observed: a Grade 2 IEC-HS (pt #12), successfully managed via on/off switch mechanism, Anakinra, and Dexamethasone. No treatment-related mortality, neurotoxicity, or GvHD were reported. CRS (Grade 1–3) occurred in 12 pts, onset typically on Day 1. Overall, the therapy was well tolerated. CAR-T cell expansion was superior to that observed with other published autologous and allogeneic CAR-Ts in AML, with peak levels exceeding 600,000 VCN copies/µg gDNA. Repeated TM cycles triggered CAR-T reactivation. Deep clinical responses were observed, e.g., among the 6 patients treated at the highest dose (DL15, 500M cells and 4.8mg/day of R-TM123) two morphological CRs with full blood count recovery (#13, #14), one MLFS in TP53-mutated AML (#17), and MRD conversions (#13, #14, #15). Most of these responses are ongoing as of May 2026. Updated data will be presented in the meeting.

Summary/Conclusion

In Phase Ia, this switchable, allogeneic CAR-T showed favorable safety and tolerability without treatment-related mortality or neurotoxicity. TM administration in cycles resulted in best-in-class CAR-T expansion, re-expansion, signs of persistence, and highly promising anti-leukemic activity, including 4/8 CR-level responses (R/R pts) and 3 MRD conversion (1 MRD+, 2 R/R AML pts) at two highest dose levels combined (DL12, DL15). The switchable RevCAR platform allowed rapid CAR-T deactivation when required. RevSTAR-123 has now advanced into Phase Ib, enrolling 20 R/R AML patients at DL15. ClinicalTrials.gov ID: NCT05949125.



Left: Swimlane, clinical responses of evaluable patients (#1, #3, #6, #9 were inevaluable/drop-outs). Right: RevCAR pharmacokinetics summary, expansion and persistence for all dosed patients, per dose level (n=17).