First-in-Human Data of ALLO-501 and ALLO-647 in Relapsed/Refractory Large B-cell or Follicular Lymphoma (R/R LBCL/FL): ALPHA Study

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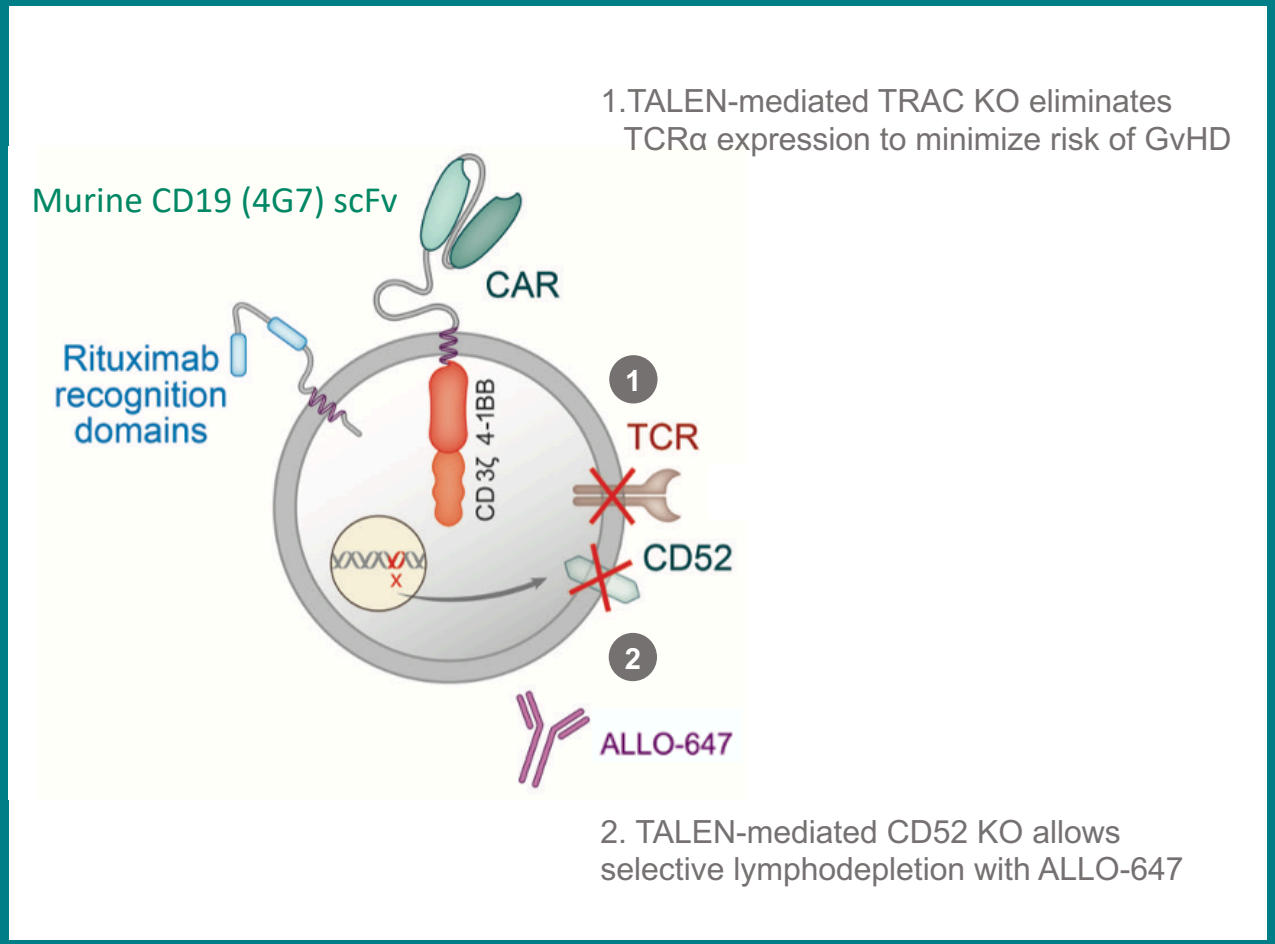
Allogeneic CAR T Cell Therapy for R/R Non-Hodgkin Lymphoma



Allogeneic CAR T therapy may provide the benefits of autologous CAR T therapy while addressing challenges:

- Access
  - Potential to treat all eligible patients
  - Convenience of repeat dosing
  - No need for complex logistics
- Speed/Reliability
  - ”Off the shelf” treatment
  - Less product variability, made from healthy T cells

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ALPHA Study (NCT03939026) Design and Endpoints

Phase 1, Open-label, Multicenter Dose Escalation Study

Primary Endpoints

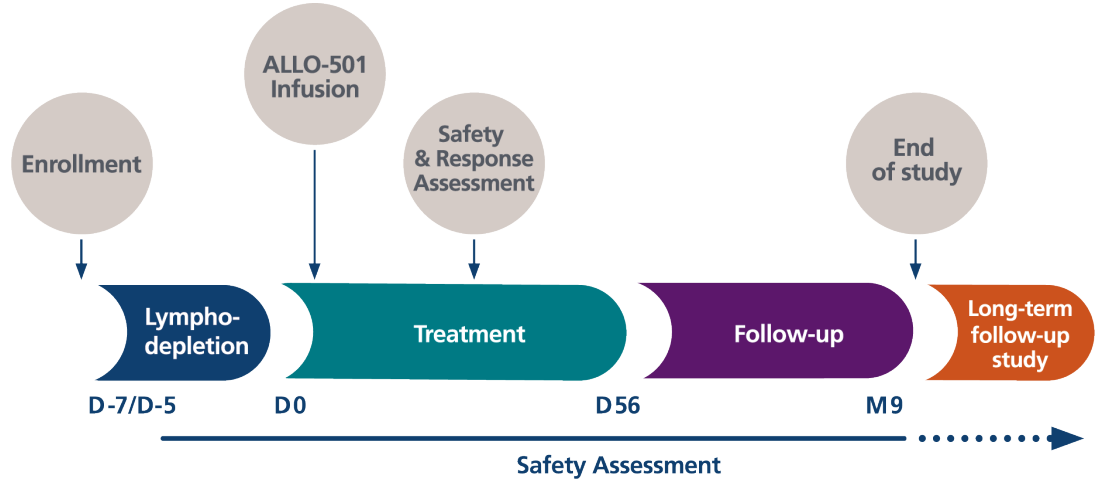
- Safety and dose-limiting toxicity of ALLO-647/Flu/Cy followed by ALLO-501

Key Secondary Endpoints

- Overall response rate
- ALLO-501 cell kinetics
- ALLO-647 PK

Key Eligibility Criteria

- R/R LBCL or FL
- At least 2 prior lines of therapy, including an anti-CD20 monoclonal antibody
- ECOG 0 or 1
- Prior autologous CAR T allowed if tumor remains CD19+
- Patients with Donor Specific Antibodies and rituximab > 15ng/ml were excluded



	DL1	DL2	DL3
Cell Dose	40 x 10^6 CAR^+ T cells	120 x 10^6 CAR^+ T cells	360 x 10^6 CAR^+ T cells

- Lymphodepletion Regimens
  - LD1: Flu/Cy and ALLO-647 13 mg/d x 3 days
  - LD2/LD3: Flu/Cy and ALLO-647 30 mg/d x 3 days (concomitant/staggered)

Fludarabine (Flu): 30 mg/m2/d x 3 days **Cyclophosphamide (Cy)**: 300 mg/m2/d x 3 days

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ALPHA Phase 1 Patient Characteristics

	Number (%) of patients			
	40 x 10^6 DL 1 (N=4)	120 x 10^6 DL 2 (N=10)	360 x 10^6 DL 3 (N=8)	All Patients (N=22)
Median Age, years (range)	57 (42, 67)	70 (37, 73)	54 (34, 67)	63 (34, 73)
Male	3 (75%)	8 (80%)	6 (75%)	17 (77%)
Lymphoma Subtypes				
Diffuse Large B-cell Lymphoma †	3 (75%)	5 (50%)	6 (75%)	14 (64%)
Follicular Lymphoma	1 (25%)	5 (50%)	2 (25%)	8 (36%)
Current Disease Stage (per Lugano 2014) #				
Stage III	1 (25%)	5 (50%)	2 (25%)	8 (36%)
Stage IV	2 (50%)	5 (50%)	6 (75%)	13 (59%)
FL(IPI) Score 3-5	1 (25%)	6 (60%)	5 (63%)	12 (55%)
Prior Treatments				
Median Number (range)	2 (2-4)	4 (3-4)	5 (3-8)	4 (2-8)
Hematopoietic Stem Cell Transplant	2 (50%)	4 (40%)	3 (38%)	9 (41%)
Autologous CAR T cell	-	1 (10%)	3 (38%)	4 (18%)

- Heavily pretreated patients with advanced-stage disease
- 14 (64%) of patients were chemo refractory*
- 4 patients received prior AutoCAR T
  - 2 had short-lasting PR as best response and 2 had PD as best response with AutoCAR T
- Analyses sets:
  - Efficacy: N=19
  - Safety: N=22

† Not otherwise specified, transformed FL, high-grade B cell lymphoma (double and triple hit), DLBCL coexistent with FL of any grade
# 1 patient with stage II disease treated at DL1
* Defined as best outcome of SD or PD following last therapy, or progression within 12 months following Hematopoietic Stem Cell Transplant

Data Cutoff Date: May 11, 2020

ALPHA Phase 1 Patient Flow

Enrolled Patients: 23*

1 patient was enrolled but removed before lymphodepletion due to acute kidney injury

Treated Patients: 22

CAR+ T cells Dose	39mg ALLO-647	90mg ALLO-647
40 x 10^6 CAR^+ T cells	4	0
120 x 10^6 CAR^+ T cells	4	6
360 x 10^6 CAR^+ T cells	3	5

- Efficacy Analysis Set (All patients with at least 1 imaging assessment): **19**
- One lot of ALLO-501 used

Median/Mean Time from Enrollment to Start of Lymphodepletion: ***5 Days***

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ALLO-501 and ALLO-647 Demonstrate Manageable Safety Profile

AE of Interest ‡	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)	All grades n (%)
Cytokine Release Syndrome *	2 (9%)	4 (18%)	1 (5%)	-	-	7 (32%)
ICANS *	-	-	-	-	-	-
Graft-versus-Host Disease	-	-	-	-	-	-
Infection	5 (23%)	4 (18%)	2 (9%)†	-	-	11 (50%)
Infusion Reaction #	1 (5%)	9 (41%)	1 (5%)	-	-	11 (50%)
Neutropenia	-	1 (5%)	7 (32%)	7 (32%)	-	15 (68%)

- No DLT, GvHD
- Manageable CRS
- ALLO-501 toxicity not dose-proportional
- Median duration of hospitalization from D0: 7 days

Serious Adverse Events (time to resolution) ‡

- **4 patients (18%):**
  - Gr2 pyrexia (2 days) and Gr2 CMV reactivation (6 days)
  - Gr3 rotavirus infection (15 days) and Gr3 hypokalemia (2 days)
  - Gr3 febrile neutropenia (2 days) and Gr3 hypotension (2 days)
  - Gr3 upper GI hemorrhage (<1 day) and Gr3 CMV reactivation (25 days)

* ASTCT Lee, 2019. ICANS: Immune Effector Cell-Associated Neurotoxicity Syndrome
† CMV reactivations and Rotavirus infection
# attributed to ALLO-647

‡ Number of patients with AE regardless of attribution unless otherwise indicated, occurring from the start of study drug up to subsequent anti-cancer therapy (for patients reporting more than one AE within a preferred term, only one AE with the maximum grade is reported).

Data Cutoff Date: May 11, 2020

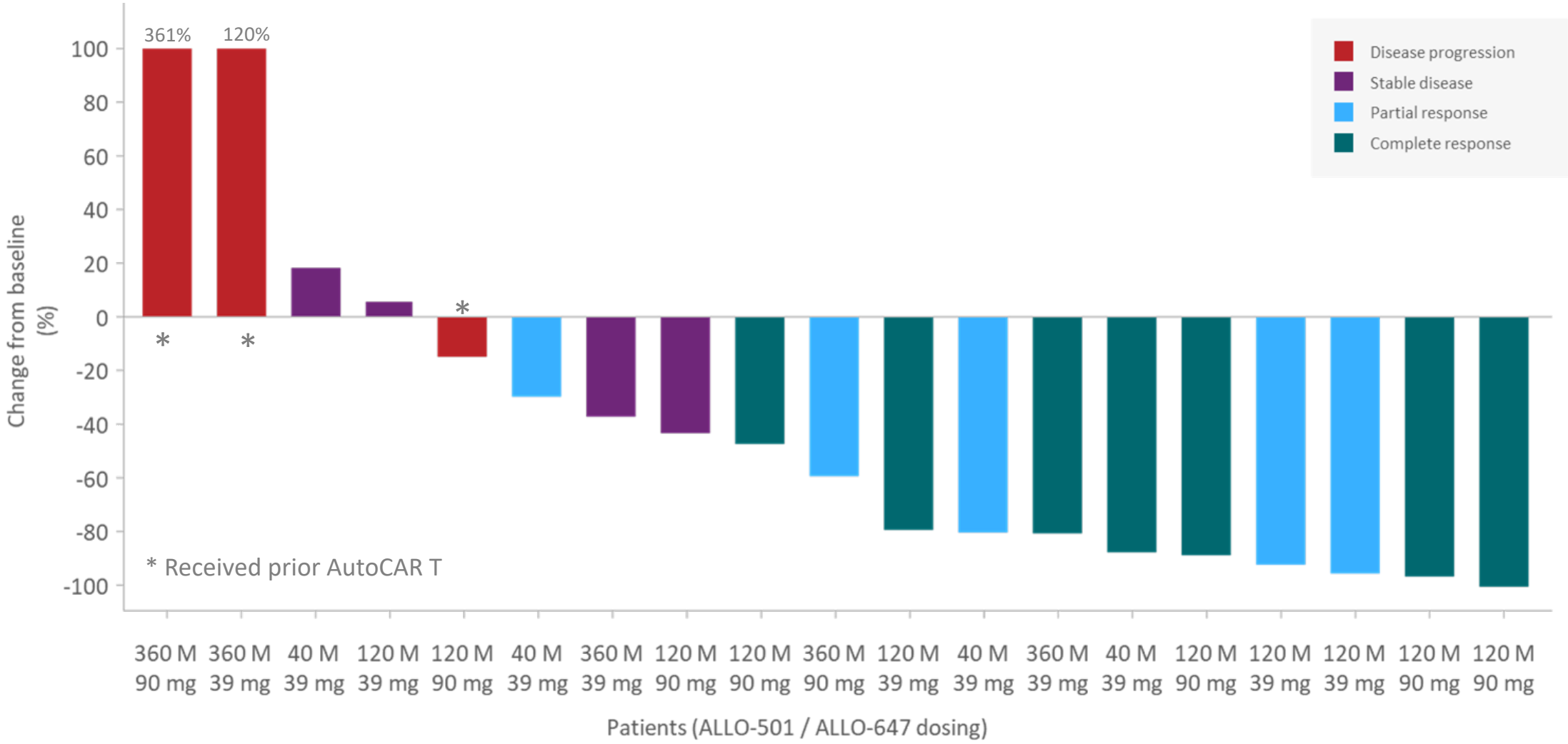
Phase 1 ALPHA Best Overall Response

Cell Dose and LD regimen	39mg ALLO-647			ALL 39mg ALLO-647 (N = 11)	90mg ALLO-647		All 90mg ALLO-647 (N=8)	All Patients (N=19) Rate (95%CI)
	40 x 10^6 CAR^+ cells (N=4)	120 x 10^6 CAR^+ cells (N=4)	360 x 10^6 CAR^+ cells (N=3)		120 x 10^6 CAR^+ cells (N=6)	360 x 10^6 CAR^+ cells (N=2)		
ORR, n (%)	3 (75%)	3 (75%)	1 (33%)	7 (64%)	4 (67%)	1 (50%)	5 (63%)	12/19 (63%) (38%, 84%)
CR , n (%)	1 (25%)	1 (25%)	1 (33%)	3 (27%)	4 (67%)	0 (0%)	4 (50%)	7/19 (37%) (16%, 62%)

Median follow-up time: 3.8 months (range: 0.7 - 6.1)

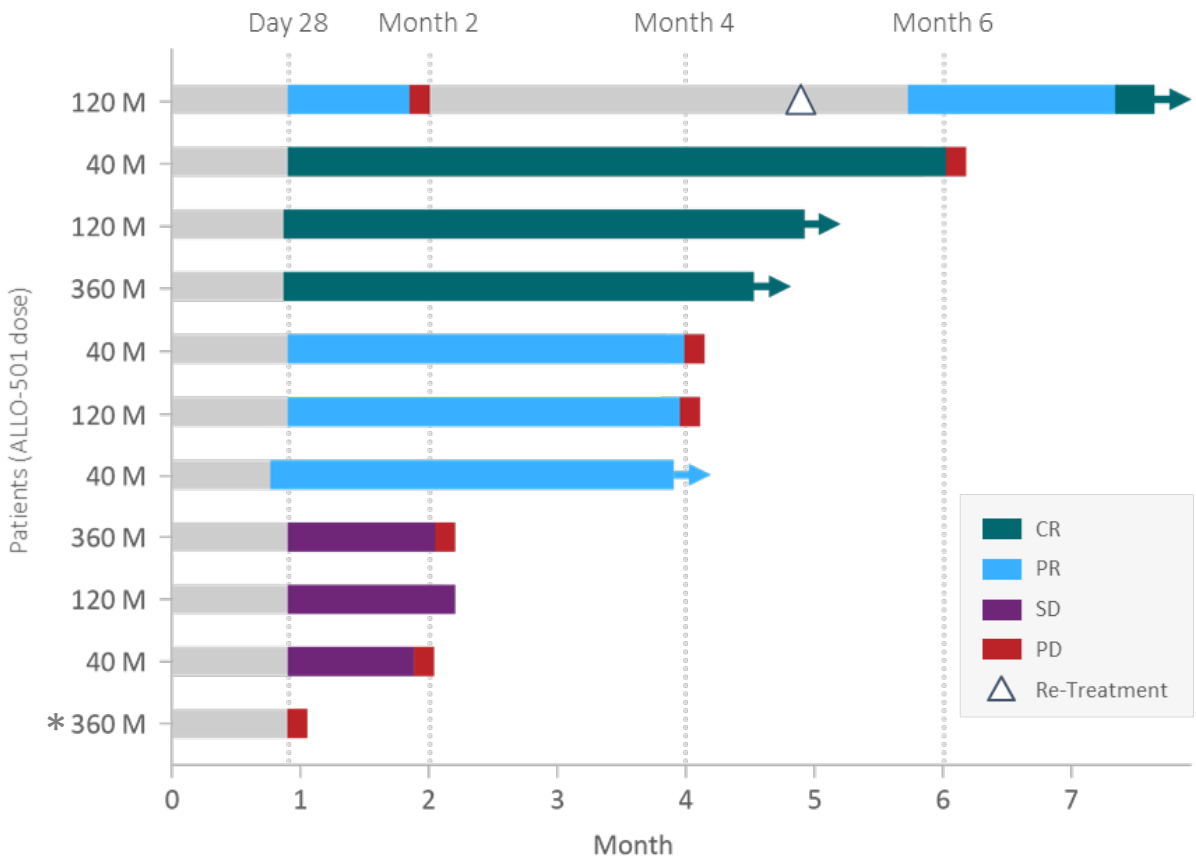
Lugano 2014; Data Cutoff Date: May 11, 2020

Reduction in Tumor Size Observed with ALLO-501



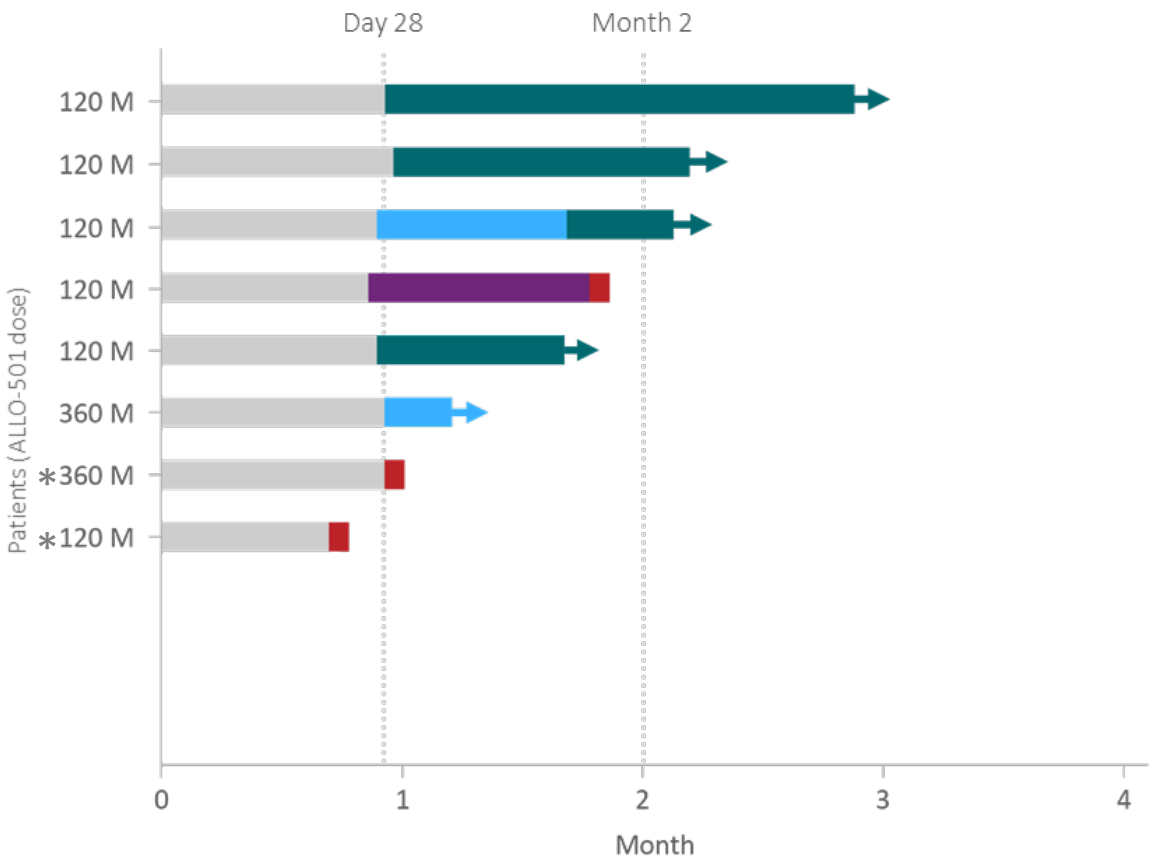
Data Cutoff Date: May 11, 2020

Nine of Twelve Responders Remain in Response



ALLO-647: 39 mg

Median follow up: 4.3 months (1.0, 6.1)



ALLO-647: 90 mg

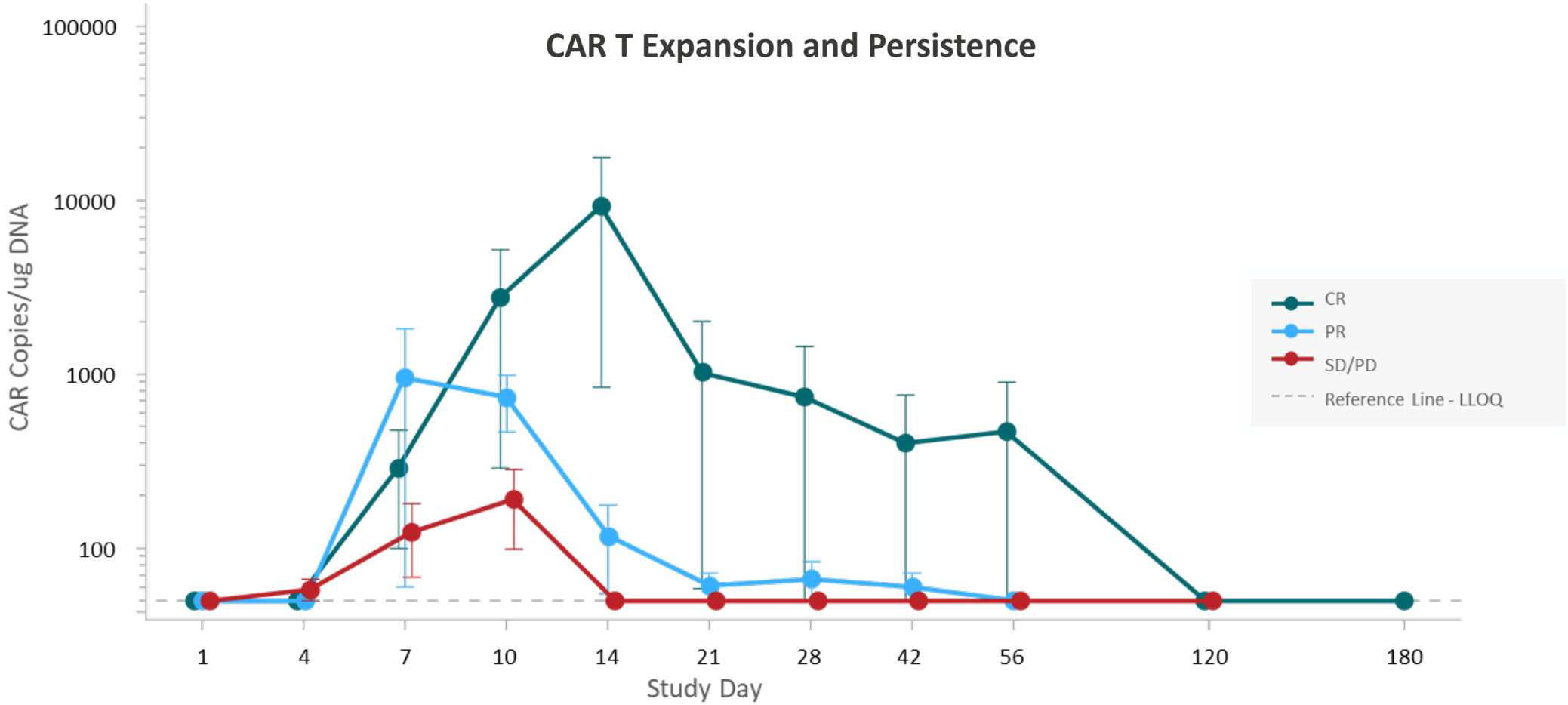
Median follow up: 1.9 months (0.7, 2.6)

One patient who progressed after a PR was re-dosed with ALLO-501 (120 x 10^6) and Flu/Cy/90mg ALLO-647 and achieved a CR

* Received prior AutoCAR T

Data Cutoff Date: May 11, 2020

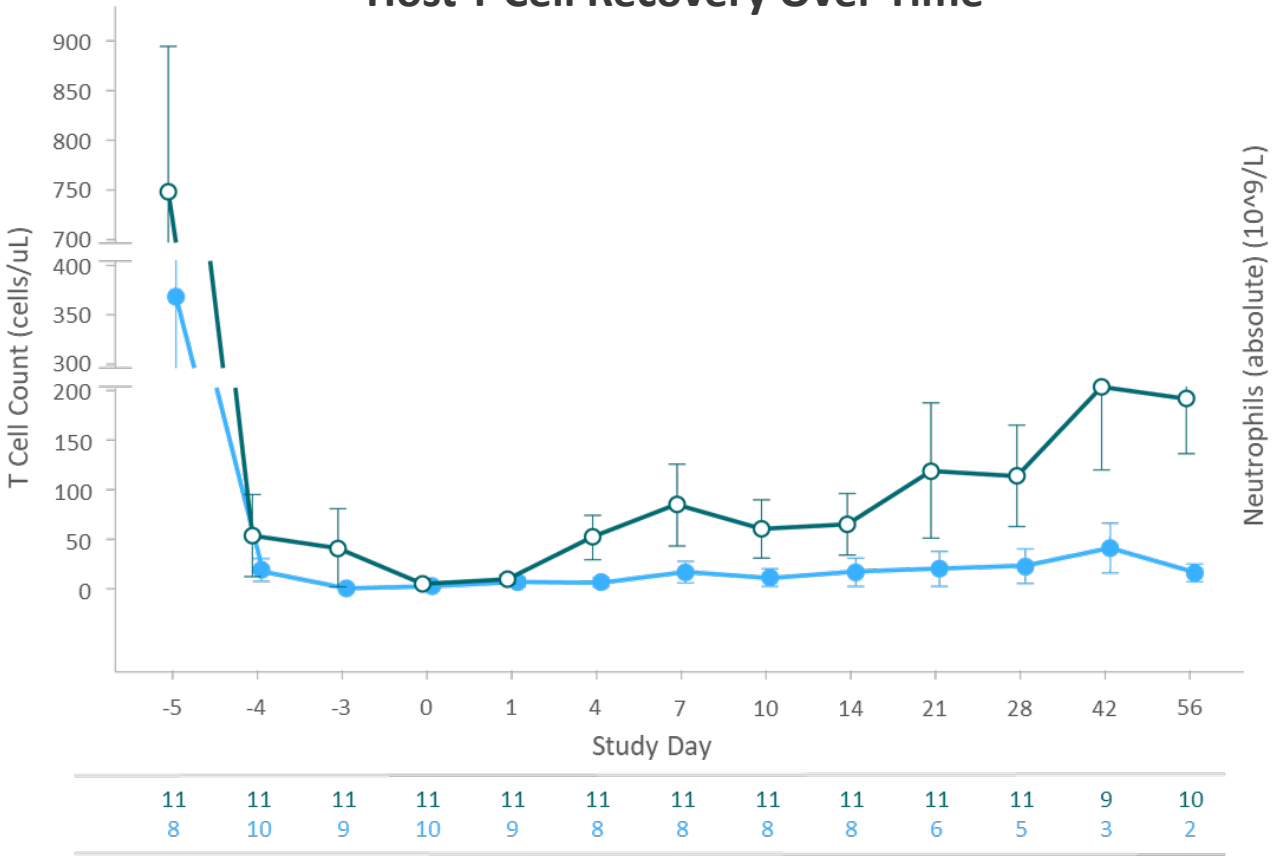
AlloCAR T Cell Expansion Is Associated with Clinical Response



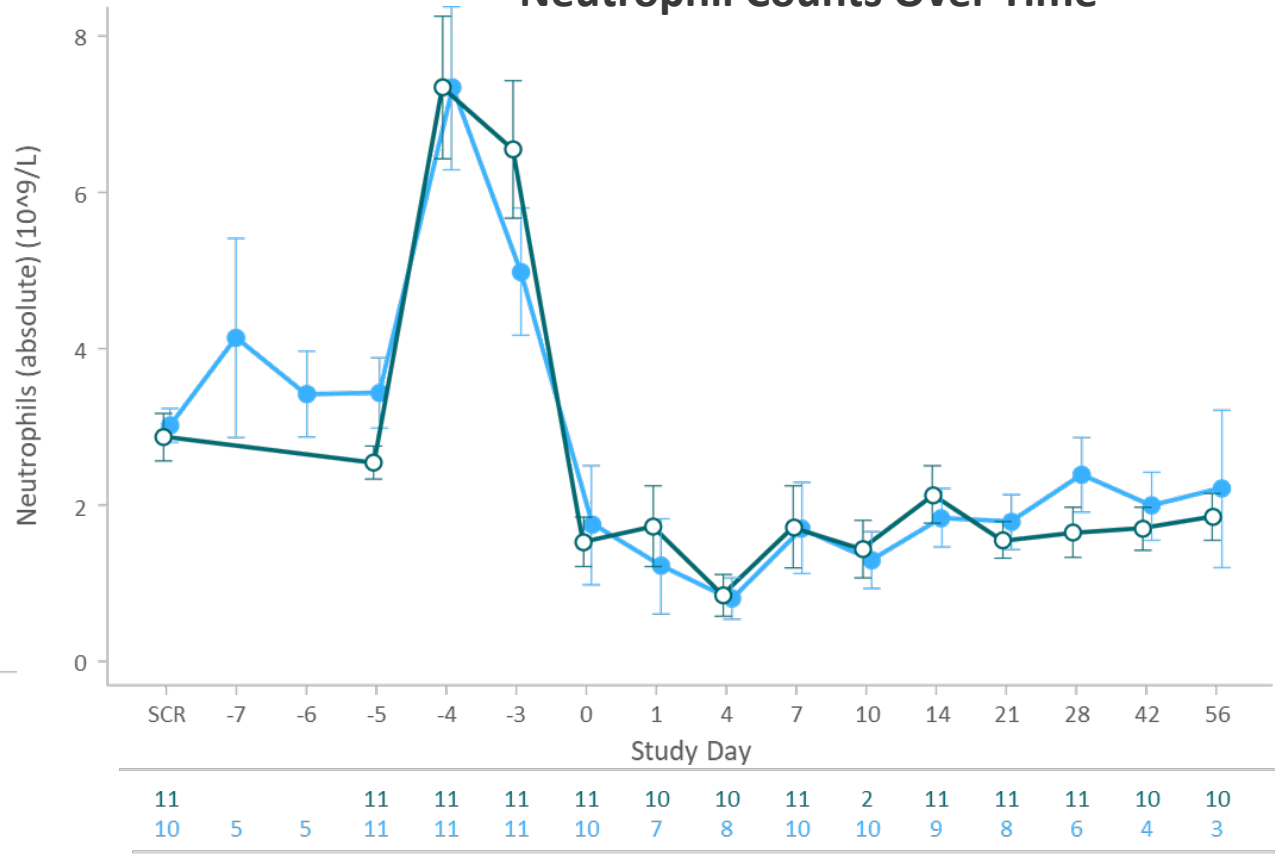
CR	6	5	5	6	6	6	6	2	2	1	1
PR	4	4	4	4	4	4	4	4	3		
SD/PD	6	6	6	6	6	6	5	2	2	1	

ALLO-647 Mediates Selective Lymphodepletion

Host T Cell Recovery Over Time



Neutrophil Counts Over Time

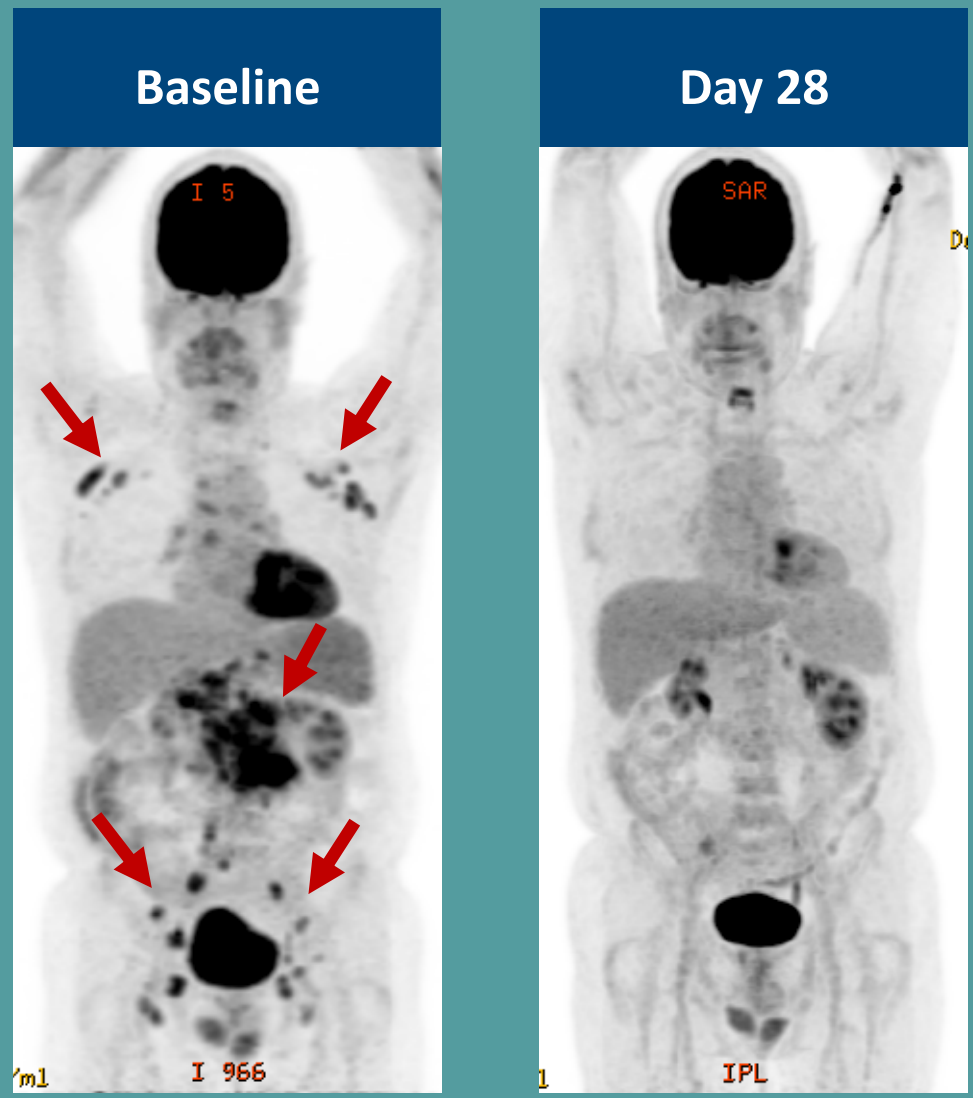


- No difference in neutrophil kinetics between ALLO-647 treatment groups
- Median time to Platelet >=100K is 8 days for 90mg ALLO-647 dose cohort

ALLO-501 Patient Case Study

- **120 x 10^6 CAR^+ T cells after Flu/Cy + 39mg ALLO-647**
- 70-year-old male with follicular lymphoma
- FLIPI 4, stage 4 (bone marrow infiltration), splenic involvement
- Primary refractory with 4 prior lines of therapy (best outcome)
    1. R-Benda x 4 cycles (PD)
    2. R-CHOP x 2 cycles (SD)
    3. R-Len x 2 cycles (PD)
    4. Copanlisib x 2 cycles (SD)
- Safety:
    - ALLO-647-related: Gr1 pyrexia

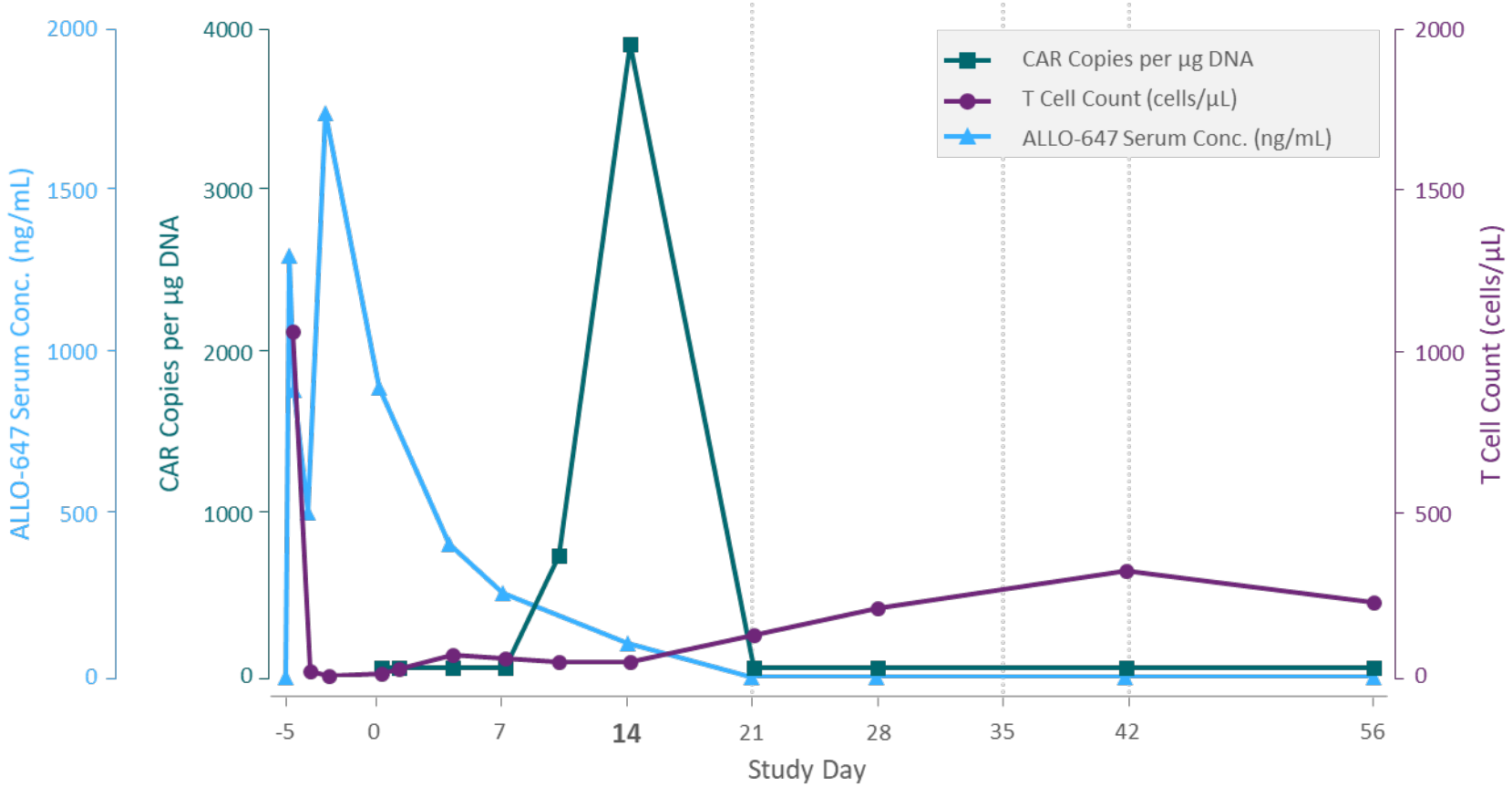
Patient remains in CR at Month 4



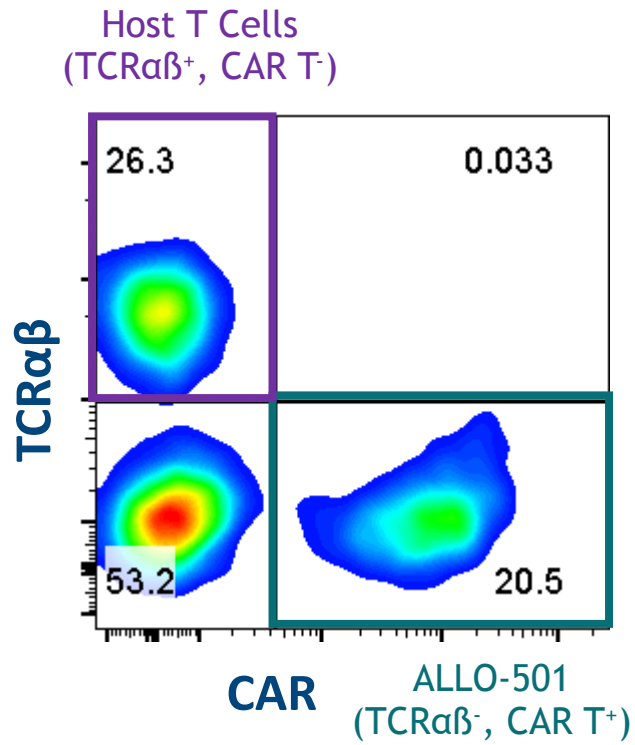
Courtesy of Sattva Neelapu

ALLO-501 Patient Case Study:
AlloCAR T Expansion Occurs During Lymphodepletion Window

ALLO-647 PK, CAR Expansion and T Cell Recovery Over Time



Flow Plot of Patient Lymphocytes on D14



Conclusions

- **ALLO-501 and ALLO-647 based lymphodepletion (LD) were well tolerated**
  - No DLT, GvHD or ICANS
  - Manageable CRS and no >Gr3 infections
- **AlloCAR T cell expansion was associated with responses**
- **Anti-tumor activity was observed across all cell dose levels**
  - Overall: ORR observed in 12/19 (63%) patients with 37% CR
  - 9 of the 12 (75%) responding patients remain in response as of the data cutoff
  - 1 patient achieved CR after the 2nd infusion of ALLO-501
- **ALLO-647 delays host T cell recovery**
  - Higher dose ALLO-647 appear to associate with deeper responses (50% CR)
- **Optimization of LD and patient follow-up is ongoing**
- **Phase I trial of ALLO-501A (ALLO-501 minus rituximab switch) is enrolling**

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Thank you

To Patients and their families, Clinical Trial Investigators and Sites, and Partners

ALLO-501 is an anti-CD19 allogeneic CAR T (AlloCAR T™) therapy being jointly developed under a collaboration agreement between Servier and Allogene based on an exclusive license granted by Cellectis to Servier. ALLO-501 uses Cellectis technologies. Servier grants to Allogene exclusive rights to ALLO-501 in the U.S. while Servier retains exclusive rights for all other countries.

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