Durable Responses With Anti-CD19 Allogeneic CAR T ALLO-501/ALLO-501A in Phase 1 Trials of Relapsed/Refractory Large B-Cell Lymphoma (r/r LBCL)

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Conflict of Interest (COI) Disclosures

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Honoraria:	Aptitude Health, ASH, BioPharma Communications CARE Education, Clinical Care Options Oncology, Imedex, Society for Immunotherapy of Cancer
Research Funding:	Allogene (Institutional), Bluebird Bio (Institutional), BMS (Institutional), CERo Therapeutics (Institutional), Kite Pharma (Institutional), Leukemia and Lymphoma Society, National Cancer Institute, Novartis (Institutional)
Travel Grants:	A2 Bio
Other Remuneration:	Several patents held by the institution in my name (unlicensed) in the field of cellular immunotherapy

Lekakis LJ No pertinent conflicts of interest to be declared

Eradat HA No pertinent conflicts of interest to be declared

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Consultant/Advisor:	ADC Therapeutics, Alexion, Bayer, Beigene, Bristol Myers Squibb, Debiopharm, Epizyme, Fosun Kite, Genmab, Innovent, Janssen, Juno/Celgene, Karyopharm, Kite Pharma, Kyowa Kirin, MorphoSys/Incyte, Novartis, Pfizer, Pharmacyclics/Abbvie, Seagen, Servier
Honoraria:	Curio, Kyowa Kirin, OncView, Physicians Education Resource, Seattle Genetics, Targeted Oncology

Tees M No pertinent conflicts of interest to be declared

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Consultant/Advisor:	Abbvie, ADC Therapeutics, Curio Science, Gilead, Janssen, Kite Pharma, Nektar, Novartis, Pfizer, TG Therapeutics
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Research Funding:	Allogene Therapeutics, Daiichi Sankyo, Kite Pharma

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Consultant/Advisor:	Cidara Therapeutics, Medigene, Merck, Miltenyi Biotec, MorphoSys, Nektar Therapeutics, Omeros, Orca Bio, Sellas Life Sciences, Servier
Honoraria:	Abbvie, Astellas, Bellicum, Bristol Myers Squibb, Celgene, Incyte, Karyopharm, Kite Pharma, Miltenyi Biotec, MorphoSys, Novartis, Takeda, VectivBio AG, Vor Biopharma
Research Funding:	Incyte, Kite
Other Remuneration:	DSMB

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Other Remuneration:	Pharmacyclics - patent & royalties

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Conflict of Interest (COI) Disclosures

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Honoraria:	Actinium, Incyte

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Malik SA No pertinent conflicts of interest to be declared

Popplewell LL No pertinent conflicts of interest to be declared

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Honoraria:	ADC Therapeutics, AstraZeneca, BioGene, Sanofi Genzyme
Research Funding:	ADC Therapeutics, Astellas Pharma, Spectrum Pharmaceuticals, Takeda

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Stock Ownership:	Allogene Therapeutics

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Stock Ownership:	Allogene Therapeutics
Other Remuneration:	Allogene Therapeutics - Patent & Royalty

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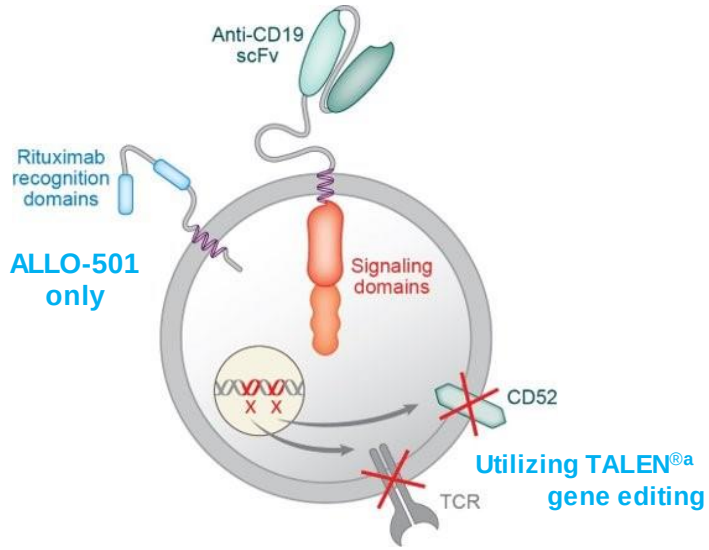
Consultant/Advisor:	Adicet Bio, Allogene Therapeutics, Aptitude Health, Bio Ascend, Bluebird Bio, Bristol Myers Squibb, Calibr, Celgene, Cell Medica/Kuur, Incyte, Kite Pharma, Legend Biotech, Medscape, Merck, Novartis, Pfizer, Precision Biosciences, Unum Therapeutics
Honoraria:	Adicet Bio, Allogene Therapeutics, Aptitude Health, Bio Ascend, Bluebird Bio, Bristol Myers Squibb, Calibr, Celgene, Cell Medica/Kuur, Incyte, Kite Pharma, Legend Biotech, Medscape, Merck, Novartis, Pfizer, Precision Biosciences, Unum Therapeutics
Research Funding:	Acerta, Adicet Bio, Allogene Therapeutics, Aptitude Health, Biosciences, Bristol Myers Squibb, Celgene, Cellectis, Karus Therapeutics, Kite Pharma, Merck, Poseida, Precision Biosciences, Unum Therapeutics
Travel Grants:	Adicet Bio, Allogene Therapeutics, Bristol Myers Squibb, Calibr, Celgene, Cell Medica/Kuur, Incyte, Kite Pharma, Legend Biotech, Merck, Novartis, Pfizer, Precision Biosciences, Unum Therapeutics
Other Remuneration:	Takeda - Patents & Royalties

Background

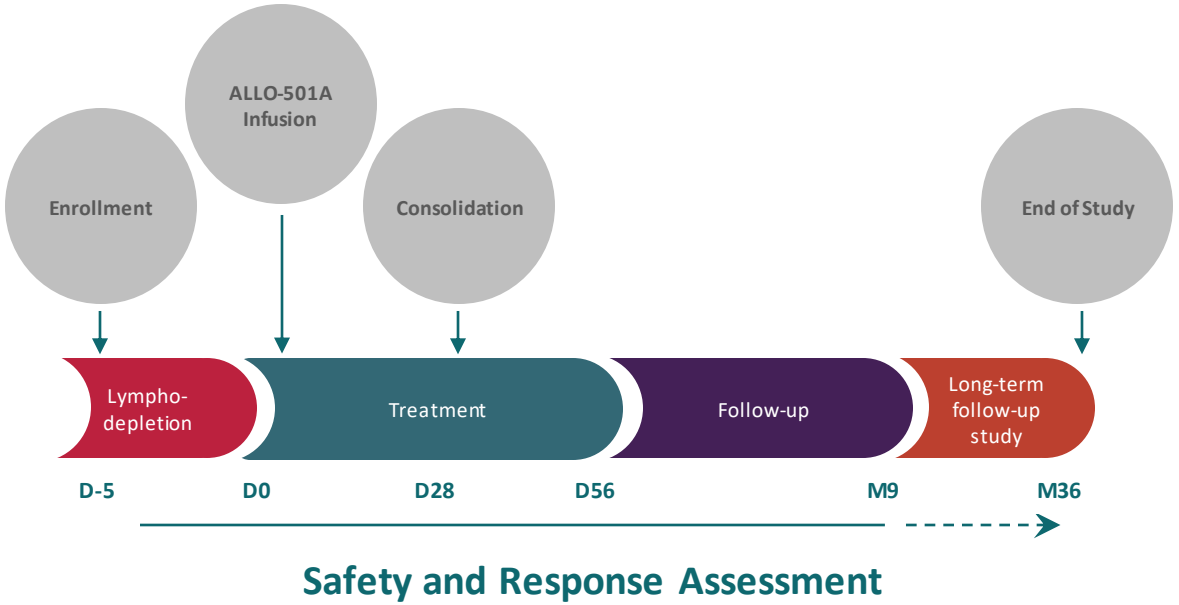
- Autologous anti-CD19 CAR T cell therapies have revolutionized the treatment of r/r LBCL. Despite this, these therapies are not available to all eligible patients due to lengthy and cumbersome manufacturing processes
- ALLO-501A, an allogeneic anti-CD19 CAR T cell product made from healthy donor T cells, may address this limitation and lack of access by providing patients with rapid access to off-the-shelf treatments that have the potential to drive durable responses
- Phase 1 data of ALLO-501A and precursor ALLO-501 have demonstrated a manageable safety profile with no dose-limiting toxicities and efficacy outcomes comparable to published results for autologous CAR T cell therapy in r/r LBCL
- This update documents clinical results achieved to date with ALLO-501/ALLO-501A following lymphodepletion with fludarabine/cyclophosphamide/ALLO-647 (FCA) in patients with CAR T-naïve r/r LBCL



A = ALLO-647 (an anti-CD52 monoclonal antibody); CAR = chimeric antigen receptor.
[a] TALEN® gene editing is a technology pioneered and controlled by Cellectis.
Data cutoff: April 20, 2023.

Study Subgroup and Schema

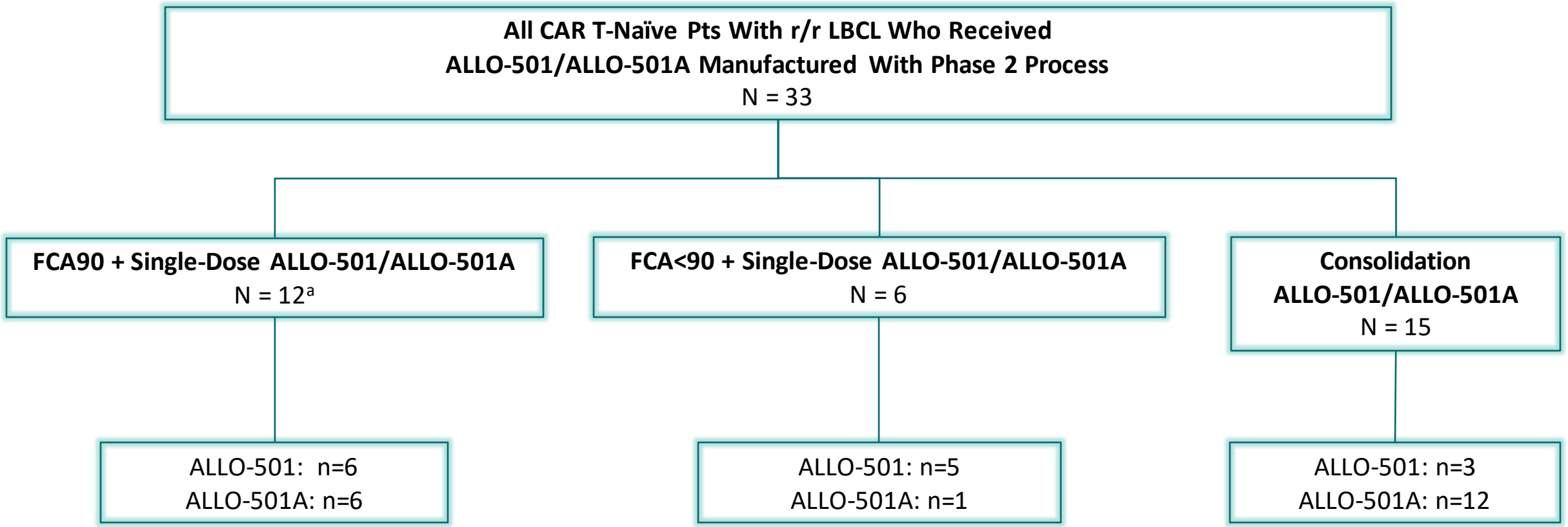
- Two Phase 1, open-label, multicenter studies of ALLO-501 and ALLO-501A (ALPHA and ALPHA2[a]) in patients with r/r NHL were conducted
- Subgroup for analysis: 33 CAR T-naïve patients with r/r LBCL treated with escalating doses of ALLO-501/ALLO-501A manufactured with the Phase 2 process given after lymphodepletion with FC and varying doses of ALLO-647



- Lymphodepletion regimens
  - Fludarabine 30 mg/m^2/day D-5 to D-3
  - Cyclophosphamide 300 mg/m^2/day D-5 to D-3
  - ALLO-647 from 13 mg/day – 30 mg/day from D-5 to D-3
- ALLO-501/ALLO-501A dosing
  - Single dose (Day 0) or two doses (Day 0 and Day 30; Consolidation regimen only)

NHL = non-Hodgkin lymphoma.
[a] NCT03939026 and NCT04416984, respectively.
Data cutoff: April 20, 2023.

Patient Disposition



[a] This treatment regimen is the Phase 2 Regimen and is the same cohort that was presented at ASCO/EHA 2023
Data cutoff: April 20, 2023.

Study Population and Treatment Experience

Baseline Characteristics of CAR T-Naïve Patients With r/r LBCL[a]	All (N=33)	Phase 2 Regimen[b] (N=12)	FCA<90 (N = 6)	Consolidation (N = 15)
Age (years), median	66	60	63	67
Stage IV disease (%)	58	67	67	47
ECOG PS of 1 (%)	79	92	50	80
Baseline LDH > ULN (%)	67	67	67	67
IPI score 3-5 (%)	58	50	33	73
Germinal center subtype (%)	55	50	50	60
Double or triple hit (%)	30	33	17	33
Median # prior regimens	3	3	3	3
Prior transplant[c] (%)	21	50	17	0
Extranodal disease (%)	58	58	67	53
Treatment Experience				
Time from enrollment to treatment initiation[d] (days)	2	3	5	2
Received product per specifications (%)	100	100	100	100
Required bridging therapy (%)	0	0	0	0
Follow-up duration (months), median	27.7	32.9	42.3	22.1

ECOG = Eastern Cooperative Oncology Group; IPI = International Prognostic Index; LDH = lactate dehydrogenase; ULN = upper limit of normal.
[a] All patients received product manufactured in the same way as the selected Phase 2 process. [b] FCA90 lymphodepletion followed by single-dose ALLO-501/ALLO-501A. [c] Conditional chemotherapy and hematopoietic stem-cell transplant.
[d] Median time from study enrollment to initiation of lymphodepletion.
Data cutoff: April 20, 2023.

Safety and Tolerability

Adverse Events of Interest	CAR T-Naïve Patients With r/r LBCL							
	All (N = 33)		Phase 2 Regimen (N = 12)		FCA<90 (N = 6)		Consolidation (N = 15)	
	All Gr n (%)	Gr ≥3 n (%)	All Gr n (%)	Gr ≥3 n (%)	All Gr n (%)	Gr ≥3 n (%)	All Gr n (%)	Gr ≥3 n (%)
CRS	8 (24)	0	4 (33)	0	1 (17)	0	3 (20)	0
Neurotoxicity	13 (39)	2 (6)	4 (33)	0	2 (33)	0	7 (47)	2 (13)
ICANS	0	0	0	0	0	0	0	0
GvHD	0	0	0	0	0	0	0	0
IRR	16 (49)	3 (9)	8 (67)	0	3 (50)	1 (17)	5 (33)	2 (13)
Infection[a]	19 (58)	5 (15)	8 (67)	1 (8)	3 (50)	1 (17)	8 (53)	3 (20)
Prolonged Gr ≥3 Cytopenia[b]	NA	4 (12)	NA	2 (17)	NA	0	NA	2 (13)

- No Gr ≥3 CRS events or any ICANS events were observed
- No GvHD events were observed
- Protocol required weekly CMV monitoring which yielded early detection of asymptomatic, low-grade viremia
- Gr ≥3 infections were CMV reactivation, pneumonia, bacteremia, sepsis, and COVID-19
- There were no fatal infections

CRS = cytokine release syndrome; Gr = Grade; GvHD = graft-versus-host disease; ICANS = immune effector cell-associated neurotoxicity syndrome; IRR = infusion-related reactions.
[a] Grade ≥3 infections and Adverse Events of Special Interest are collected through month 60 in patients without progression.
[b] Prolonged cytopenia is any grade 3 or higher cytopenia that is present 2 months after treatment and has been ongoing for at least 21 days.
Data cutoff: April 20, 2023

Efficacy: Response Rates

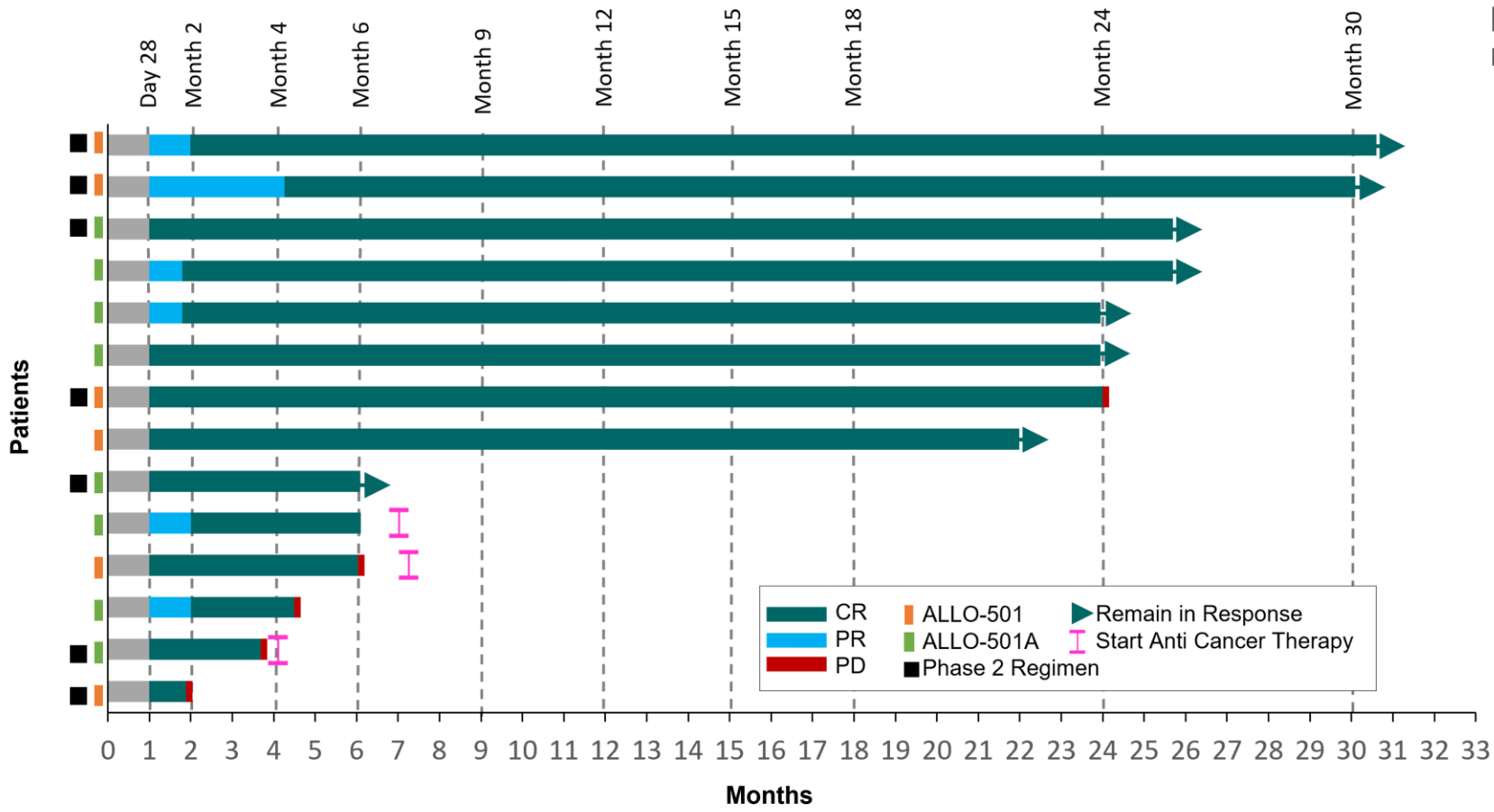
	CAR T-Naïve Patients With r/r LBCL			
	All (N=33)	Phase 2 Regimen (N=12)	FCA<90 (N = 6)	Consolidation (N = 15)
ORR, n (%)	19 (58)	8 (67)	3 (50)	8 (53)
CR, n (%)	14 (42)	7 (58)	1 (17)	6 (40)
6 months CR,[a] n (%)	10 (30)	5 (42)	0	5 (33)

- Overall response rate was similar across regimens
- Complete responses were more common with lymphodepletion regimens containing 90 mg of ALLO-647
- Six-month durable responses were most common in patients who received the Phase 2 Regimen

CR = complete response; ORR = overall response rate.
[a] Analysis of patients who had the opportunity to be followed through Month 6 or experienced disease progression prior to Month 6.
Data cutoff: April 20, 2023.

Durable Remissions in Patients Who Received ALLO-501/ALLO-501A

Patients With CR (n=14)

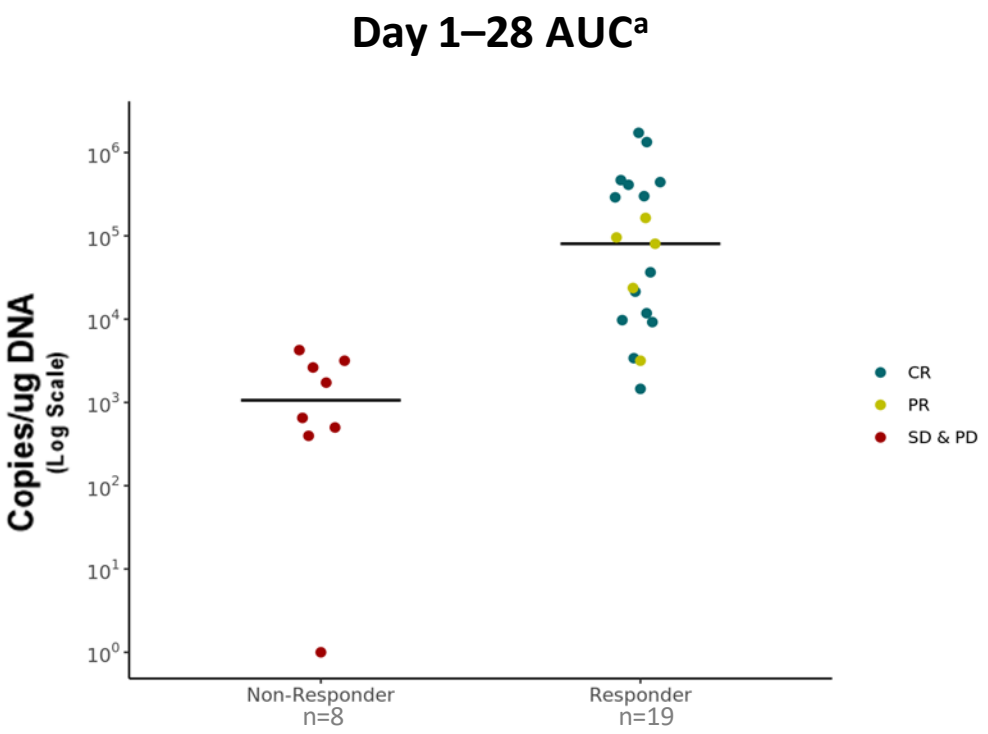


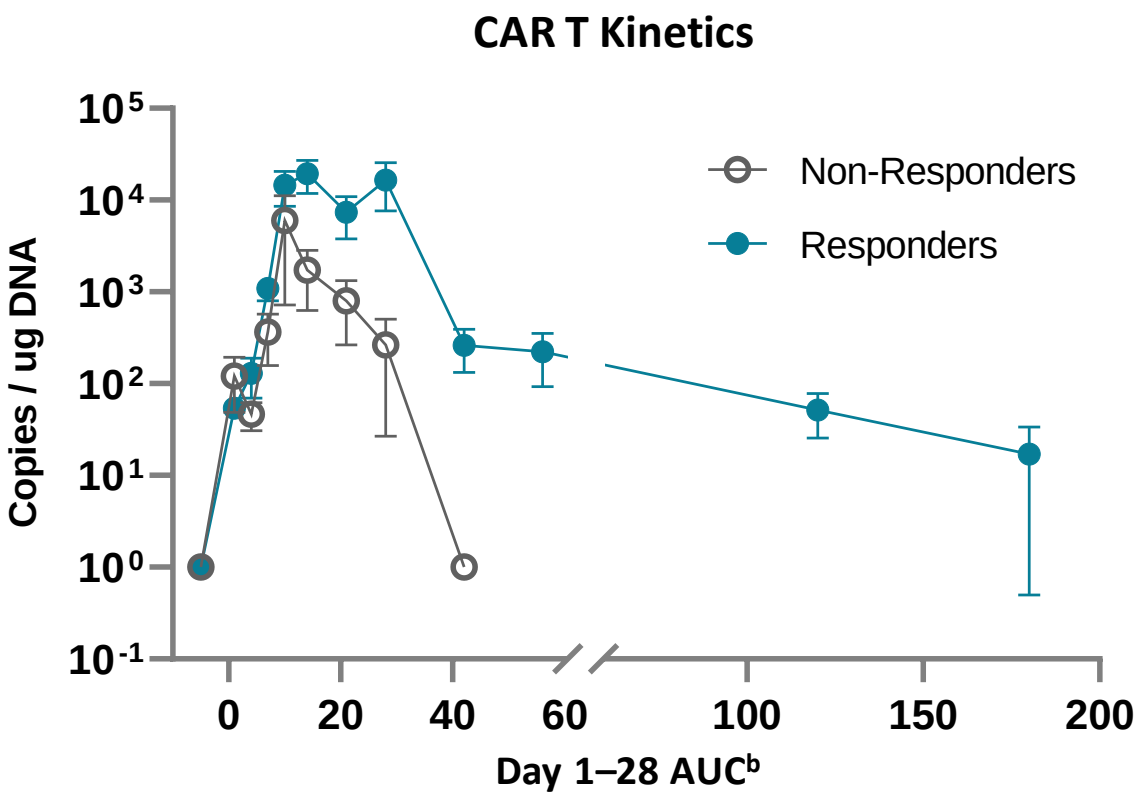
Durable responses were observed in patients who received lymphodepletion regimens containing 90 mg of ALLO-647

- Overall and Phase 2 Regimen median DOR was 23.1 months
- 30% (10/33) of patients had a CR lasting ≥ 6 months
- 42% (5/12) of patients who received the Phase 2 Regimen had a CR lasting ≥ 6 months
- 80% of patients overall (8/10) and of those treated with the Phase 2 Regimen (4/5) who were in CR at 6 months remained in CR as of the data cut date
- 6 patients remain in remission beyond 24 months
- Longest ongoing remission is 31+ months

CR = complete response; DOR = duration of response.
Data cutoff: April 20, 2023.

CAR T Cell Expansion Is Associated With Response

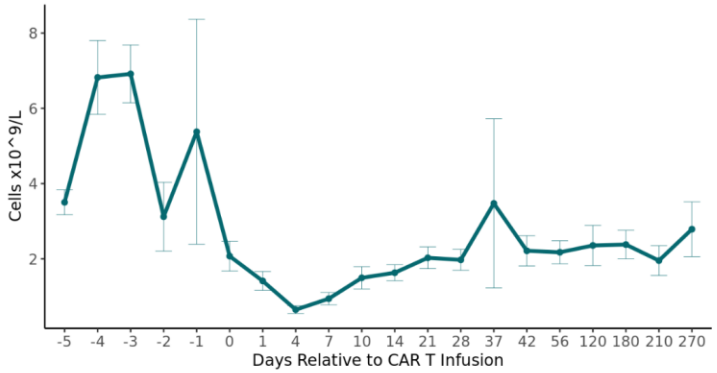




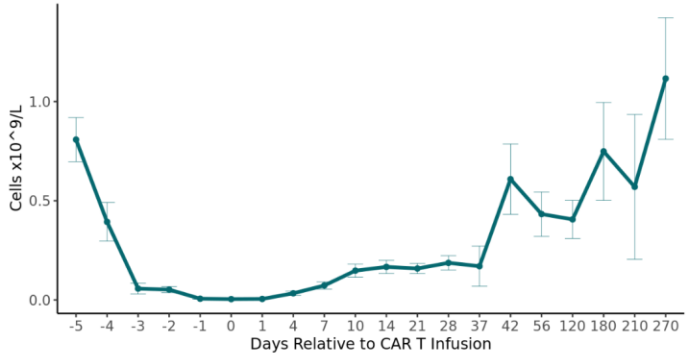
AUC = area under the curve; p = 0.0000554 by unpaired t-test.
[a] 6 subjects excluded from AUC for having missing data.
[b] Data shown for visits before, or without, consolidation or re-treatment.
Data cutoff: April 20, 2023.

Recovery of Leukocyte Counts

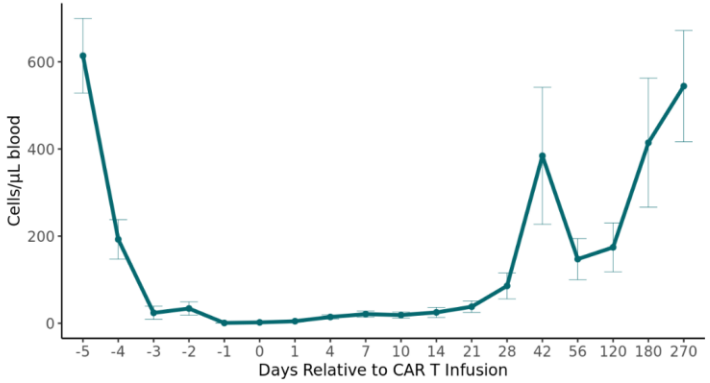
ANC



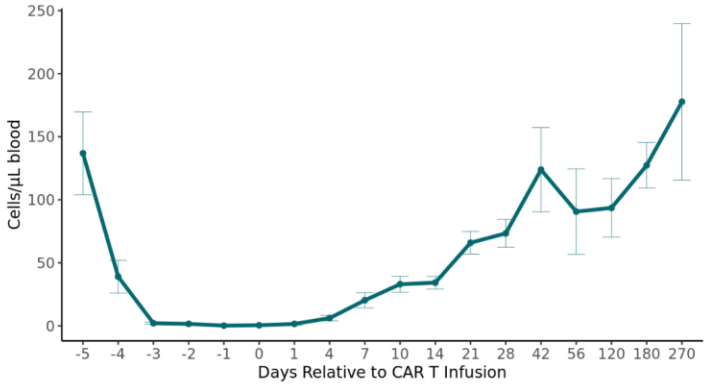
ALC



T Cell Counts



NK Cell Counts



- Neutrophils recovered[a] at a median of 7 days after ALLO-501/ALLO-501A
- Lymphocytes recovered[a] at a median of 17.5 days after ALLO-501/ALLO-501A
- T and NK cells recovered to baseline levels within 6–9 months post-infusion

ALC = absolute lymphocyte count; ANC = absolute neutrophil count; NK = natural killer.
[a] Defined as Common Terminology Criteria for Adverse Events (CTCAE) v5.0 < Grade 4.
Data cutoff: April 20, 2023.

Conclusions

1. ALLO-501/ALLO-501A, an off-the-shelf, anti-CD19 allogeneic CAR T cell product, expands, persists and generates durable complete responses in patients with r/r LBCL.
2. Efficacy was observed with all treatment regimens, however, benefit:risk and convenience appeared optimal with the regimen selected for Phase 2 – FCA90 lymphodepletion followed by a single dose of ALLO-501/ALLO-501A.
3. Response rate (67%) and durable CR rate (42%) were highest in patients who received the Phase 2 Regimen. These results are consistent with outcomes achieved with autologous CAR T cell therapies in r/r LBCL.
4. Safety with ALLO-501/ALLO-501A compared favorably to autologous CAR T therapy; there was no grade ≥3 CRS, and no ICANS or GvHD. Infections and leukocyte recovery were comparable to the experience with autologous CAR T cell therapy.
5. CAR T cell expansion was superior in responders vs non-responders with persistence up to 6 months.
6. FCA90 followed by a single dose of ALLO-501A CAR T cells is being evaluated in the potentially pivotal Phase 2 ALPHA2 (NCT04416984) and EXPAND (NCT05714345) trials.