Preliminary Results of BALLI-01: A Phase I Study of UCART22 (Allogeneic Engineered T-cells Expressing Anti-CD22 Chimeric Antigen Receptor) in Adult Patients with Relapsed or Refractory CD22+ B-Cell Acute Lymphoblastic Leukemia (NCT04150497)

Nitin Jain, MD[1], Gail J. Roboz, MD[2], Marina Konopleva, MD, PhD[1], Hongtao Liu, MD, PhD[3], Elias Jabbour, MD[1], Camille Poirot, PharmD[4], Cécile Schiffer-Mannioui, PhD[4], Agnès Gouble, PhD[4], Asifa Haider, PhD[5], Oleg Zernovak, MD[5], and Richard A. Larson, MD[3]

[1]Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX; [2]Division of Hematology and Oncology, Weill Cornell Medicine and The New York-Presbyterian Hospital, New York, NY; [3]Department of Medicine, Section of Hematology-Oncology, University of Chicago, Chicago, IL; [4]Cellectis SA, Paris, France; [5]Cellectis Inc., New York, NY

FORWARD-LOOKING STATEMENTS

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.

Factors that may cause actual results to differ from those in any forward-looking statement, include the duration and severity of the COVID-19 pandemic and responsive measures; inconclusive clinical trial results or clinical trials failing to achieve one or more endpoints; early data not being repeated in ongoing or future clinical trials; failures to secure required regulatory approvals; disruptions from failures by third-parties on whom we rely in connection with our clinical trials; delays or negative determinations by regulatory authorities; changes or increases in oversight and regulation; increased competition; manufacturing delays problems; inability to achieve enrollment disagreements with our collaboration partners of collaboration partners to pursue product legal challenges or intellectual property disputes; disruptions to access to raw materials or starting material.

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.

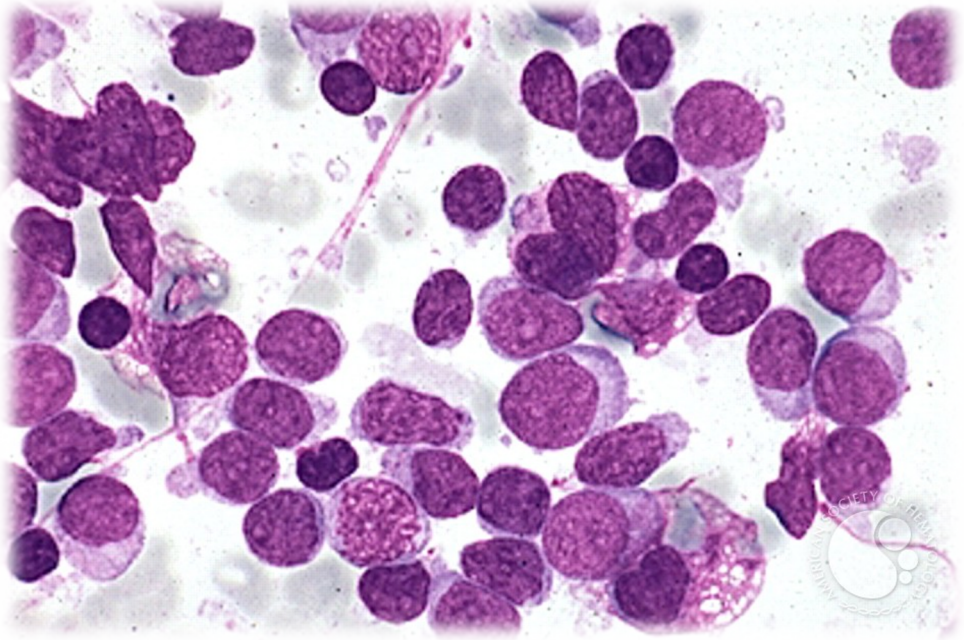
Disclosures (N. Jain)

- Research funding
  - Cellectis, Pharmacyclics, AbbVie, Genentech, AstraZeneca, BMS, Pfizer, ADC Therapeutics, Incyte, Servier, Adaptive Biotechnologies, Precision Biosciences, Aprea Therapeutics, Fate Therapeutics

- Advisory committee / Honoraria
  - Cellectis, Pharmacyclics, Janssen, AbbVie, Genentech, AstraZeneca, Adaptive Biotechnologies, Servier, Precision Biosciences, Beigene, TG Therapeutics, ADC Therapeutics

Adult B Cell Acute Lymphoblastic Leukemia

- Standard therapy for adults with B-ALL involves multiagent chemotherapy ± allogeneic SCT
- 30-60% of patients with newly diagnosed B-ALL who attain CR will relapse[1]
- Prognosis is poor for patients with R/R B-ALL (~10% at 5 years)[1]
- UCART19, with LD using FCA, demonstrated efficacy in R/R B-ALL patients[2]
- CD22 is an FDA-approved therapeutic target in B-ALL



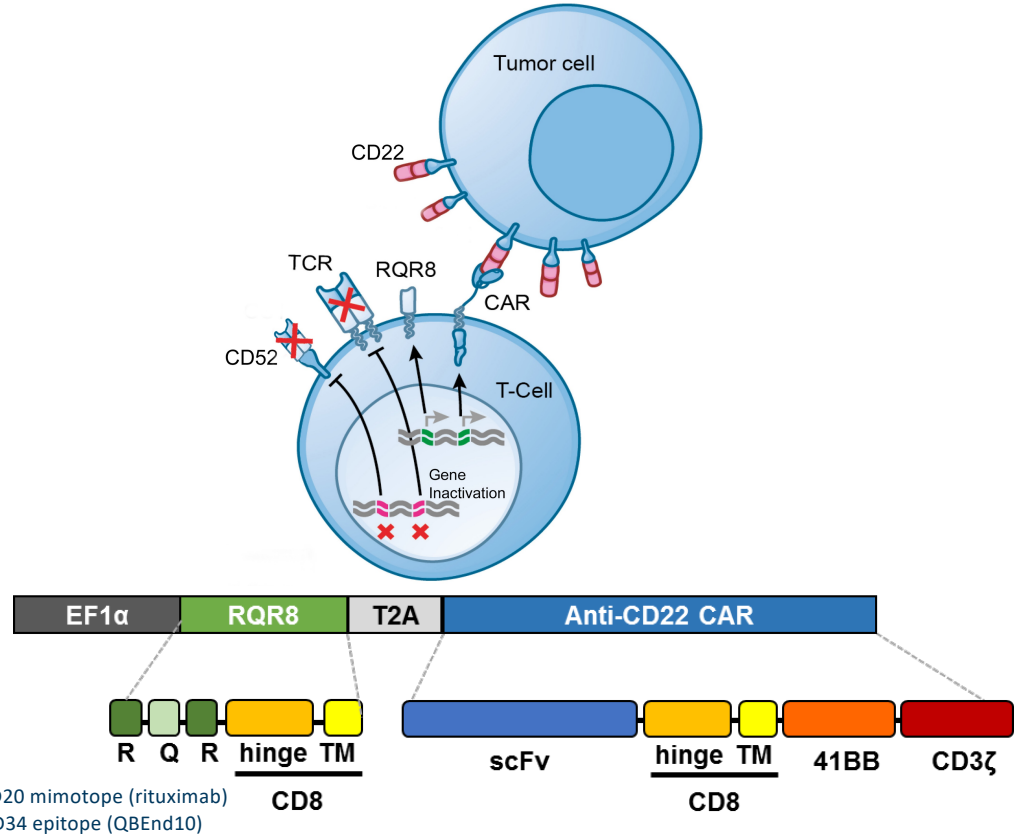
1. Gökbuget et al. *Haematologica*. 2016;101(12):1524-1533. 2. Benjamin, et al. *Blood* 2018;132(Suppl 1):Abstract 896.

B-ALL, B cell acute lymphoblastic leukemia; CR, complete remission; FCA, fludarabine + cyclophosphamide + alemtuzumab; LD, lymphodepletion; R/R, relapsed/refractory; SCT, stem cell transplant.

UCART22: Allogeneic "Off-the-shelf" T Cell Product

UCART22 (anti-CD22 scFv-41BB-CD3ζ):

- Immediately available, standardized, manufactured at large scale
- Ability to re-dose
- CAR expression redirects T cells to tumor antigens
- CD20 mimotope for rituximab "safety switch"
- *TRAC* disrupted using TALEN® to eliminate TCRαβ from the cell surface and reduce risk of GvHD
- *CD52* disrupted using TALEN® to eliminate sensitivity to LD with alemtuzumab

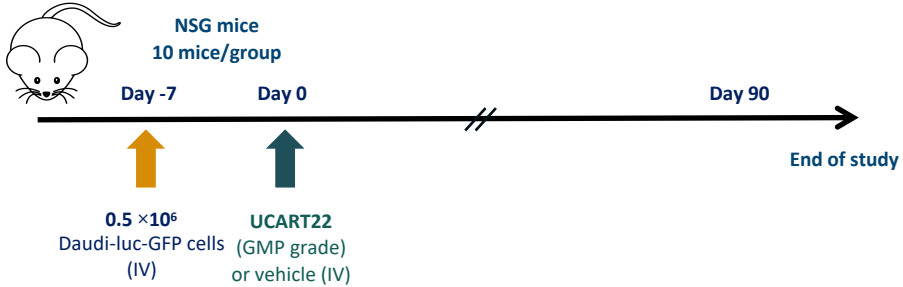


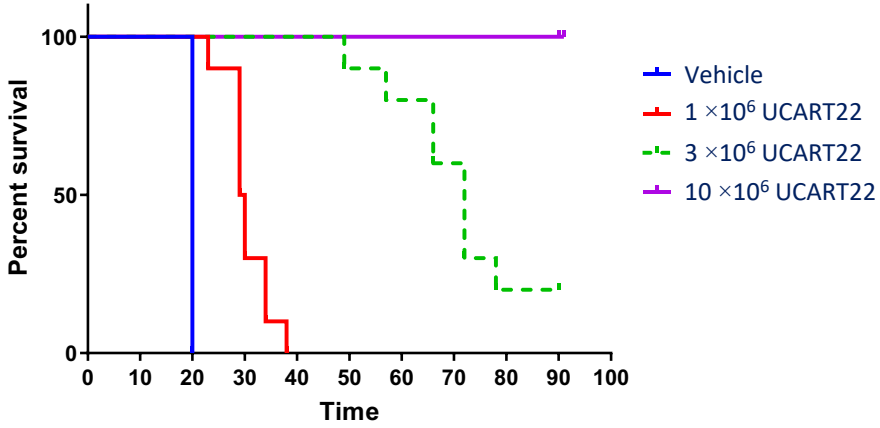
R= CD20 mimotope (rituximab)
Q= CD34 epitope (QBEnd10)

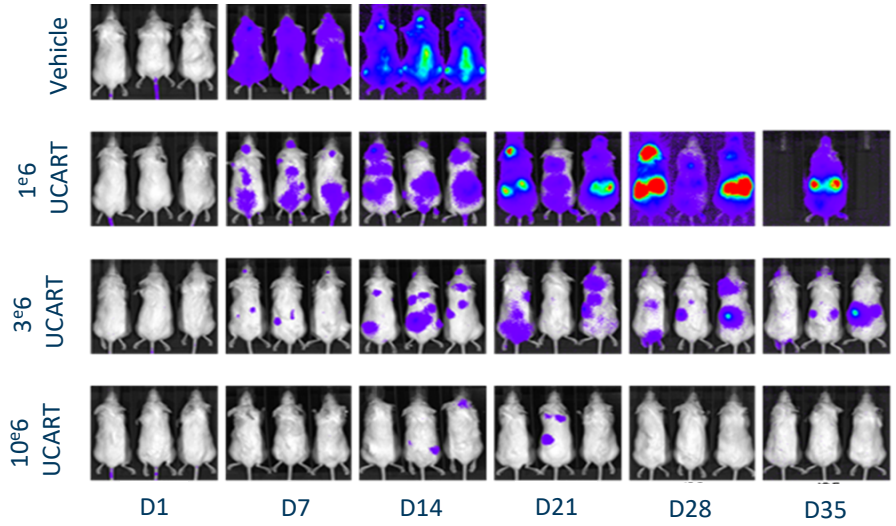
CAR, chimeric antigen receptor; GvHD, graft-versus-host disease; LD, lymphodepletion; TCR, T cell receptor; TRAC, T cell receptor alpha constant.

In Vivo Anti-tumor Activity of UCART22

- UCART22 extended survival of immune-compromised mice engrafted with Daudi cells (CD22+ Burkitt's lymphoma cells) in a dose-dependent manner





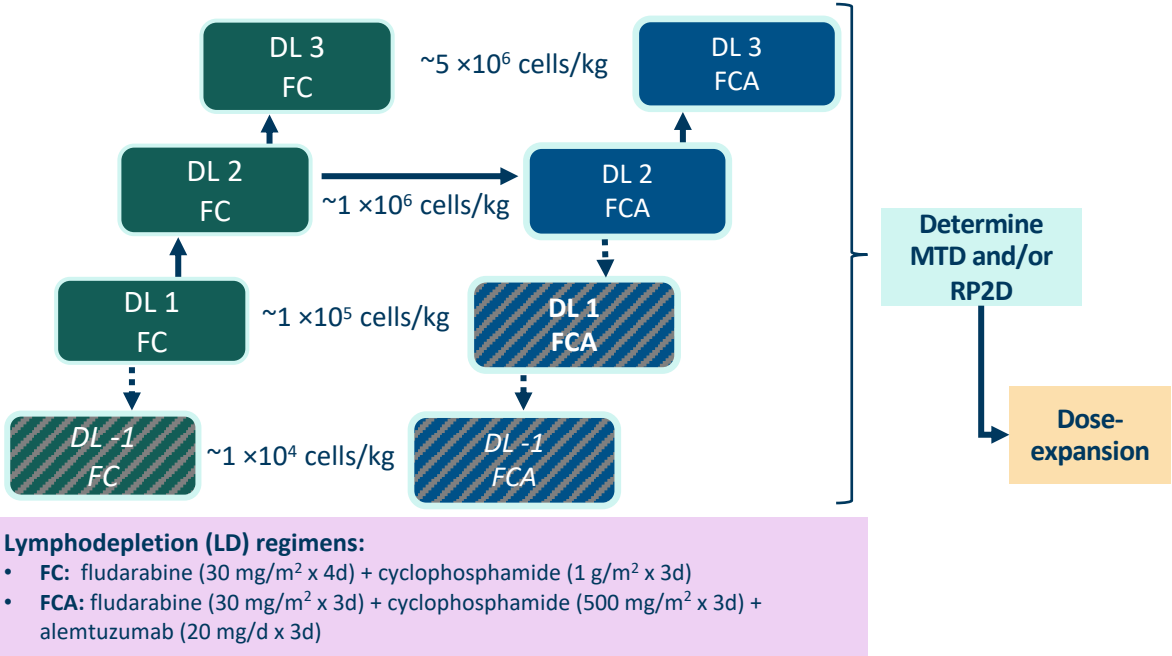


BALLI-01 Study Design

- **Key inclusion criteria**
  - Age 18-70 years, adequate organ function, ECOG PS ≤1
  - B-ALL blast CD22 expression ≥90%
  - Received ≥1 standard chemotherapy regimen and ≥1 salvage regimen
- **Endpoints**
  - Safety & tolerability
  - MTD/RP2D
  - Response (NCCN criteria[1]; investigator assessed)
  - UCART22 expansion and persistence, VCN and chimerism in WB and BM
  - Immune reconstitution

Dose-escalation

Up to 30 patients • mTPI design • 2-4 patients/cohort



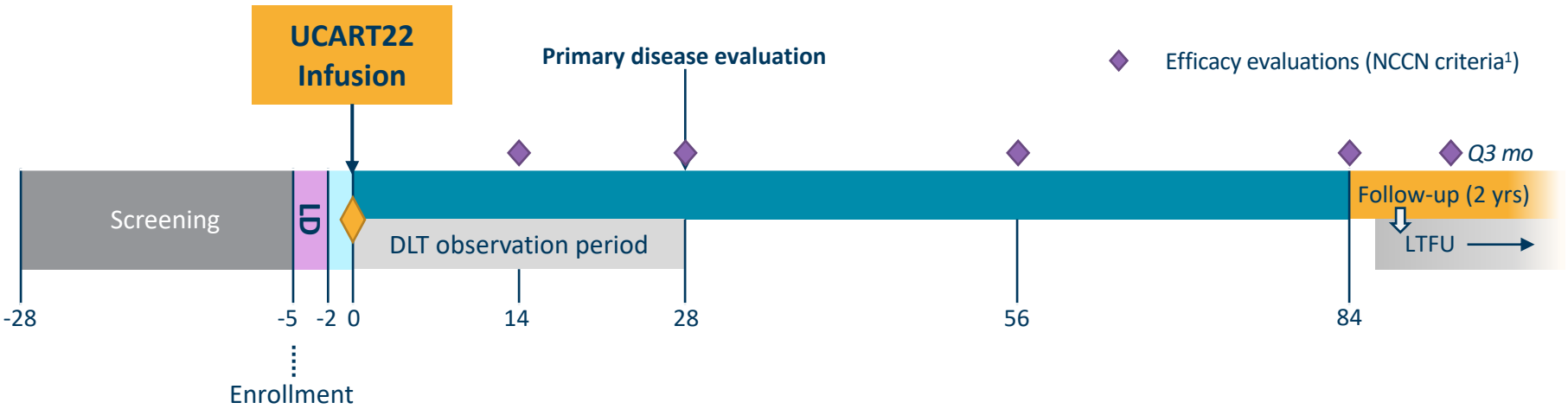
Lymphodepletion (LD) regimens:

- **FC:** fludarabine (30 mg/m² x 4d) + cyclophosphamide (1 g/m² x 3d)
- **FCA:** fludarabine (30 mg/m² x 3d) + cyclophosphamide (500 mg/m² x 3d) + alemtuzumab (20 mg/d x 3d)

1. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology – Acute Lymphoblastic Leukemia v2.2020.

B-ALL, B cell acute lymphoblastic leukemia; BM, bone marrow; DL, dose level; DLT, dose-limiting toxicity; ECOG PS, Eastern Cooperative Oncology Group performance status; FC, fludarabine + cyclophosphamide; FCA, fludarabine + cyclophosphamide + alemtuzumab; MTD, maximum tolerated dose; mTPI, modified Toxicity Probability Interval; RP2D, recommended phase 2 dose; VCN, vector copy number; WB, whole blood.

Timeline of Study Events



1. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology – Acute Lymphoblastic Leukemia v2.

DLT, dose-limiting toxicity; LTFU, long-term follow-up; LD, lymphodepletion; NCCN, National Comprehensive Cancer Network; Q3mo, every 3 months; yrs, years.

Patients

- 7 patients screened as of 1 July, 2020
  - 1 patient failed screening, 6 patients enrolled
  - 1 patient discontinued before receiving UCART22 due to an AE (hypoxia due to pneumonitis related to LD)
- 5 patients treated with UCART22
  - DL 1 n=3
  - DL 2 n=2
- Baseline characteristics (n=5):
  - Median age 24 years (range 22-52)
  - Median of 3 prior therapies (range 2-6)
  - Median 35% BM blasts before LD (range 10%-78%)

AE, adverse event; BM, bone marrow; DL, dose level; LD, lymphodepletion.

Baseline Characteristics

Characteristic	DL1 (1 ×10^5 cells/kg) n=3			DL2 (1 ×10^6 cells/kg) n=2	
Age, years	22	52	33	24	24
Sex	M	M	F	M	F
ECOG PS score	0	1	0	0	1
Cytogenetics	Diploid	Diploid	Complex Karyotype	Complex Karyotype	Complex Karyotype
Molecular Abnormalities	*CRLF2*	*CRLF2* *JAK2* *NRAS*	*CDKN2A* loss	*KRAS* *PTPN11*	*IKZF1*
Number of prior treatments	2	3	3	3	6
Prior transplant	No			Y/Haplo	No
Prior CD19- or CD22-directed therapy	No	Blinatumomab	Inotuzumab	CAR19	Blinatumomab, Inotuzumab, CAR19
Disease status at study entry	Refractory	Refractory	Relapsed	Relapsed	Refractory

DL, dose level; ECOG PS, Eastern Cooperative Oncology Group performance status; F, female; LD, lymphodepletion; M, male.

Safety

No patient experienced a DLT, ICANS, GvHD, AESI, or UCART22-related Grade ≥3 AE or SAE

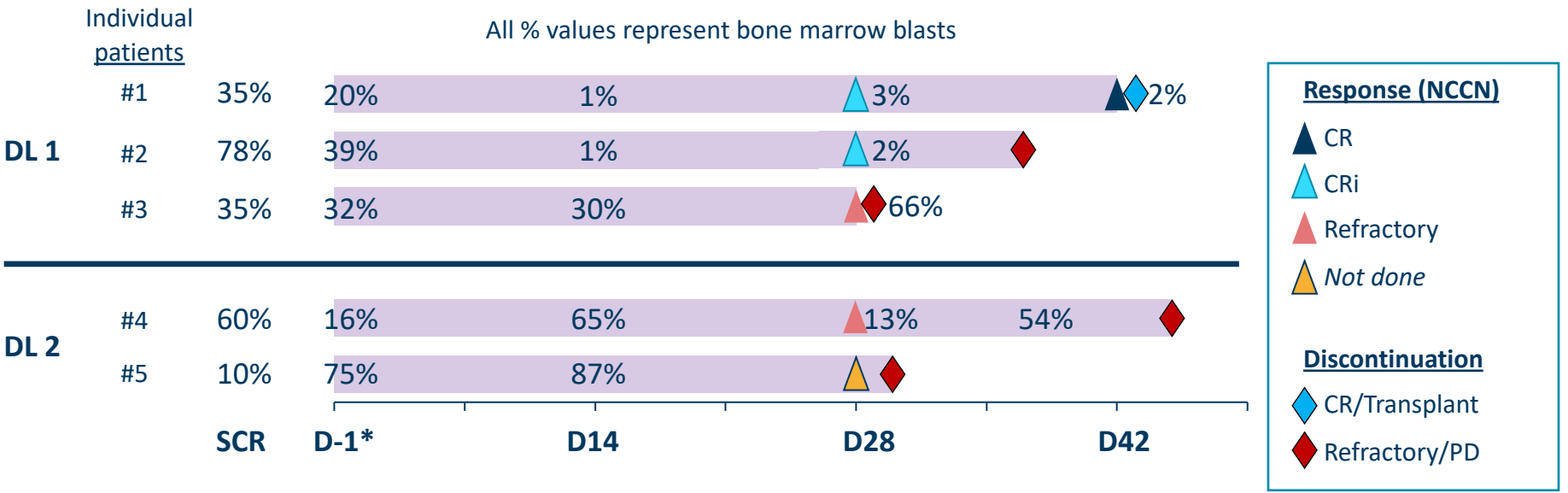
Treatment-emergent adverse events of interest with DL1 and DL2					
	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Graft-versus-host disease (GvHD)	0	0	0	0	0
Cytokine release syndrome (CRS)*	2	1	0	0	0
ICANS	0	0	0	0	0
SAEs			3	1	1

- Grade ≥3 TEAEs (not related to UCART22 treatment): hypokalemia (G3); anemia (G3); bilirubin increase (G4); acute hypoxic respiratory failure (G4)
- 3 patients experienced 4 treatment-emergent SAEs not related to UCART22 treatment: porta-hepatis hematoma (G3); sepsis (G3); bleeding (G4); sepsis (G5) in the context of progressive disease
- No patient discontinued treatment due to a UCART22-related TEAE

*CRS durations ranged from 2-4 days; no patient received tocilizumab or steroids

AESI, adverse event of special interest; DLT, dose-limiting toxicity; G, grade; ICANS, immune effector cell-associated neurotoxicity syndrome; SAE, serious adverse event.

Anti-leukemic Activity



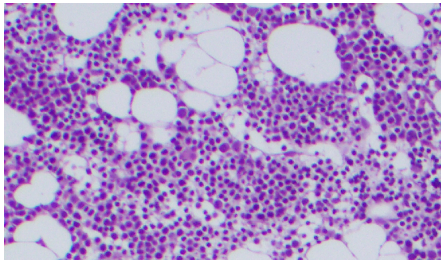
- 2 patients at DL1 achieved CRi at D28; 1 of them attained CR (MRD+) at D42 and received transplant after subsequent therapy with inotuzumab
- 1 patient at DL2 had significant BM blast reduction at D28 and then progressed

*D-1 sample is after LD and before UCART22 dosing

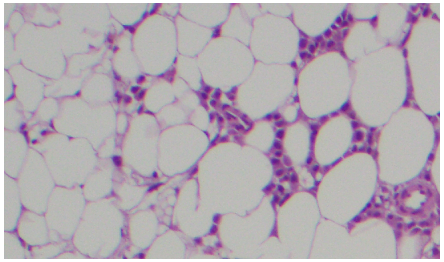
CR, complete remission; CRi, complete remission with incomplete hematologic recovery; D, day; DL, dose level; EOT, end of treatment; LD, lymphodepletion; MRD, measurable residual disease; NCCN, National Comprehensive Cancer Network; PD, progressive disease; SCR, screening.

UCART22 Case Study: CRi to CR to Transplant

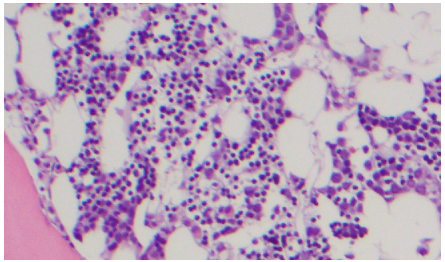
- Patient #1 characteristics:
  - 22-year-old male
  - 2 prior treatments for B-ALL
  - Treated with UCART22 at DL1 ($1x10^5$ cells/kg)
- Safety and efficacy
  - No CRS, ICANS, GvHD, SAE
  - All TEAEs Grade 1
  - CRi at D28
  - At D42 CR with MRD+; started treatment with inotuzumab and proceeded to transplant



Screening
35% blasts



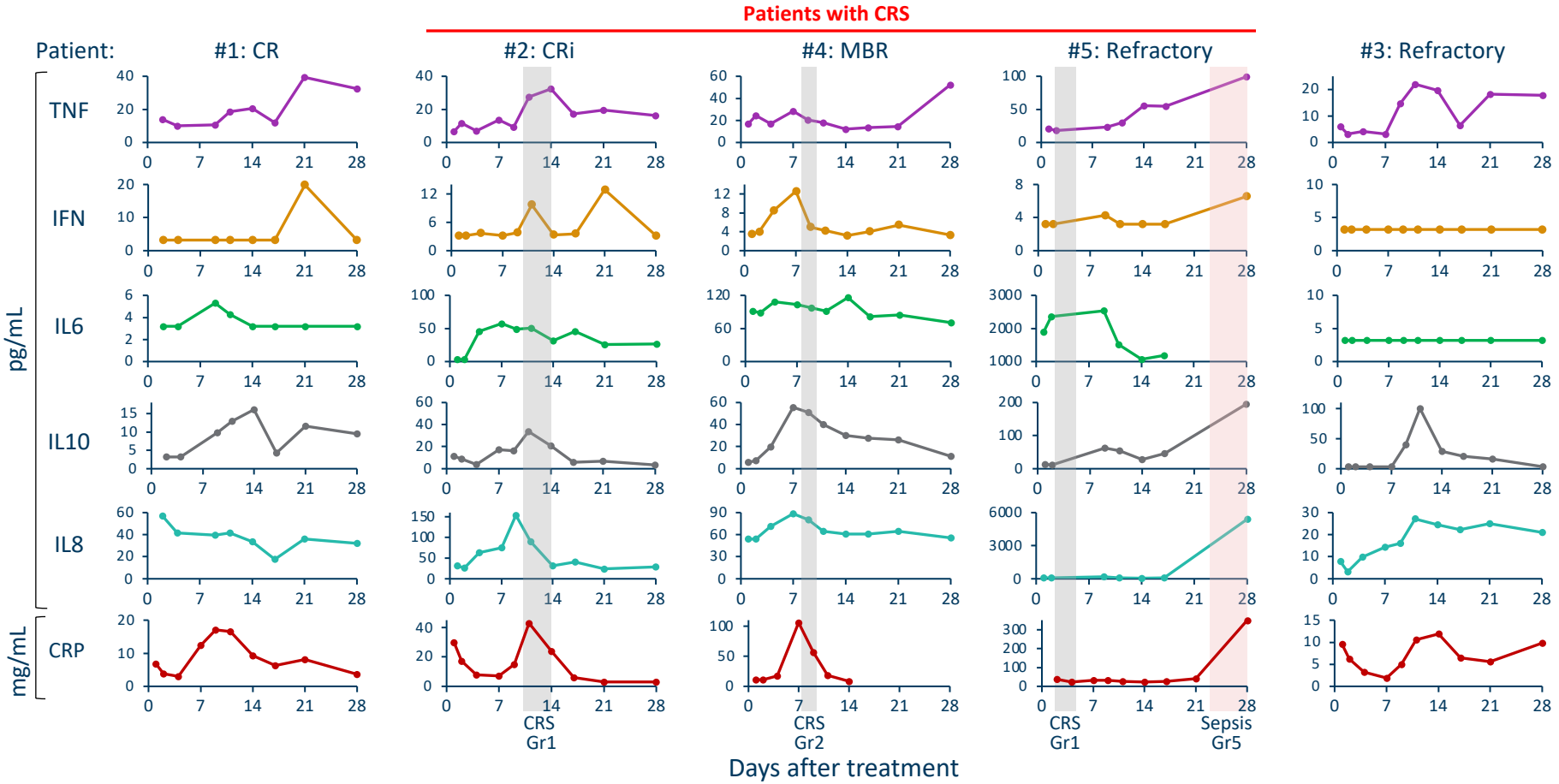
Day 14
1% blasts



Day 28
3% blasts

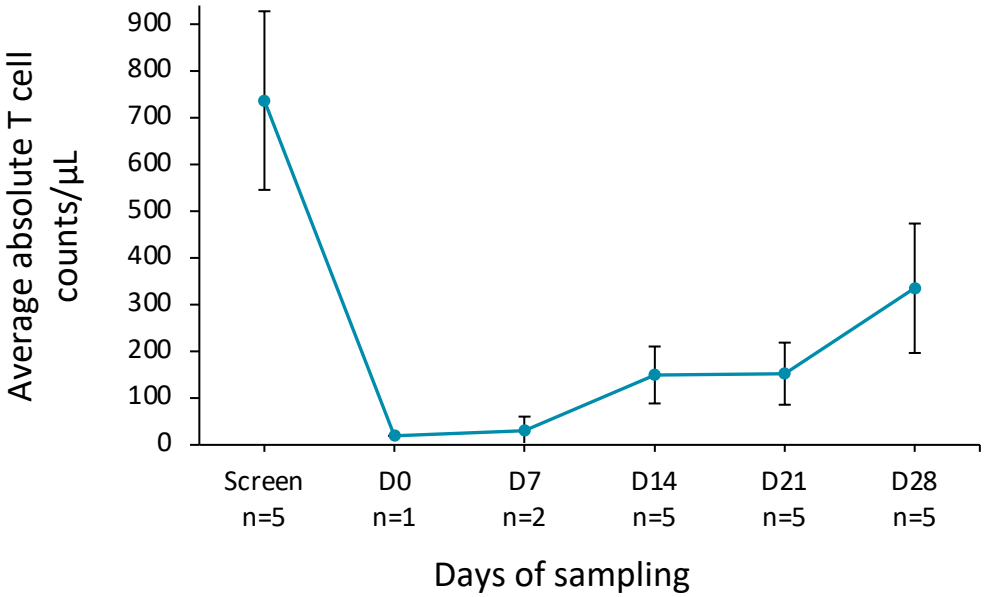
CR, complete remission; CRi, complete remission with incomplete hematologic recovery; CRS, cytokine release syndrome; D, day; DL, dose level; GvHD, graft-versus-host disease; ICANS, immune effector cell-associated neurotoxicity syndrome; MRD, measurable residual disease; TEAE, treatment-emergent adverse event.

Proinflammatory Markers After UCART22 Dosing



CRP, C-reactive protein; CRS, cytokine release syndrome; Gr, grade; IFN, interferon gamma; IL, interleukin; MBR, major blast reduction; SCR, screening; TNF, tumor necrosis factor.

Host T Cell Reconstitution and UCART22 Detection



- Host T cell reconstitution observed in all patients within DLT observation period

UCART22

- Not detectable in WB or BM samples (flow cytometry), or molecular analysis (DL1 only)
- Low cell counts in WB limited effective analysis of UCART22 cells at early timepoints

BM, bone marrow; DL, dose level; DLT, dose-limiting toxicity; WB, whole blood.

Conclusions

- UCART22 showed no unexpected toxicities at doses of $1x10^5$ cells/kg and $1x10^6$ cells/kg with the FC LD regimen
  - No patient had a DLT, GvHD, AESI, or ICANS; no SAEs related to UCART22 treatment
- CRS occurred in 3 patients, all grade 1 or 2 and of short duration (2-4 days), no patient required tocilizumab or steroids
- CR and CRi achieved in 2 patients and blast reduction in 1 patient
- Cytokine profiles show minor changes
- Host immune recovery observed early; addition of alemtuzumab to FC LD regimen is currently being explored to achieve deeper and more sustained T cell depletion and promote expansion and persistence of UCART22
  - FCA LD cohorts are enrolling

AESI, adverse event of special interest; CR, complete remission; CRi, complete remission with incomplete hematologic recovery; CRS, cytokine release syndrome; DLT, dose-limiting toxicity; FC, fludarabine + cyclophosphamide; FCA, fludarabine + cyclophosphamide + alemtuzumab; GvHD, graft-vs-host disease; ICANS, immune effector cell-associated neurotoxicity syndrome; LD, lymphodepletion; SAE, serious adverse event.

Acknowledgments

- We thank the patients, families, co-investigators and all study personnel who made this trial possible
- The BALLI-01 study is funded by Cellectis S.A.

- For questions or comments, please contact Dr. Nitin Jain: njain@mdanderson.org

Scan QR code for a copy of this presentation