First-In-Human Data of ALLO-501A, An Allogeneic Chimeric Antigen Receptor (CAR) T Cell Therapy, and ALLO-647 in Relapsed/Refractory Large B Cell Lymphoma (R/R LBCL): ALPHA2 Study

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Background

- Allogeneic chimeric antigen receptor (CAR) T cell therapy is promising to address logistical and manufacturing challenges of autologous CAR T cell therapy
- ALLO-501 is an anti-CD19 CAR T with rituximab recognition domains. Data from ALLO-501 support development of ALLO-501A, which excludes rituximab recognition domains
- ALLO-501A* (anti-CD19) is an allogeneic CAR T cell product whose utilizing TALEN® gene editing to 1) disrupted TCRα constant gene may reduce graft-versus-host disease (GvHD) risk, and 2) edited CD52 gene may permit use of ALLO-647 (a humanized anti-CD52 mAb) to selectively deplete host T cells

ALPHA Trial (Supporting Data)

Study Design - ALPHA

- Phase 1 study in patients (pts) with relapsed/refractory large B-cell lymphoma (R/R LBCL) or follicular lymphoma (FL) and ≥2 prior lines of therapy

Results - ALPHA

- 41 of 42 pts enrolled received ALLO-501 including 9 pts received prior autologous CAR T; 21 had FL, 20 had LBCL
- Treatment-failure-free (TFF) survival is defined as the time from the first dose of ALLO-501 to the last observed progression or death from any cause (Table 4)

Table 1. Patient Disposition, Demographics, and Disease Characteristics

	DL1 40M (N=4)	DL2 120M (N=16)	DL3 360M (N=18)	Consol. (N=3)	All patients (N=41)
Mean age (yrs)	56	62	57	60	59
Stage IV disease (%)	75	56	50	33	54
ECOG baseline of 0/1 (%)	75/25	50/44	28/72	67/33	44/54
Baseline LDH > ULN (%)	25	56	56	-	49
IPI score ≥3 (%)	25	50	50	-	44
Mean # prior regimens (SD)	3 (1)	4 (2)	4 (1)	6 (4)	4 (2)
Germinal center subtype (%)	50	6	39	33	27
Double or triple hit (%)	-	13	22	33	17

Table 2. ALPHA Adverse Events of Special Interest

	ALLO-647 39 mg (N=11)		ALLO-647 60 mg (N=6)		ALLO-647 90 mg (N=24)		All patients (N=41)	
n (%)	All Gr	Gr 3+	All Gr	Gr 3+	All Gr	Gr 3+	All Gr	Gr 3+
IRR	5 (46)	-	3 (50)	-	18 (75)	1 (4)	26 (63)	1 (2)
CRS	2 (18)	-	1 (17)	-	8 (33)	-	11 (27)	-
ICANS	-	-	-	-	1 (4)	1 (4)	1 (2)	1 (2)
GvHD	-	-	-	-	-	-	-	-
Infection	7 (64)	1 (9)	1 (17)	1 (17)	17 (71)	8 (33)	25 (61)	10 (24)
SAE-TEAE/ ALLO-501	1 (9)	-	-	-	-	3 (13)	4 (10)	4 (10)

Table 3. ORR for AutoCAR-Naïve by Disease Subtype (mITT†)

	FL	LBCL	All patients
n (%)	All FL (N=21)	(N=11)	(N=32)
ORR	17 (81)	7 (64)	24 (75)
95% CI	58, 95	31, 89	57, 89
CR	10 (48)	5 (46)	15 (47)
95% CI	26, 70	17, 77	29, 65

*TALEN® gene editing is a technology pioneered and controlled by Cellectis.

†ITT for FL is as in Table 3. ITT for LBCL was 58% (ORR) and 42% (CR).

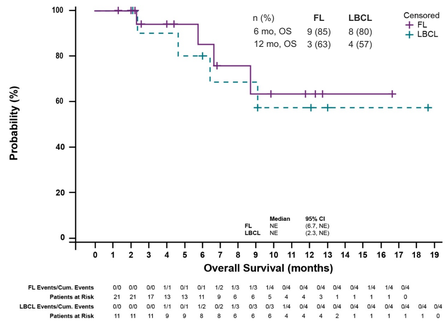
ALPHA Trial (Supporting Data)

Table 4. Treatment-Failure-Free Survival for AutoCAR Naïve Patients

KM Estimate % (95% CI)	FL (N=21)	LBCL (N=11)	All patients (N=32)
3 Month	76 (48, 90)	61 (27, 84)	71 (50, 84)
6 Month	64 (36, 82)	61 (27, 84)	63 (42, 78)

- Among the 5 LBCL AutoCAR-naïve pts who attained CR, 3 remain‡ in ongoing CR with DOR of 5.1, 11.1, and 11.2 months. Ongoing responses§ indicate one pt is in CR at month 15
- 2 pts with FL remain in CR at month 12 and 15, respectively

Figure 1. Kaplan-Meier Curves for Overall Survival for AutoCAR-Naïve Patients by Disease Subtype



ALPHA2 Methods

Study Design - ALPHA2

- Using the learnings of ALPHA, ALPHA2 was designed as a single-arm, open-label, Phase 1/2 study of ALLO-501A in non-HLA matched pts with R/R LBCL (DLBCL, tFL, tMZL, PMBCL, FL 3B) and ≥2 prior lines of therapy, including an anthracycline and anti-CD20 monoclonal antibody
- Retreatment was allowed for PD or SD with suboptimal CAR T expansion
- In a recent amendment, pts who had ≥SD at D28 received consolidation therapy with an additional 30 mg dose of ALLO-647 (total dose of 90 mg) and ALLO-501A cell infusion

Endpoints

- Primary: Safety, tolerability, and cell kinetics of ALLO-501A following LD
- Secondary: ORR by investigator assessment; ALLO-501A cell kinetics

Table 5. Patient Disposition, Demographics, and Disease Characteristics

	DL1 (N=1)	DL2 (N=6)	Consolidation (N=6)	All patients (N=13)
Mean age (yrs)	60	52	57	55
Stage IV disease (%)	100	33	33	39
ECOG baseline of 0/1 (%)	0/100	17/83	50/50	31/69
Baseline LDH > ULN (%)	100	100	33	69
IPI score ≥3 (%)	100	17	67	46
Mean # prior regimens (SD)	5 (NE)	4 (2)	2 (1)	3 (2)
Prior anti-CD19 (%)	100	33	17	31
Germinal center subtype (%)	100	33	67	54
Double or triple hit (%)	100	33	50	46

‡At last protocol specified scan.

§Unaudited results.

ALPHA2 Results

Safety Results

- No patient experienced dose limiting toxicities (DLTs)
- In the consolidation arm, a second dose of ALLO-647 and cell infusion were planned to be administered. No CRS, no ICANS, no DLTs, no dose reductions, and no related SAEs occurred (Table 6)
- Most common adverse events (AEs) were neutropenia, leukopenia, lymphopenia thrombocytopenia and anemia (Table 7)

Table 6. ALPHA2 Adverse Events of Special Interest

	DL1 40M (N=1)		DL2 120M (N=5)		Consolidation 120M + 120M (N=6)		All patients (N=13¶)	
n (%)	All Gr	Gr 3+	All Gr	Gr 3+	All Gr	Gr 3+	All Gr	Gr 3+
IRR	1 (100)	-	2 (40)	-	2 (33)	-	5 (39)	-
CRS	1 (100)	1 (100)	1 (20)	-	-	-	2 (15)	1 (8)
ICANS	-	-	-	-	-	-	-	-
GvHD	-	-	-	-	-	-	-	-
Infection	1 (100)	-	4 (80)	1 (20)	2 (33)	-	7 (54)	1 (8)
SAE-TEAE/ALLO-501A	-	-	1 (20)	-	-	-	1 (8)	-

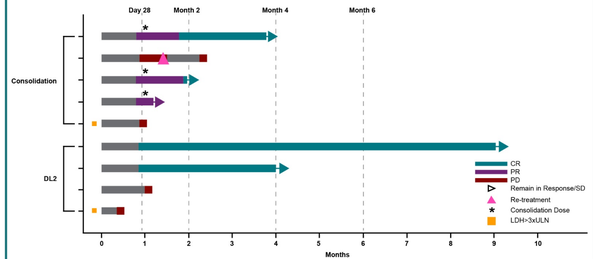
Table 7. Gr 3+ Treatment Emergent AEs (Safety Analysis Set)

	DL1 (N=1)	DL2 (N=5)	Consolidation (N=6)	All patients (N=13¶)
n (%)				
Pts with any TEAE	1 (100)	5 (100)	3 (50)	10 (77)
Neutropenia	-	5 (100)	3 (50)	9 (70)
Leukopenia	1 (100)	5 (100)	1 (17)	8 (62)
Lymphopenia	-	4 (80)	2 (33)	7 (54)
Thrombocytopenia	1 (100)	3 (60)	1 (17)	6 (46)
Anemia	1 (100)	4 (80)	-	5 (39)

Table 8. ORR for AutoCAR Naïve Patients and Responders to Prior AutoCAR Therapy

	DL2 (N=4)	Consolidation (N=5)	All patients# (N=9)
n (%)			
ORR	2 (50)	3 (60)	5 (56)
95% CI	7, 93	15, 95	21, 86
CR	2 (50)	2 (40)	4 (44)
95% CI	7, 93	5, 85	14, 79

Figure 2. Swimmer Plot of Tumor Response to Study Treatment

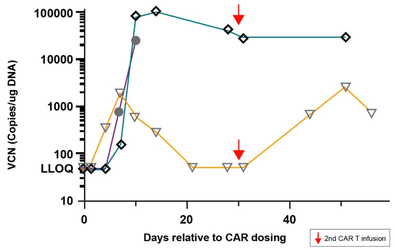


¶One subject was treated with ALLO-647 and not treated with ALLO-501A.

#One patient was not treated. One patient at DL1 had no response so is not included.

ALPHA2 Results

Figure 3. Vector Copy Number for Consolidated Patients Shows Expansion After 2nd CAR T Dose



In Figure 3, each line represents one patient.

Table 9. Responses in Patients Who Received Consolidation Dose Across Studies

Study/disease	Time from 1st dose (months)	D28	D56	Month 4
ALPHA2/LBCL	4	PR	CR	CR
ALPHA2/LBCL	3	PR	CR	-
ALPHA2/LBCL	1	PR	-	-
ALPHA/FL	3	CR	CR	-
ALPHA/FL	1	PR	-	-
ALPHA/FL	1	PR	-	-

In Table 9, dash (-) represents pts who have not yet reached the timepoint and only includes subjects who received their second consolidation dose.

Conclusions

- Allogeneic CD19 CAR T therapy, ALLO-501, produced a deep durable response in pts with R/R NHL
  - In ALPHA study, 75% ORR including 47% CR were seen, on par with the RR seen in autologous CD19 CAR T therapies, with the longest ongoing remission ≥ 1+ year as of last scan
  - Re-dosing appeared to provide clinical benefit with an overall TFFS rate of 63% at 6 months (Table 4)
- ITT results were nearly identical to mITT results and pts were treated within a median of 5 days from enrollment to LD
- ALLO-501A mirrored the efficacy and safety results seen in ALLO-501
  - In the ALPHA2 study, 56% ORR, including 44% CR were seen in CAR T naïve pts with R/R LBCL (Table 8)
  - The benefits of consolidation dosing was demonstrated in 3/3 pts who had a scan after the second dose (Table 9)
- Across both studies, ALLO-501 and ALLO-501A (one or two doses) in combination with ALLO-647 lymphodepletion were well-tolerated with no GvHD and one event each of Gr3 ICANS and Gr3 CRS
- Re-dosing at the time of disease progression or an upfront consolidation can be safely administered with emerging evidence of meaningful clinical benefit

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

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Data Cutoff Date: April 19, 2021.