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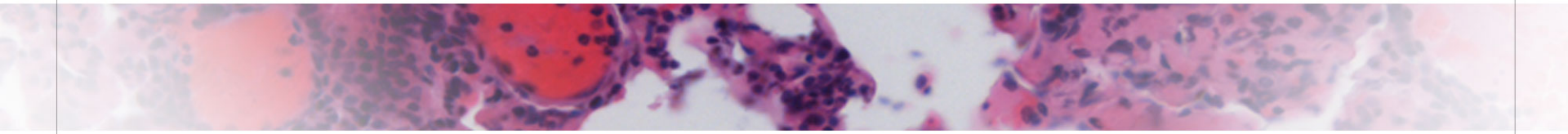

Preliminary Data on Safety, Cellular Kinetics and Anti Leukemic Activity of UCART19, an Allogeneic Anti-CD19 CAR T-cell Therapy in Adult and Pediatric Patients with CD19^{+} Relapsed/Refractory B-cell Acute Lymphoblastic Leukemia – A Pooled Analysis of the CALM and PALL Phase 1 Trials

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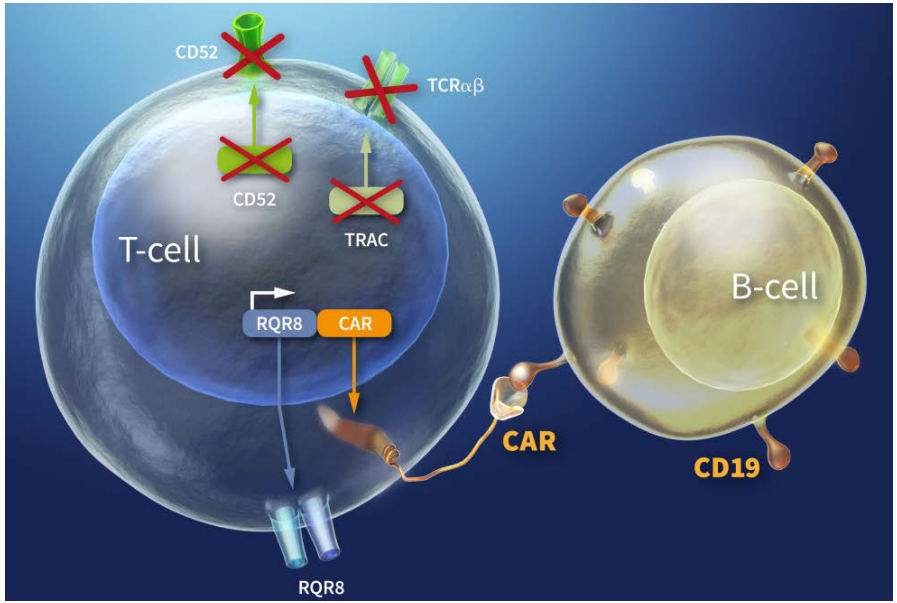
R/R B-cell ALL in Children and Adults

- Prognosis of R/R ALL is very poor (<10% overall survival)
- Standard therapy involves combination of chemotherapy ± allogeneic SCT
- New treatments include BiTEs, ADCs and autologous CAR T-cell therapies
- Still unmet medical need in advanced R/R ALL
- The "off-the-shelf" UCART19 may overcome some hurdles faced with autologous CAR T-cell therapies

UCART19: the First “Off the Shelf” Anti-CD19 Allogeneic CAR T-cell Therapy



Transgene expression using lentiviral transduction

- **CAR**: anti-CD19 scFv and CD3ζ + 4-1BB
- **RQR8** (= CD20 mimotope): safety switch

Gene knock-out using TALEN® technology

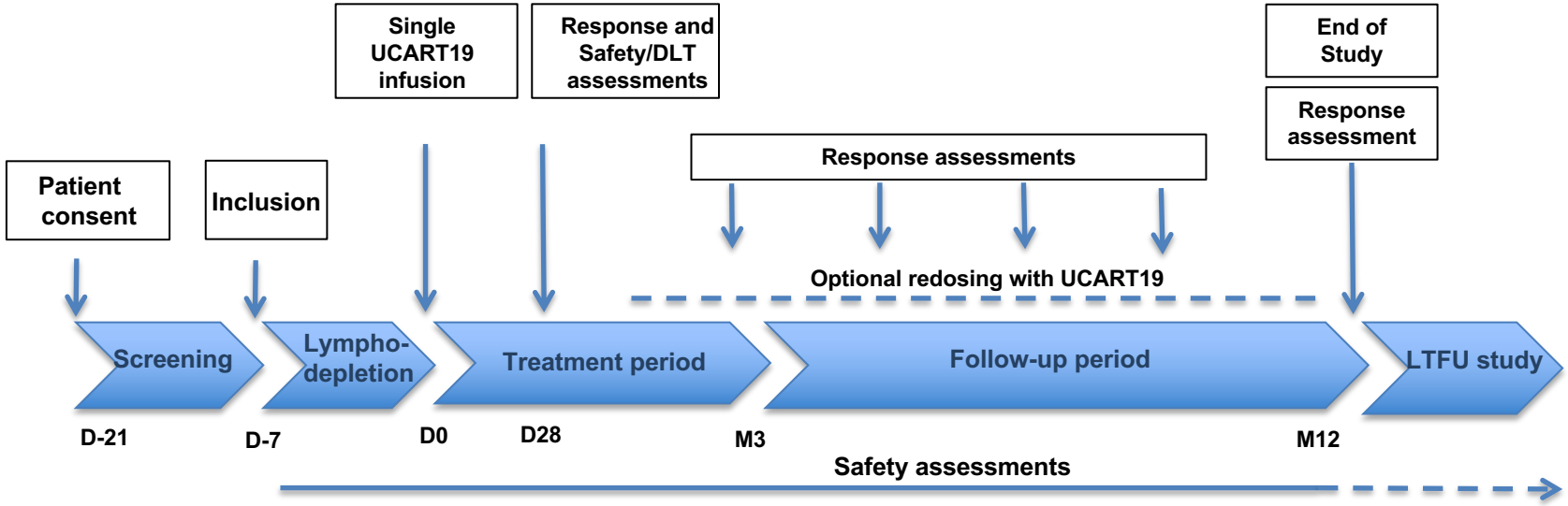
- **TRAC KO**: to prevent TCR mediated recognition of patient’s HLA antigens
- **CD52 KO**: to permit anti CD52 mAb use in lymphodepletion

TALEN® (= transcription activator-like effector nuclease) is a proprietary technology owned by Cellectis

PALL / CALM – Study Main Objectives

Objectives	PALL (pediatric study)	CALM (adult study)
Primary	• Safety and tolerability of UCART19	• Safety and tolerability of UCART19 • Determine maximum tolerated dose (MTD) and lymphodepleting (LD) regimen
Secondary	• Remission rate at D28	
Exploratory	• Anti-leukemic activity at each time-point up to M12 • Proportion of patients undergoing allo-SCT • Expansion and persistence of UCART19 • Proportion of patients undergoing UCART19 redosing	

PALL / CALM Study Schema



LD regimen (FC or FCA)	Doses in PALL	Doses in CALM
Fludarabine (F)	150 mg/m^2	90 mg/m^2
Cyclophosphamide (C)	120 mg/kg	1500 mg/m^2
Alemtuzumab (A)	1 mg/kg (capped at 40 mg)	1 mg/kg or 40 mg

PALL dose	CALM dose levels	
weight-banded dose [range 1.1 to 2.3 x10^6 cells/kg]	DL1: 6x10^6	≈ 1x10^5 cells/kg
	DL2: 6 or 8x10^7	≈ 1x10^6 cells/kg
	DL3: 1.8 or 2.4x10^8	≈ 3x10^6 cells/kg

PALL / CALM Key Eligibility Criteria

Inclusion Criteria

- Age: PALL from 6 months to <18 yrs; CALM from 16 yrs to <70 yrs
- Patients with CD19+ relapsed or refractory (R/R) B-ALL
  - ✓ R/R defined as ≥ 2nd BM relapse or any BM relapse after allo-HSCT or chemorefractory
  - ✓ morphologically confirmed (≥ 5% leukemic blasts) or quantifiable MRD+ (≥ 1x10^{-3})
  - ✓ and who have exhausted available treatment options

Exclusion Criteria

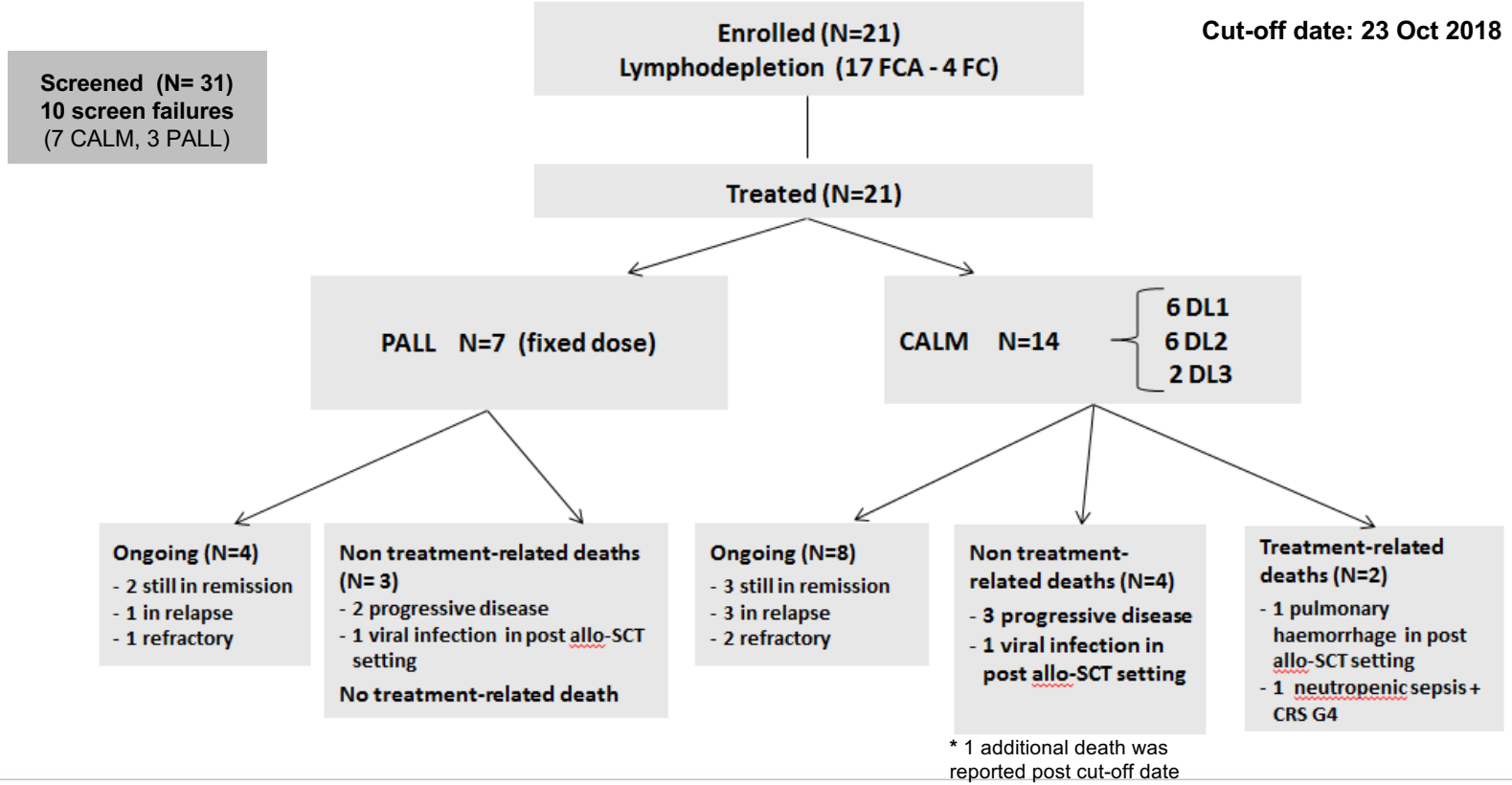
- Clinically suspected extra-medullary involvement, CNS-3
- Evidence of active infection within 7 days of inclusion
- Presence of UCART19 donor-specific anti-HLA antibodies

High-Risk, Heavily Pretreated Patients

	PALL (N =7)	CALM (N =14)	POOLED (N =21)
Median age (range) - years	2.7 (0.8-16.4)	29.5 (18-62)	**22 (0.8-62)**
Number of previous lines of therapy			
1 to 3	3	4	**7**
≥ 4	4	10	**14**
Median (range)	4 (2-6)	4 (1-5)	**4 (1-6)**
High cytogenetic risk *	3	6	**9**
Prior allo-SCT	3	10	**13**
Time to relapse following prior allo-SCT			
< 6 months	0	4	**4**
≥ 6 months	3	6	**9**
Bone marrow tumor burden prior to LD (% of blasts)			
< 5	3	3	**6**
5 to 25	2	4	**6**
> 25	2	7	**9**
Median (range)	6 [0-80]	19 [0-96]	**8 [0-96]**

* High cytogenetic risk includes complex karyotypes, MLL rearrangements, Ph+

PALL / CALM - Patients Status



UCART19 Shows an Acceptable Safety Profile

N=21	G1 n (%)	G2 n (%)	G3 n (%)	G4 n (%)	G5 n (%)	All grades n (%)
AEs related to UCART19						
Cytokine release syndrome	4 (19.0)	12 (57.1)	2 (9.5)	1* (4.8)	-	19 (90.5)
Neurotoxicity events	7 (33.3)	1 (4.8)	-	-	-	8 (38.1)
Acute skin graft-versus-host disease **	2 (9.5)	-	-	-	-	2 (9.5)
AEs related to lymphodepletion and/or UCART19						
Prolonged cytopenia***	-	-	-	6 ‡ (28.5)	-	6 (28.5)
Viral infections †	1 (4.8)	2 (9.5)	4 (19.0)	1 (4.8)	-	8 (38.1)
Neutropenic sepsis				1 (4.8)	1* (4.8)	2 (9.5)
Febrile neutropenia/ septic shock					1 (4.8)	1 (4.8)
Pulmonary haemorrhage					1‡ (4.8)	1 (4.8)

n: number of patients with at least one event by worst grade

* 1 DLT at DL1 related to UCART19: G4 CRS associated with G5 neutropenic sepsis (death at D15 post-infusion)

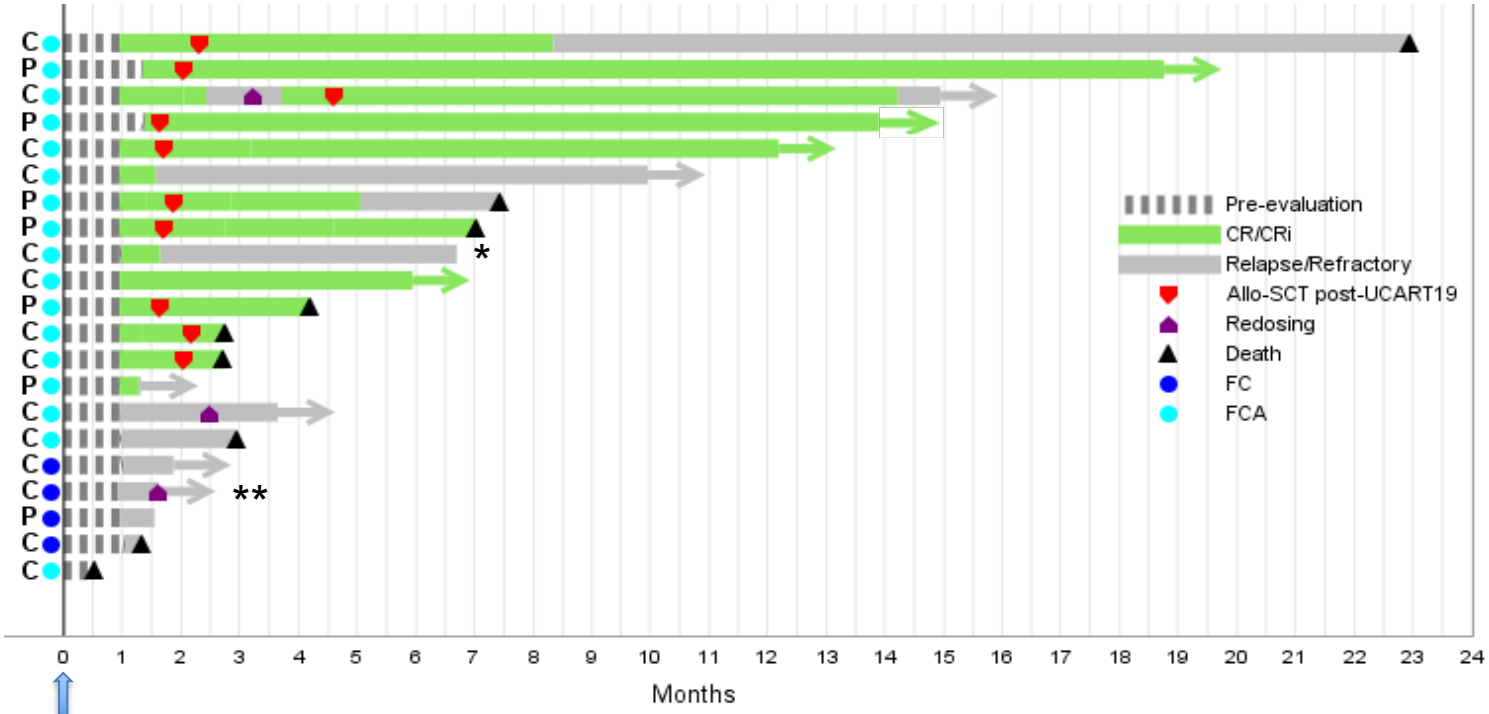
** GvHD confirmed by biopsy in 1 out of 2 cases

*** Persistent Grade 4 neutropenia and/or thombocytopenia beyond Day 42 post UCART19 infusion, except if >5% bone marrow blasts

‡ 1 DLT at DL2 related both to UCART19 and LD: G4 prolonged cytopenia associated with infection and pulmonary hemorrhage (death at D82 post-infusion)

† Viral infections: CMV, ADV, BK virus, metapneumovirus

82% Achieved CR/CRi in FCA-treated Population



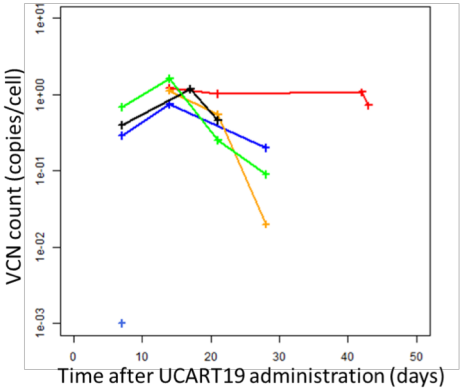
- CR/CRi: 14/17 pts in FCA-treated pts
- MRD-: 10/14 pts (71%)
- Allo-SCT: 11/14 pts (78%)
- Overall CR/CRi: 14/21 pts (67%)

* This patient died post cut-off date

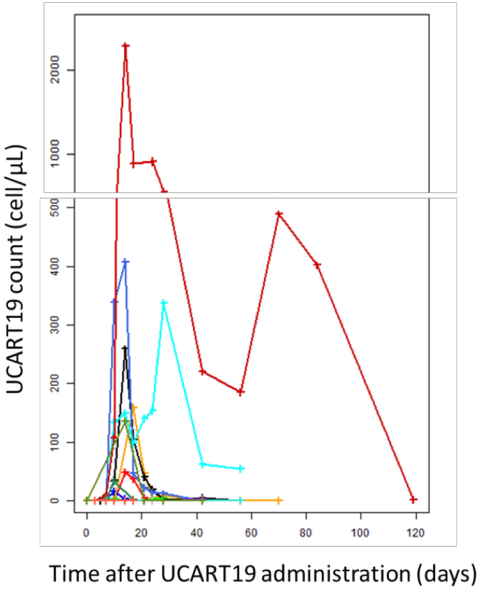
** Patient in MRD- status after 2nd dose, underwent allo-SCT (data reported post cut-off date)

UCART19 Kinetics Measured by qPCR and Flow

UCART19 by qPCR
PALL (n=6)

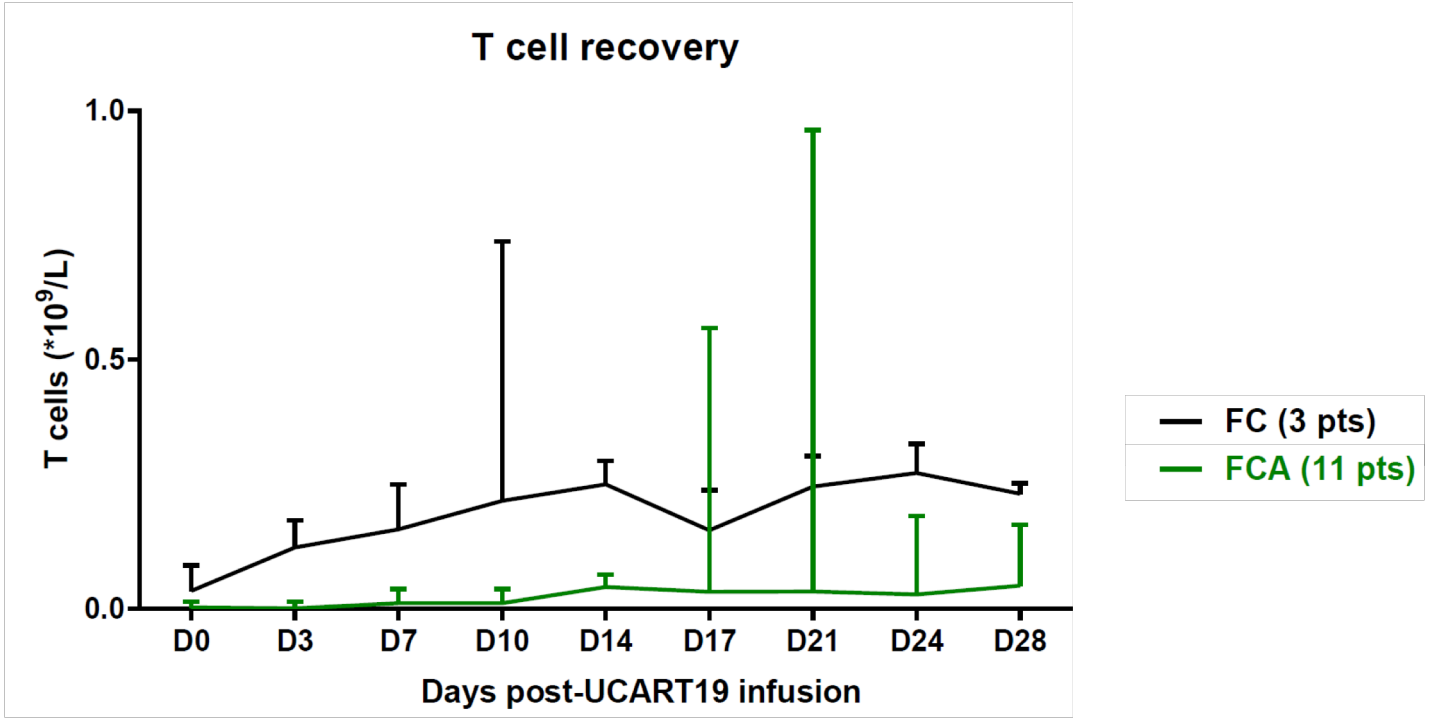


UCART19 by flow
CALM (n=14) + PALL (n=1)



- UCART19 expansion observed in 15/17 pts with FCA
- UCART19 expansion observed in 0/4 pts with FC
- 3 pts had UCART19 persistence beyond D42 and upto D120 in 1 pt
- Response is linked to expansion observed in D0-28 period

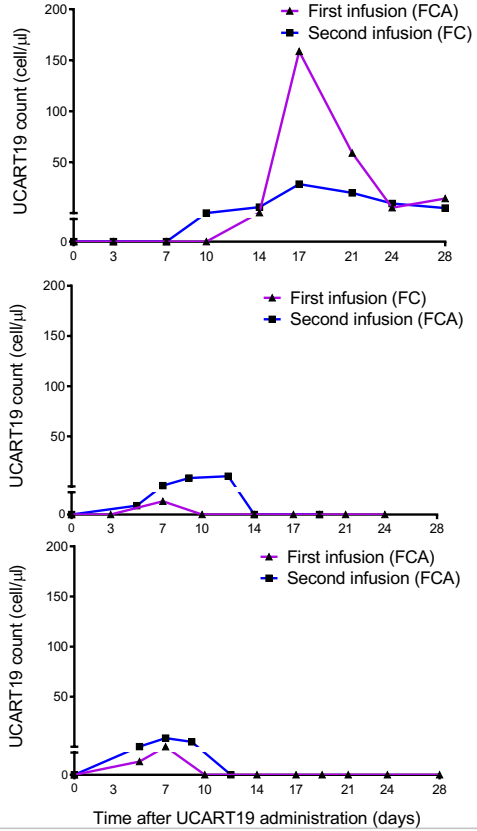
Trend for a Deeper and More Sustained Host T-cell Depletion with FCA



Maximum value of the cell range is plotted from the CALM study

Redosing Allowed Further UCART19 Expansion and 2 out of 3 pts Achieved MRD-

- ✓ Patient 1
  - MRD- at D28
  - Relapse and 2nd infusion 3 months after 1st dose
  - MRD- at D28 after redosing
- ✓ Patient 2
  - Refractory at D28
  - 2nd infusion 1.6 months after 1st dose
  - MRD- at D28 after redosing
- ✓ Patient 3
  - Refractory at D28
  - 2nd infusion 2.4 months after 1st dose
  - Progression at D28



Key Messages

- 82% (14/17) CR/CRi rate in FCA-treated pts
  - 71% (10/14) achieved MRD- status
  - 67% (14/21) CR/CRi rate in overall population
  - No UCART19 expansion and no response in 4/4 FC-treated pts
- UCART19 has shown an acceptable safety profile:
  - no moderate/severe acute GvHD, no severe neurotoxicities, and mainly moderate CRS
  - viral reactivations and prolonged cytopenias are observed
- FCA lymphodepletion appears to be required for UCART19 expansion
- Redosing with UCART19 resulted in cell expansion and MRD- status in 2/3 pts
- UCART19 evaluation in pediatric and adult B-ALL is ongoing

Acknowledgements

- Patients participating in CALM & PALL trials and their families
- Teams involved in UCART19 studies at study centres, Servier and Allogene teams

PALL trial active centers
- Great Ormond Street Hospital, London, UK - W. Qasim
- Hospital Robert Debré, Paris, France - A. Baruchel

CALM trial active centers
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- MD Anderson Cancer Centre, Houston, US - N. Jain
- Massachusetts General Hospital, Boston, US - M. Maus
- Hospital Saint Louis, Paris, France - N. Boissel
- Hospital Saint Antoine, Paris, France - M. Mohty