



CTX110 Allogeneic CRISPR-Cas9–Engineered CAR T Cells in Patients (Pts) with Relapsed or Refractory (R/R) Large B-Cell Lymphoma (LBCL): Results From the Phase 1 Dose Escalation CARBON Study

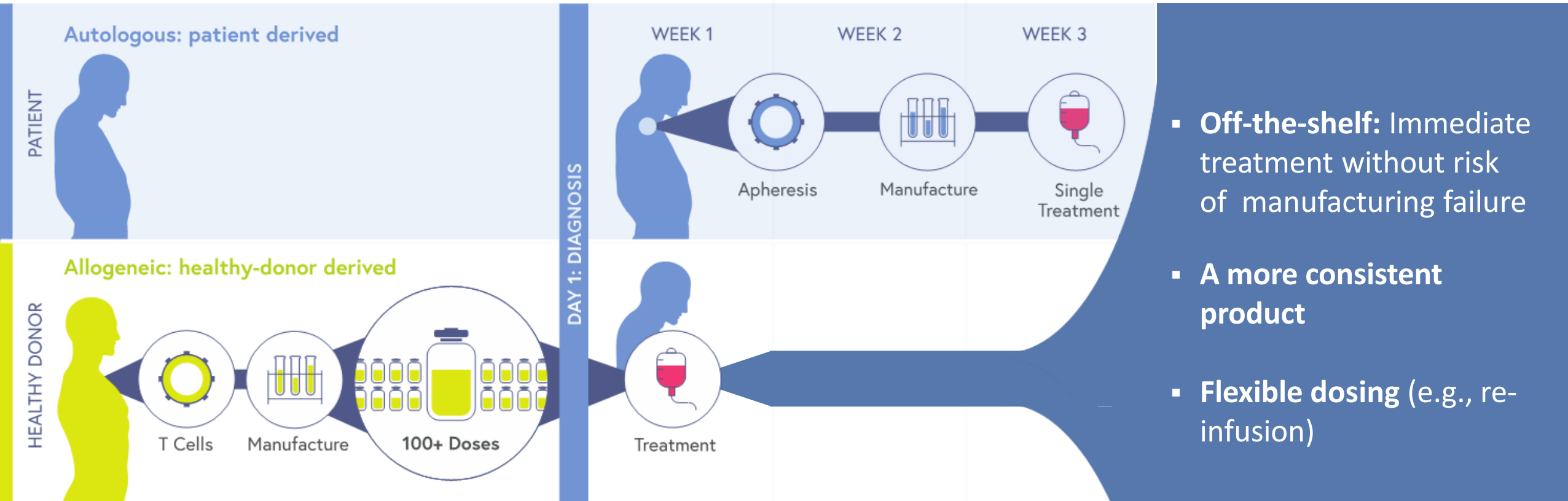
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Disclosures

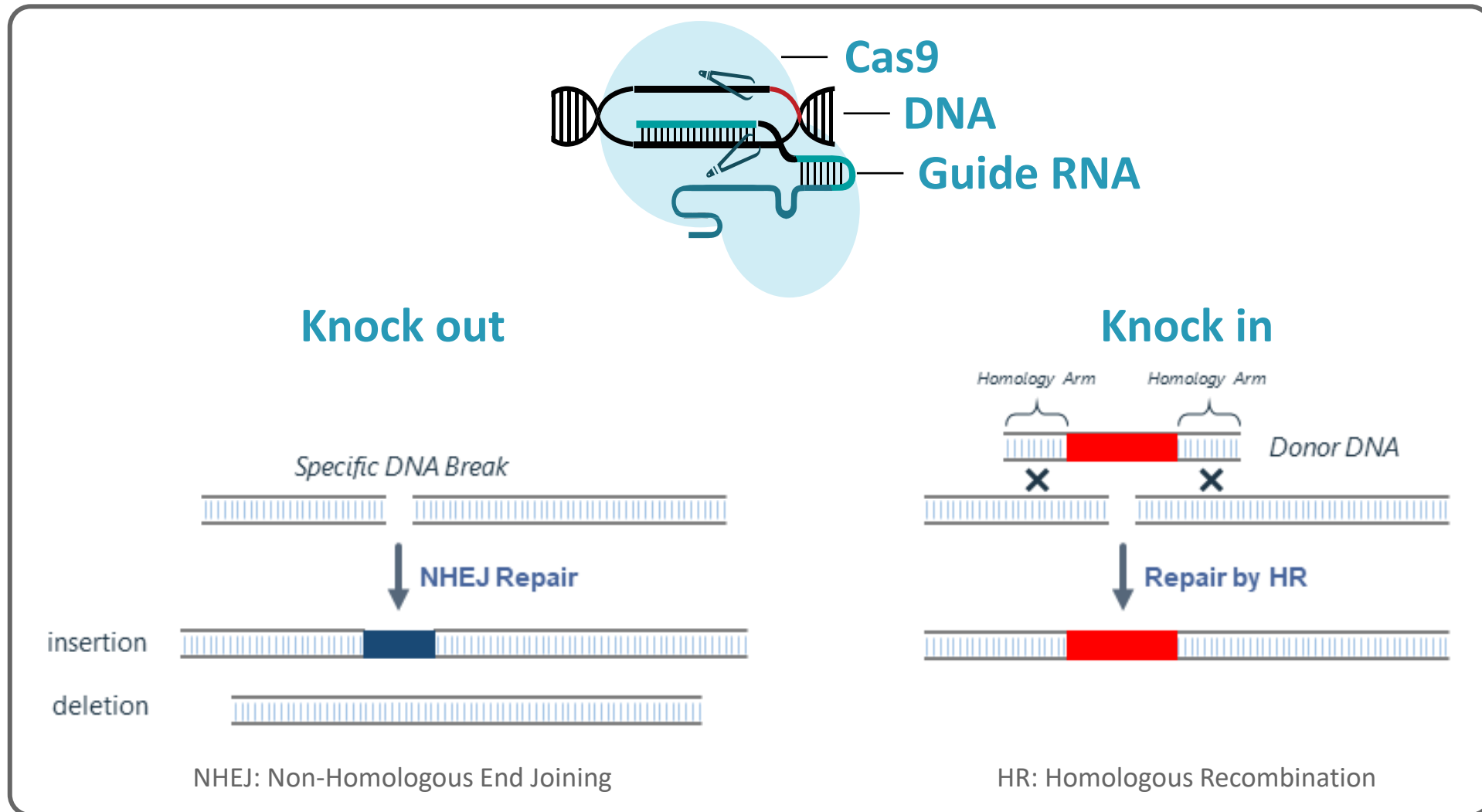
- Novartis: Consultancy, Honoraria; AlloVir: Consultancy, Honoraria, Research Funding, Speakers Bureau; Juno Therapeutics: Consultancy, Honoraria, Research Funding; Magenta Therapeutics: Consultancy, Honoraria, Research Funding; Kite, a Gilead Company: Consultancy, Honoraria, Research Funding, Speakers Bureau; Nektar: Consultancy, Honoraria; BMS: Consultancy, Honoraria, Speakers Bureau; Orca Bio: Research Funding; Sana: Honoraria; CRISPR Therapeutics: Consultancy; In8bio, Inc.: Other: IIT Clinical Trial

Healthy Donor Derived Allogeneic CAR-T Therapy



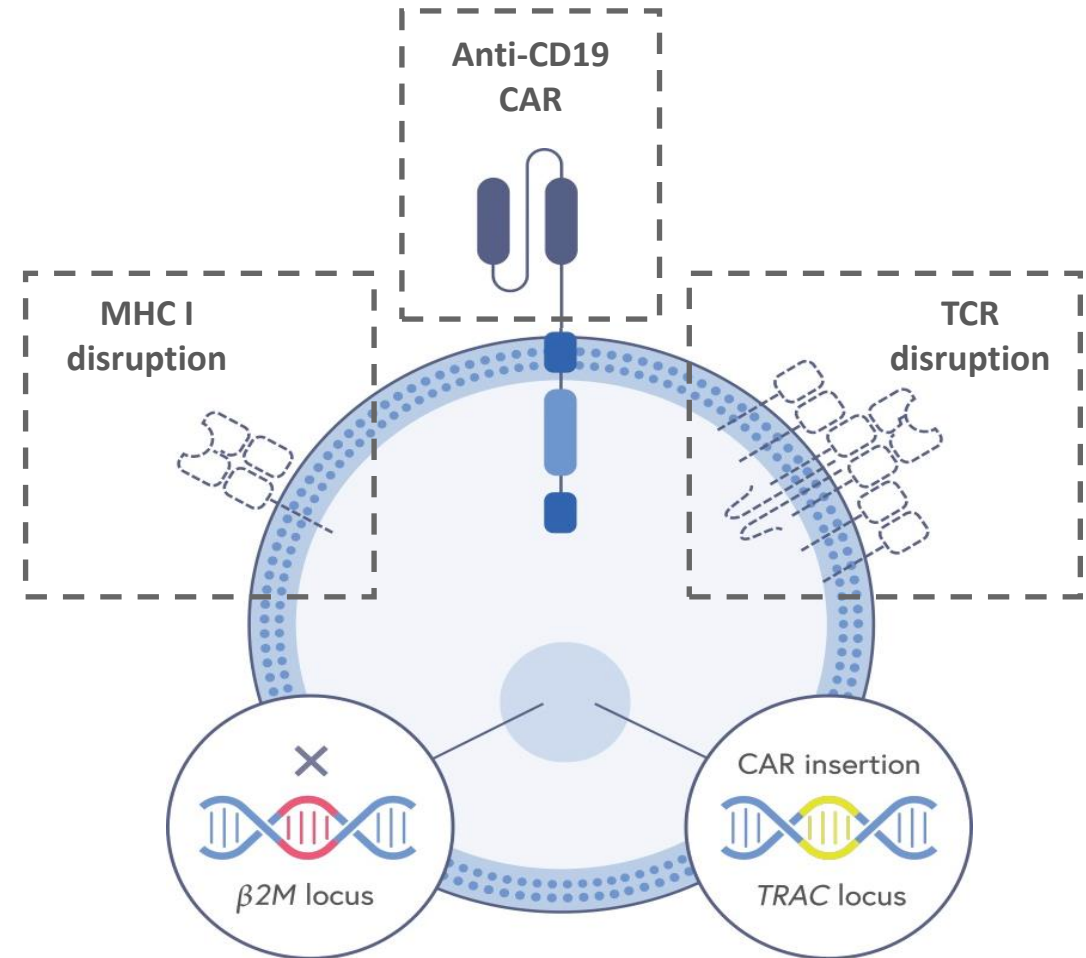
*Specificity, efficiency, and versatility of **CRISPR gene editing** facilitates consistent, multiplex editing to produce allogeneic cell therapies and enhance immune cell performance*

CRISPR/Cas9 Gene Editing Mechanism

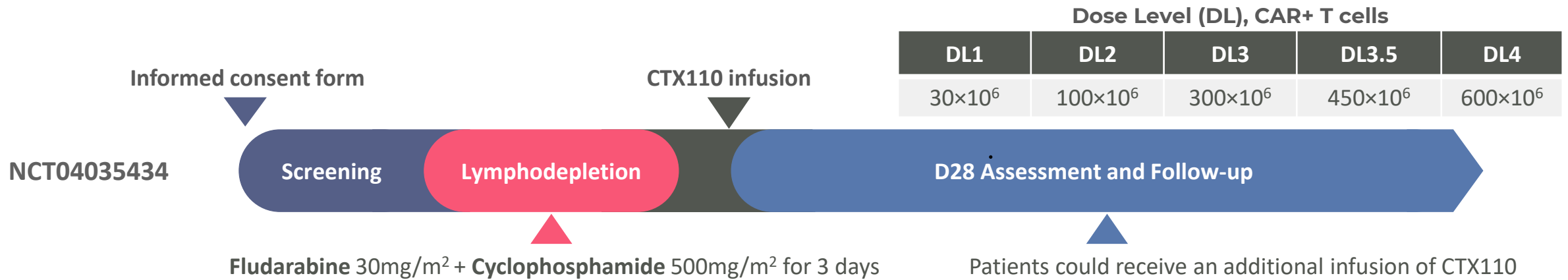


CTX110™

- Investigational allogeneic anti-CD19 CAR T cell therapy
- CRISPR/Cas9 editing to disrupt the TRAC locus and β 2 microglobulin (β 2M)
 - **TRAC disruption** removes T-cell receptor (TCR) expression to minimize risk of graft-versus-host disease (GvHD)
 - **β 2M disruption** eliminates major histocompatibility complex (MHC) class I expression to mitigate host T-cell-mediated clearance of CTX110
- **Anti-CD19 CAR transgene** construct is precisely inserted into the TRAC locus using an AAV vector
- We designed a phase 1 study to evaluate the safety and efficacy of CTX110 in patients with R/R LBCL and report here results from the dose-escalation phase of the study



CARBON™ Dose Escalation Trial Design



Allogeneic CAR T enables simplified trial design:

- Short screening timeframe
- No bridging chemotherapy
- No apheresis
- On-site availability of CAR-T cell product

Open-label, multicenter, Phase 1 study evaluating the safety and efficacy of CTX110 in subjects with relapsed or refractory B-cell malignancies.

Key eligibility criteria

- Age ≥18 years
- R/R DLBCL NOS, double- or triple-hit DLBCL, or transformed or grade 3b FL, as evidenced by ≥2 lines of prior therapy
- No prior allogeneic stem cell transplant (SCT) or treatment with CAR-T therapy
- No history of central nervous system (CNS) lymphoma involvement
- No minimum complete blood count requirements

Patients could receive an additional infusion of CTX110 if they achieved initial benefit and subsequently progressed. Additionally, a subset of patients were eligible for a second planned infusion on Day 35

Primary endpoint

- Incidence of adverse events (AEs), defined as dose-limiting toxicities (DLTs)
- Objective response rate (ORR, per Lugano 2014 criteria)

Secondary endpoints

- Complete response (CR) rate
- Duration of response (DOR)
- Overall survival (OS)

Patient Demographics and Baseline Characteristics

	DL1 30x10 ⁶ N=3	DL2 100x10 ⁶ N=3*	DL3 300x10 ⁶ N=6	DL3.5 450x10 ⁶ N=6	DL4 600x10 ⁶ N=14	Total N=32
Median age, y (range)	52 (50-61)	64 (58-74)	69 (62-74)	67.5 (25-74)	64 (35-75)	64 (25-75)
Female, n (%)	1 (33.3)	1 (33.3)	4 (66.7)	2 (33.3)	2 (14.3)	10 (31.3)
ECOG PS at screening, n (%)						
0	2 (66.7)	1 (33.3)	2 (33.3)	4 (66.7)	4 (28.6)	13 (40.6)
1	1 (33.3)	2 (66.7)	4 (66.7)	2 (33.3)	10 (71.4)	19 (59.4)
Refractory disease, n (%)	3 (100)	3 (100)	2 (33.3)	1 (16.7)	8 (57.1)	17 (53.1)
Prior anticancer therapies						
Median prior therapies, n (range)	2 (2-8)	3 (2-3)	2 (2-4)	2.5 (2-10)	2.5 (2-10)	2 (2-10)
≥3 prior therapies, n (%)	1 (33.3)	2 (66.7)	2 (33.3)	3 (50)	7 (50)	15 (46.9)
Prior stem cell transplant, n (%)	0	0	3 (50)	4 (66.7)	4 (28.6)	11 (34.4)
NHL subtype, n (%)						
DLBCL, NOS	1 (33.3)	2 (66.7)	2 (33.3)	4 (66.7)	8 (57.1)	17 (53.1)
HGBLCL w MYC/BCL2 and/or BCL6 rearr.	0	1 (33.3)	1 (16.7)	1 (16.7)	2 (14.3)	5 (15.6)
Transformed FL	1 (33.3)	0	2 (33.3)	1 (16.7)	3 (21.4)	7 (21.9)
Grade 3b FL	0	0	0	0	1 (7.1)	1 (3.1)
Other†	1 (33.3)	0	1 (16.7)	0	0	2 (6.2)
Bulky disease, baseline SPD >50 cm ² , n (%)	1 (33.3)	1 (33.3)	2 (33.3)	1 (16.7)	6 (42.9)	11 (34.4)
Baseline LDH > ULN, n (%)	1 (33.3)	2 (66.7)	2 (33.3)	5 (83.3)	7 (50)	17 (53.1)

*1 pt received two CTX110 infusions with the first infusion at DL2 and the second at DL3. †1 pt enrolled in DL1 had Richter's transformation of CLL, and 1 pt in DL3 had both grade 3b FL and DLBCL.

CLL, chronic lymphocytic leukemia; DL, dose level; DLBCL, diffuse large B-cell lymphoma; ECOG, Eastern Cooperative Oncology Group; FL, follicular lymphoma; HGBLCL, high-grade large B-cell lymphoma; LDH, lactate dehydrogenase; NOS, not otherwise specified; PS, performance status; SPD, sum of the perpendicular diameters; ULN, upper limit of normal.

CTX110 Demonstrated a Tolerable Safety Profile Across All Dose Levels

- No infusion reactions with CTX110
- Gr ≥3 infections occurred in 4/32 patients (12.5%) including 1 pt who died with HHV6 encephalitis¹
- 7 patients experienced SAEs attributed to CTX110; these included CRS, ICANS, and febrile neutropenia

	DL1-DL2 30-100x10 ⁶ N=6		DL3 300x10 ⁶ N=6		DL3.5 450x10 ⁶ N=6		DL4 600x10 ⁶ N=14		Total N=32	
	Gr 1-2	Gr ≥3	Gr 1-2	Gr ≥3	Gr 1-2	Gr ≥3	Gr 1-2	Gr ≥3	Gr 1-2	Gr ≥3
CRS	4 (50.0)	0	2 (33.3)	0	3 (50)	0	10 (71.4)	0	18 (56.3)	0
ICANS	1 (0.16)	0	0	0	0	0	0	2 (14.3) ¹	1 (3.1)	2 (6.2)
GvHD	0	0	0	0	0	0	0	0	0	0
Infections	0	1 (0.16)	1 (16.7)	1 (16.7)	2 (33.3)	0	1 (7.1)	2 (14.3)	4 (12.5)	4 (12.5)

All events listed in table are treatment-emergent adverse events.

1. ICANS event confounded by HHV6 encephalitis. Independent DSMB reviewed case and attributed cause of death to HHV6 encephalitis.

CRS, cytokine release syndrome; DLT, dose-limiting toxicity; Gr, grade; GvHD, graft versus host disease; ICANS, immune effector cell associated neurotoxicity syndrome; LDC, lymphodepleting chemotherapy; TLS, tumor lysis syndrome.

CTX110 Demonstrated Encouraging Efficacy at Dose Level ≥ 3

- As of Oct 6, 2022, **34 patients with LBCL** were enrolled for dose escalation and 32 received CTX110. Only 2 enrolled patients did not receive CTX110 due to intercurrent infections (COVID-19 and pneumonia)
- **2-day median time from enrollment** to the beginning of lymphodepleting chemotherapy (LDC)
- Among patients who received ≥ 1 infusion of CTX110 at doses of $\geq 300 \times 10^6$ CAR T cells (DL ≥ 3 ; N=27)
 - Best ORR and CRR were 66.7% (18/27) and 40.7% (11/27), respectively
 - 6-mo CR rate with single infusions of CTX110 was 19% (5/27)
 - 3 patients have achieved and maintained ongoing CR for more than 24 months¹

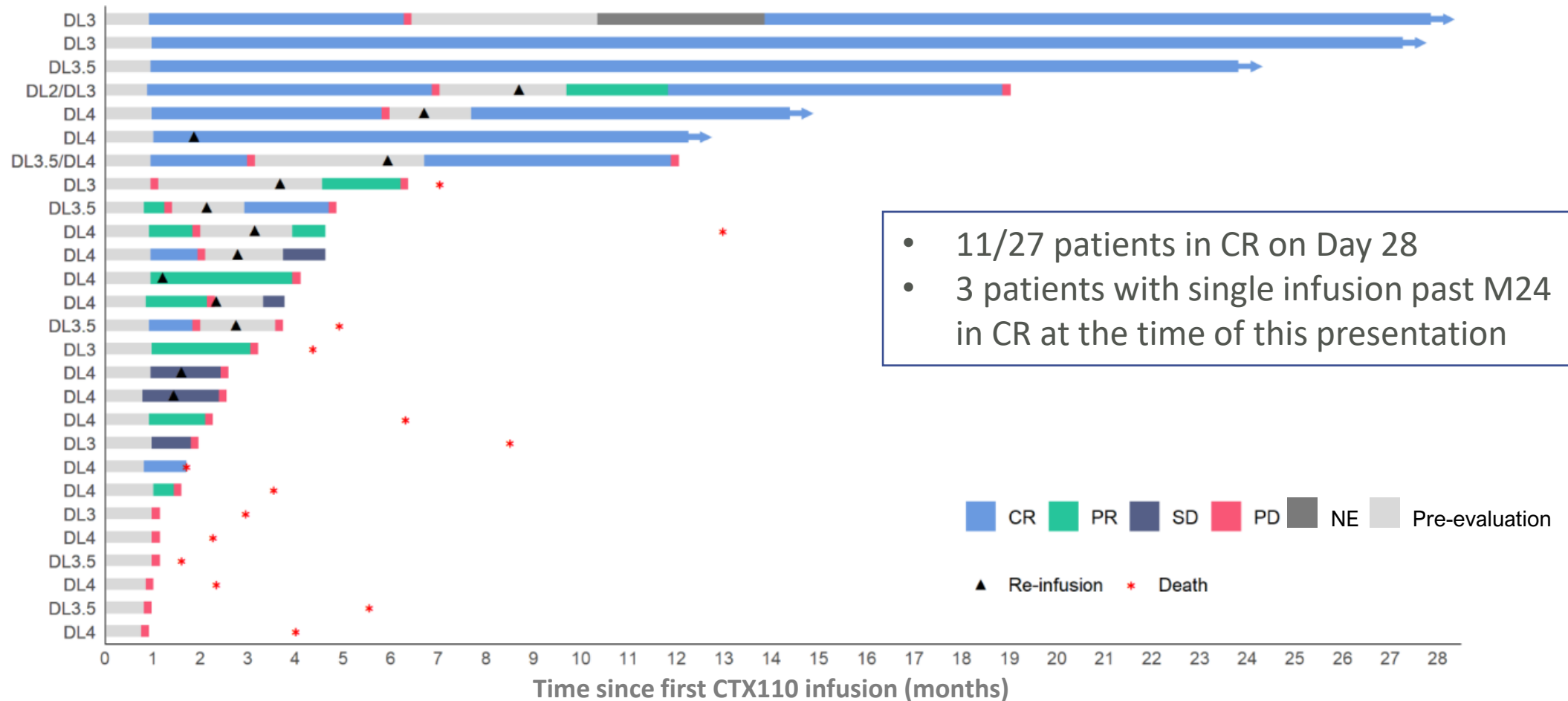
Cell dose (CAR+ T cells)	DL1-DL2 30-100x10 ⁶ N=6 ²	DL3 300x10 ⁶ N=6	DL3.5 450x10 ⁶ N=6	DL4 600x10 ⁶ N=14	≥ 1 Infusion at DL≥ 3 N=27
Overall Response Rate (ORR), n (%)	1 (0.16)	4 (66.7)	4 (66.7)	9 (64.3)	18 (66.7)
CR	1 (0.16)	2 (33.3)	4 (66.7)	4 (28.6)	11 (40.7)
PR	0	2 (33.3)	0	5 (35.7)	7 (25.9)

1. Two patients in CR at more than 24 months at the time of the data cutoff; 3 patients in CR at over 24 months ongoing as of the EBMT presentation.

2. One patient enrolled to DL2 received two CTX110 infusions with the first infusion at DL2 and the second at DL3.

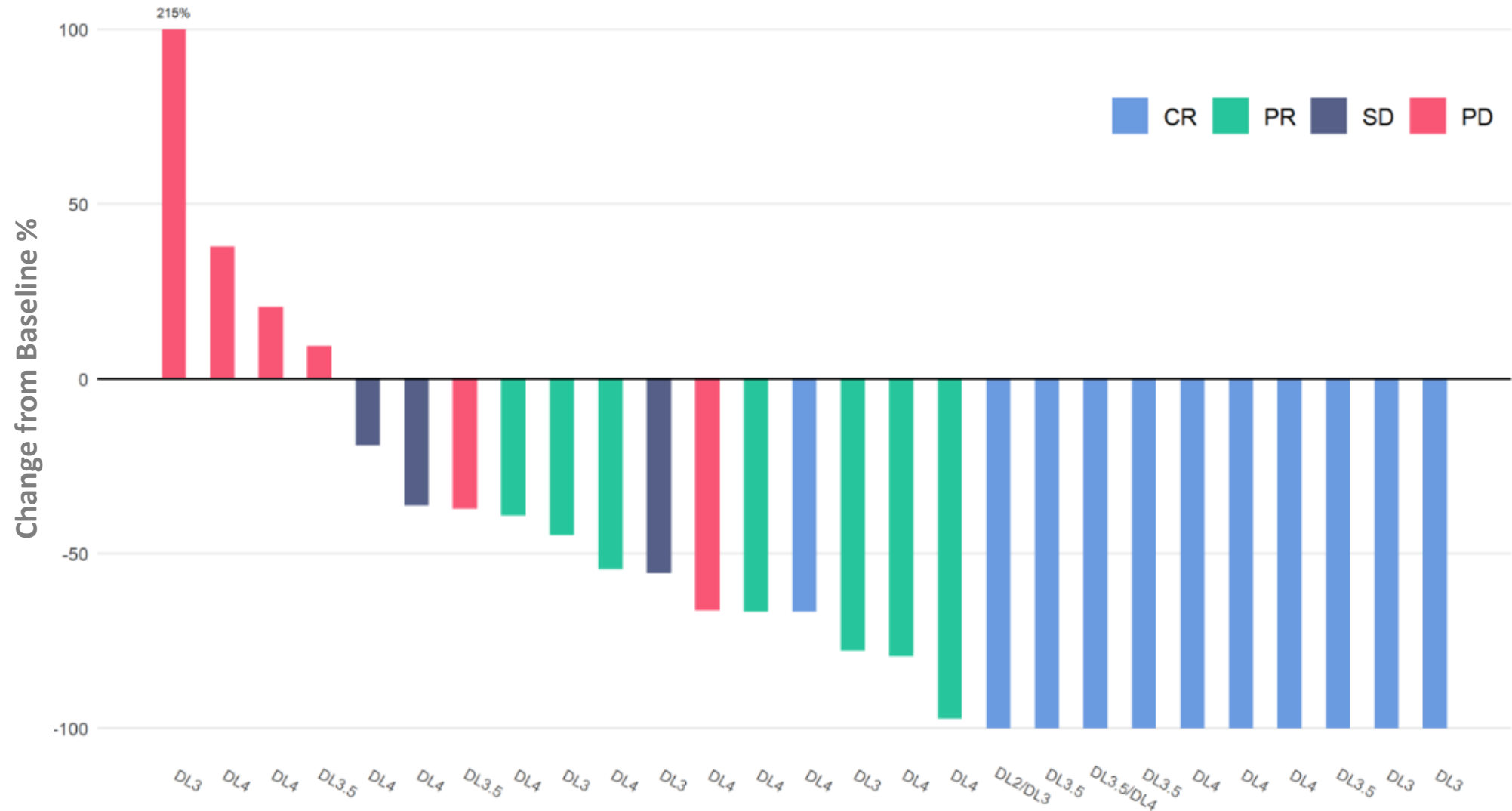
CAR, chimeric antigen receptor; CR, complete response; DL, dose level; ORR, overall response rate; PR, partial response; lymphoma; SD, stable disease.

Durable Responses at Clinically Active Doses



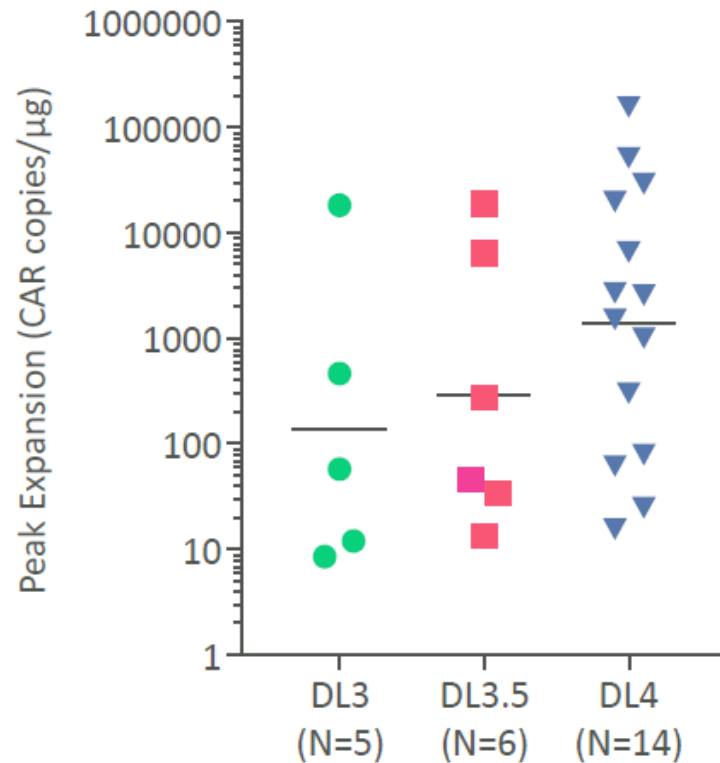
*PET CT identified a single new small FDG-avid node located in the left upper arm. The lesion was completely excised. The patient remained clinically well and required no subsequent anti cancer therapy including no steroids, no radiotherapy and no chemotherapy. **On the Month 9 scan, the PET CT identified unspecific localized small FDG uptake in the right upper arm. The patient did not have subsequent surgery nor anti cancer therapy, and the lesion spontaneously resolved. CR, complete response; DL, dose level; FDG, fluorodeoxyglucose; NE, not evaluable; PET-CT; positron emission tomography-computed tomography; PD, progressive disease; PR, partial response; SD, stable disease. Data cut Oct 6, 2022 Previously presented at ASH 2022

Deep Responses at Clinically Active Doses

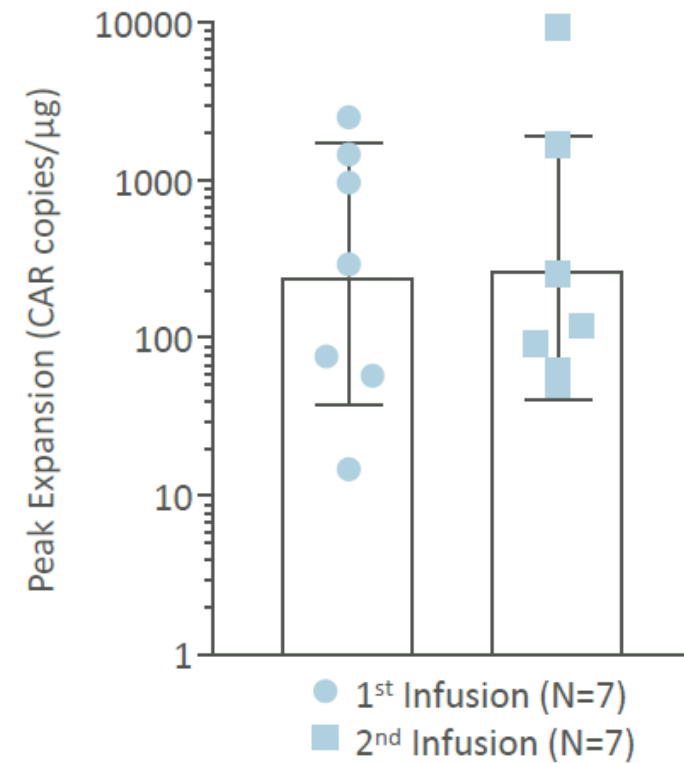


Dose Dependent Pharmacokinetics and Comparable Expansion After 2nd Infusion

Dose dependent increase in peak CTX110 expansion following 1st infusion



Comparable peak CTX110 expansion following 1st and 2nd infusion



CAR T cell expansion observed in all patients who received a 2nd infusion with comparable overall safety profile

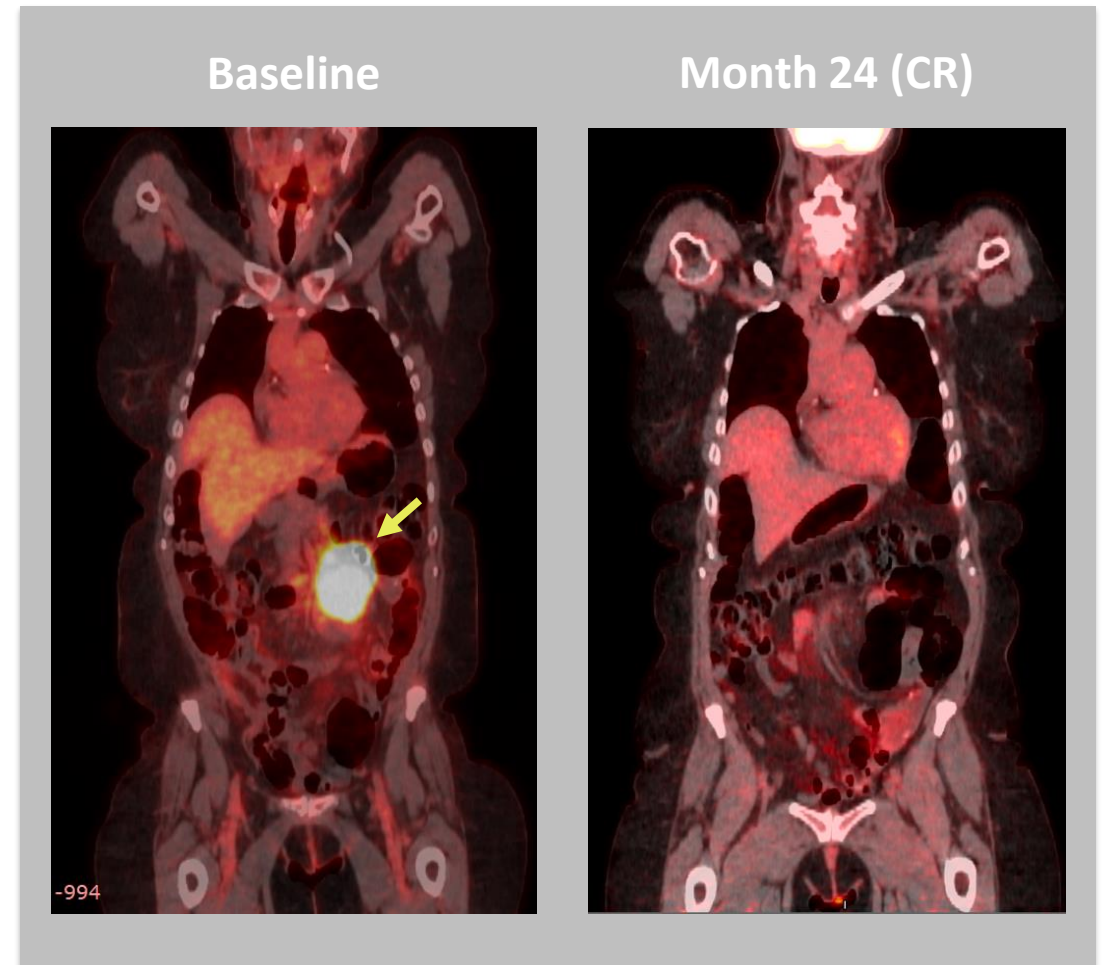
Ongoing CMR 24 Months After Single Infusion

Patient characteristics

- 62-year-old female diagnosed with DLBCL
- Relapsed following 2 prior lines of therapy, including autologous SCT
- Treated with CTX110 at DL3 (300x10⁶ CAR+ T cells)

Safety and efficacy

- CR at Day 28 after a single CTX110 infusion
- No CRS or ICANS
- **CR on-going 24+ months**



Summary

CTX110 offers a potential off-the-shelf treatment option for patients

The **median time from enrollment to lymphodepletion was just 2 days**. Only 2 enrolled patients were unable to receive CTX110

In a heavily pre-treated patient population with R/R LBCL, CTX110 at DL \geq 3 resulted in **clinically meaningful overall response rate (66.7%), complete response rate (40.7%), and durable remissions**, accompanied by a **favorable safety profile** during dose escalation

Nearly half of all patients who achieved a CR maintained this response for at least 6 months

Administration of a second CTX110 infusion was well tolerated, and CAR T cells expanded following the second infusion

Path Forward

Pivotal single arm expansion phase initiated with a single course regimen consisting of 2 infusions 4-8 weeks apart

Emerging data shows:

- Tolerable safety profile
- Comparable peak expansions after initial and repeat doses
- Deepening of responses with the second infusion, with deepening of complete responses and conversions of SD and PR to ongoing CR after the second dose

Acknowledgments

Thank you to all the patients, families, caregivers,
and investigators involved in the CARBON Study



CARBON (NCT04035434) Study Sites

