AMELI-01: Phase I, Open Label Dose-escalation and Dose-expansion Study to Evaluate the Safety, Expansion, Persistence and Clinical Activity of UCART123 (Allogeneic Engineered T-cells Expressing Anti-CD123 Chimeric Antigen Receptor), Administered in Patients with Relapsed/Refractory Acute Myeloid Leukemia

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This presentation contains “forward-looking” statements that are based on our management’s current expectations and assumptions and on information currently available to management.

Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from those expressed or implied by the forward-looking statements.

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Further information on risks and factors that may affect company business and financial performance, is included in our annual report on form 20-F and the financial report (including the management report) for the year ended December 31, 2019 and subsequent filings Cellectis makes with the Securities and Exchange Commission from time to time.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.

Disclosures

- Consultancy
  - Agios, Amphivena, Astex, Celgene, Janssen, Novartis, Pfizer, Abbvie, Array Biopharma, Bayer, Celltrion, Eisai, Jazz, Roche/Genentech, Sandoz, Actinium, Argenx, Astellas, Daiichi Sankyo, Orsenix, Otsuka, Takeda, Trovagene, Jasper Therapeutics, Epizyme, Helsinn, MEI Pharma
- Research funding
  - Cellectis

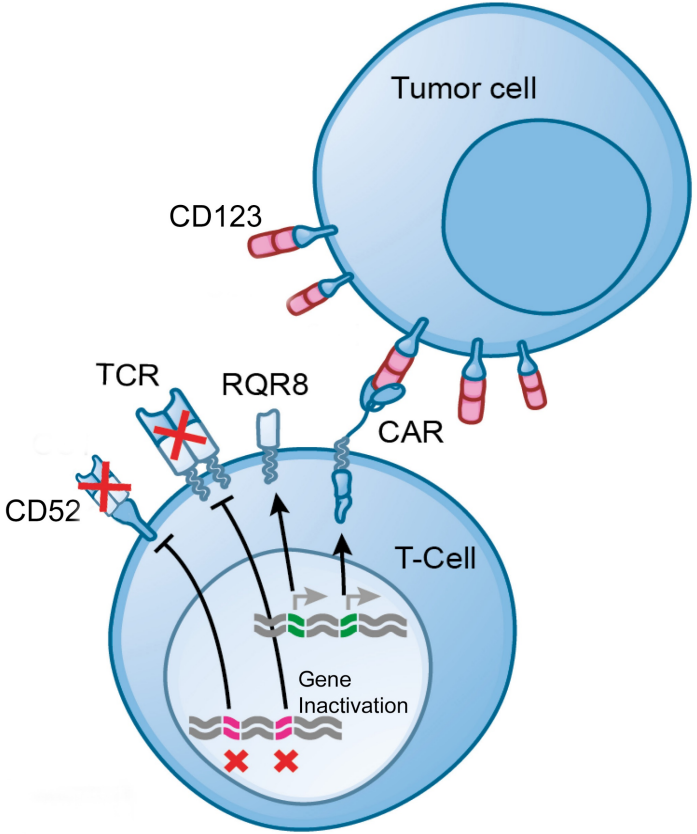
Background

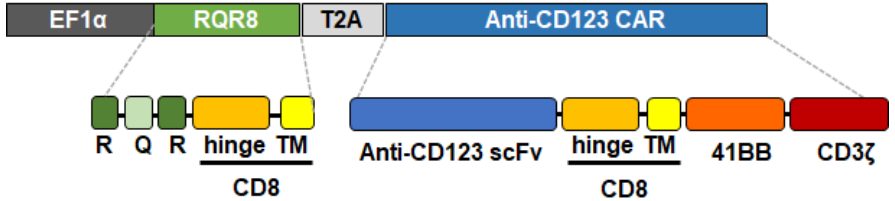
- AML is a clonal hematopoietic stem cell (HSC) neoplasm characterized by uncontrolled proliferation and accumulation of leukemic blasts in BM and peripheral blood[1]
- Despite modest remission rates, most patients with AML will relapse[2-4]
- Prognosis is dismal for patients with relapsed/refractory (R/R) AML,[5] and new therapeutic options are needed
  - Most of the recently approved treatments for R/R AML are targeted agents with activity against mutations present in smaller patient populations (*IDH1/2*, *FLT3*)
- CAR T-cell therapies have shown substantial activity in select hematologic malignancies (B cell lymphoma, ALL) but none are approved for treatment of AML
- Autologous CAR T cells require a complex manufacturing process and healthy patient T-cell population
- The cell surface antigen, CD123 (IL-3Rα) is overexpressed on leukemic (AML) cells
- UCART123 is a genetically modified, allogeneic anti-CD123 CAR T product for R/R AML

1. Döhner et al, *N Engl J Med*. 2015;373(12):1136. 2. Schlenk et al. *Leukemia.* 2017;31:1217. 3. Ramos et al. *J Clin Med.* 2015;4(4):665. 4. Rollig et al. *J Clin Oncol.* 2011;29(20):2758. 5. McMahon et al. *Semin Hematol.* 2019;56(2):102-109.

ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; BM, bone marrow; CAR, chimeric antigen receptor; HPC, hematopoietic progenitor cell; HSC, hematopoietic stem cell; R/R, relapsed refractory.

UCART123: Allogeneic "Off-the-shelf" T Cell Product





R=CD20 mimetope (rituximab)
Q= CD34 epitope (Qben10)

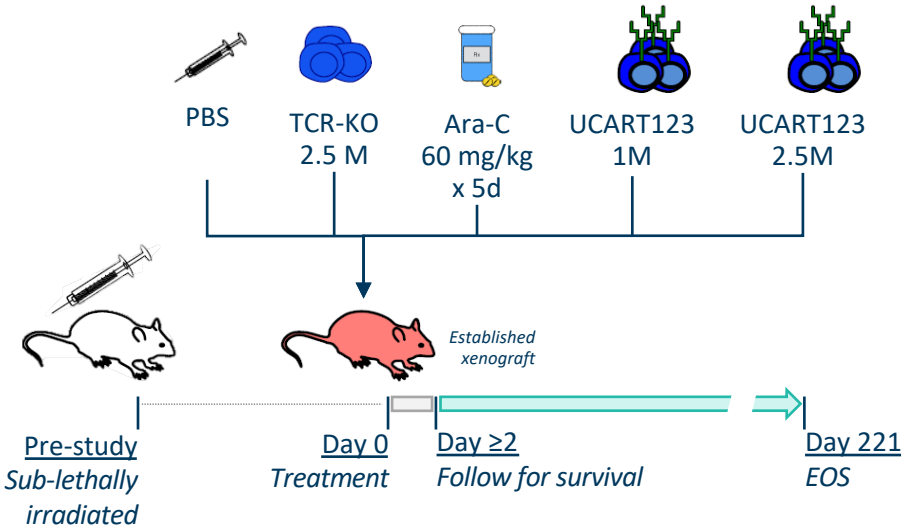
UCART123:

- ✓ Second-generation CAR targeting CD123
- ✓ Mouse-derived scFv
- ✓ Derived from healthy donor T cells
- ✓ Reduces risk of GvHD (TCR K/O and TCRab-purification)
- ✓ CD20 mimotope for rituximab "safety switch"
- ✓ Alemtuzumab resistance (CD52 K/O)
- ✓ Available "off the shelf"
- ✓ Manufactured at large scale

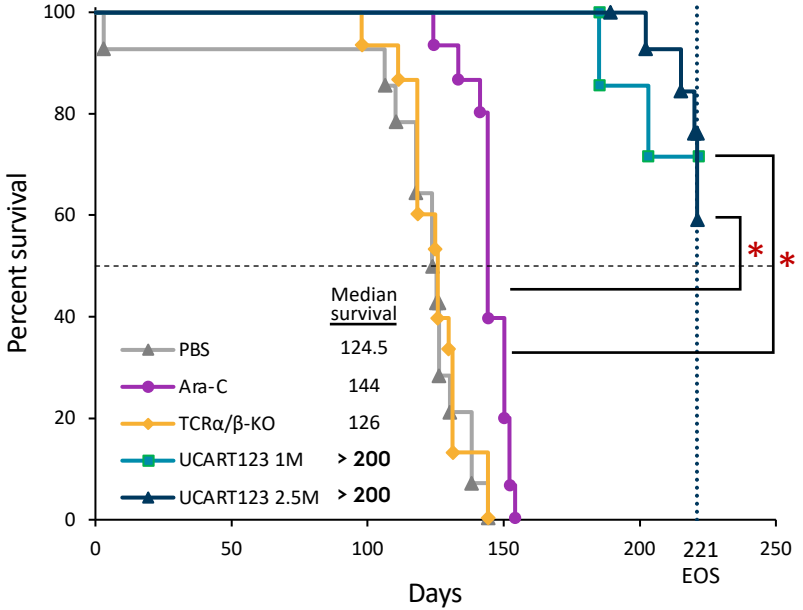
CAR, chimeric antigen receptor; GvHD, graft-versus-host disease; K/O, knock-out; scFv, single-chain variable antibody fragment; TCR, T-cell receptor.

Patient-derived Xenograft Models

UCART123 improves overall survival (OS) in PDX AML models[1]



PDX-AML2 (*NPM1*+/*FLT3*-ITD+) Survival



*$P < 0.0001$.

1. Guzman et al. *Blood.* 2016;128(22):765.

AML, acute myeloid leukemia; Ara-C, cytarabine; EOS, end of study; KO, knockout; OS, overall survival; PBS, phosphate-buffered saline; PDX, patient-derived xenograft; TCR, T-cell receptor.

AMELI-01 Study Design

Phase I, open label, dose-escalation and dose-expansion study of UCART123 in patients with R/R AML

KEY ELIGIBILITY CRITERIA:

Inclusion:

- Age 18–65
- R/R AML with ≥ 5% blasts in BM or PB
- CD123+ blast cells (flow cytometry)
- ECOG PS score ≤1
- Adequate organ function
- *(Dose-escalation)* Identified donor and transplant strategy prior to lymphodepletion (LD)

Exclusion:

- APL or CNS leukemia
- Previous investigational gene or cell therapy (including CAR)
- ≥ 2 prior allogeneic SCTs
- Prior treatment with rituximab or other anti-CD20 therapy within 3 months
- Any known active or uncontrolled infection

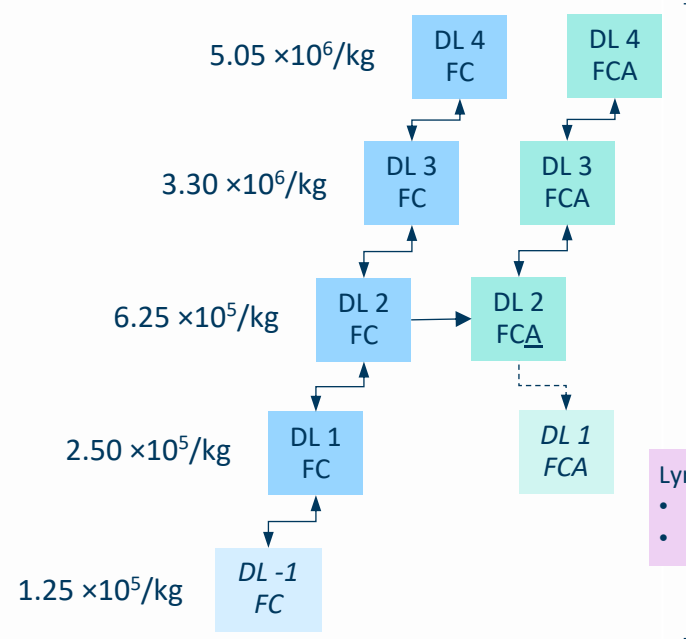
AML, acute myeloid leukemia; APL, acute promyelocytic leukemia; BM, bone marrow; CAR, chimeric antigen receptor; CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance status; PB, peripheral blood; R/R, relapsed/refractory; SCT, stem cell transplant.

Dose-escalation and Dose-expansion

DOSE ESCALATION

Up to 28 Patients • MTPI design • 2–4 patients/cohort

Dose level*



Determine MTD/RP2D

DOSE EXPANSION

18–37 patients • Simon's two-stage design

UCART123 at MTD / RP2D with recommended LD regimen

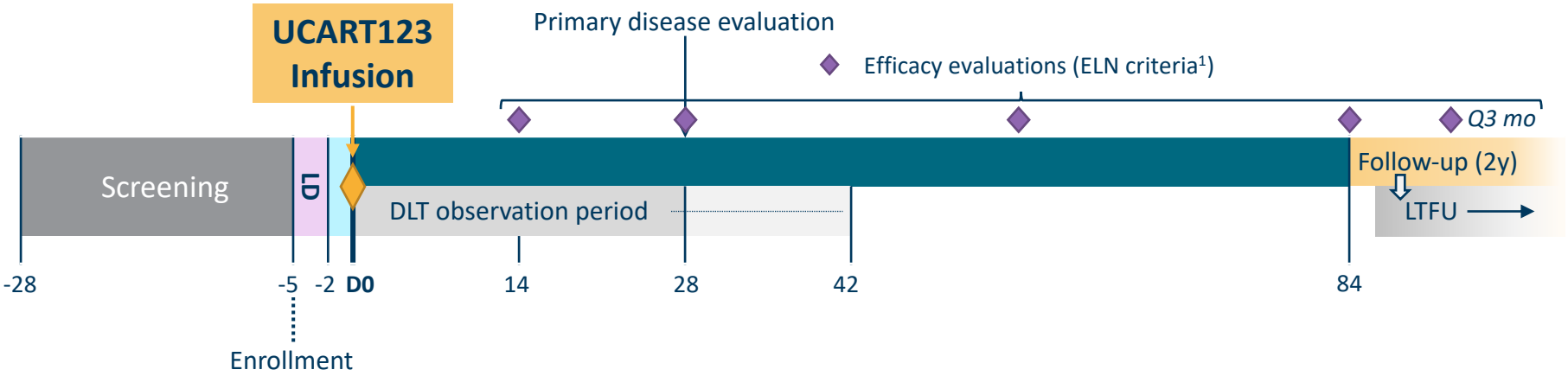
Lymphodepletion (LD) regimens:

- FC: fludarabine + cyclophosphamide
- FCA: fludarabine + cyclophosphamide + alemtuzumab

*Up to 80-kg equivalent.

DL, dose level; FC, fludarabine + cyclophosphamide; FCA, fludarabine + cyclophosphamide + alemtuzumab; LD, lymphodepletion; MTD, maximum tolerated; MTPI, modified Toxicity Probability Interval; RP2D, recommended phase 2 dose.

Timeline of Study Events



1. Döhner et al. *Blood* 2017;129:424-447.
D, day; DLT, dose-limiting toxicity; ELN, European LeukemiaNet; EOT, end of treatment; LD, lymphodepletion; LTFU, long-term follow-up.

Objectives and Statistical Considerations

STUDY OBJECTIVES

Primary:

- Safety & tolerability
- Establish MTD and identify RP2D

Secondary:

- Efficacy

Exploratory:

- UCART123 expansion, trafficking, and persistence
- Profile cytokine, chemokine, growth factor, and C-reactive protein levels post-infusion
- Investigate correlation between CD123 expression levels and clinical outcomes
- Confirm the absence of replication competent lentivirus (RCL)

STATISTICAL CONSIDERATIONS

- No formal statistical hypothesis for dose-escalation phase
- For the dose expansion a futility analysis will apply and will follow a Simon's two-stage Minimax design.
  - Stage 1: Enroll 18 patients; Target CR rate 3/18
    - ≥ 3/18 patients: Proceed to Stage 2
    - < 3/18 patients: Terminate study
  - Stage 2: Enroll 19 additional patients (total 37)
    - Target CR rate 9/37

CR, complete remission; MTD, maximum tolerated dose; RP2D, recommended phase 2 dose.

Summary

- There is an important unmet need for novel therapies to treat patients with R/R AML
- This phase I study will evaluate the safety, tolerability, RP2D, and preliminary efficacy of UCART123, a genetically modified allogeneic anti-CD123 CAR T cell product
  - Disruption of the TCRα constant and CD52 genes reduces risk of GvHD and allows use of alemtuzumab for selective and prolonged host lymphodepletion
  - Allogeneic cells from healthy donors allows for large-scale production and “off-the-shelf” availability immediately upon treatment decision
- This study is currently enrolling; if you know of a patient who could benefit from participation in this trial, please contact the Cellectis Clinical Operations team (clinops@cellectis.com)

AML, acute myeloid leukemia; CAR, chimeric antigen receptor; GvHD, graft-vs-host disease; R/R, relapsed/refractory; RP2D, recommended phase 2 dose; TCR, T cell receptor.

Acknowledgements

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For questions or comments, please contact Dr. Gail Roboz: gar2001@med.cornell.edu.

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