CB-010 ANTLER Phase 1 trial: Results from dose escalation phase

Allogeneic anti-CD19 CAR-T cell with a PD-1 knockout for r/r B cell non-Hodgkin lymphoma (B-NHL)

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iwCAR-T meeting (Miami, FL)

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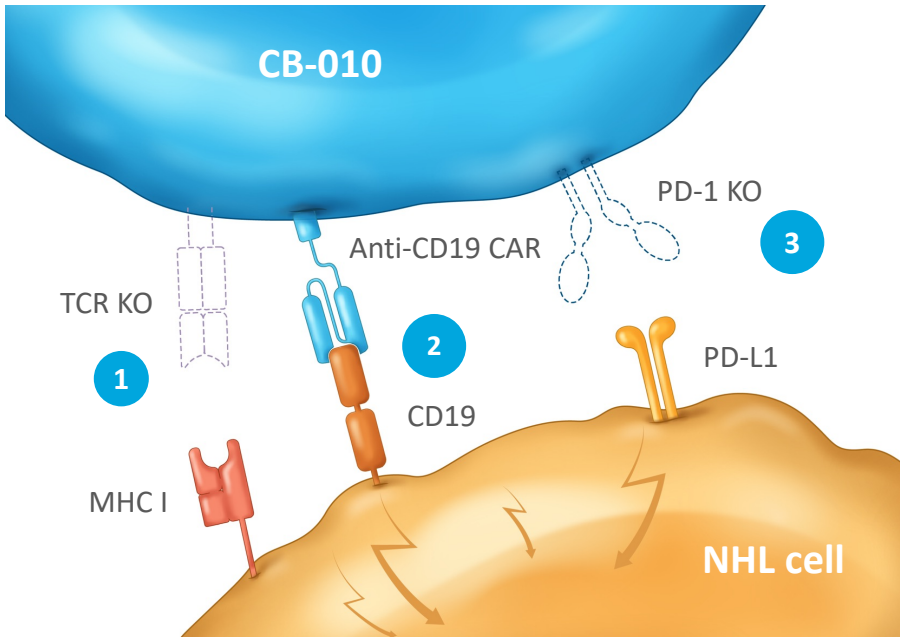
CB-010 has a PD-1 KO designed to reduce CAR-T cell exhaustion



Armored with 3 genome edits

1. ***TRAC* gene knockout (KO)**
   - Eliminates TCR expression, reduces GvHD risk
2. **Anti-CD19 CAR site-specific insertion into *TRAC* locus**
   - Eliminates random integration, targets tumor antigen
3. **PD-1 KO for enhanced antitumor activity**
   - Reduces CAR-T cell exhaustion
   - Potentially contributes to initial tumor debulking

- 1st CAR-T in the clinic with **checkpoint disruption** via PD-1 KO[1]
- Cas9 chRDNA editing for **reduced off-target editing** and enhanced genomic integrity
- **Anti-CD19** scFv FMC63 with a 4-1BB costimulatory domain

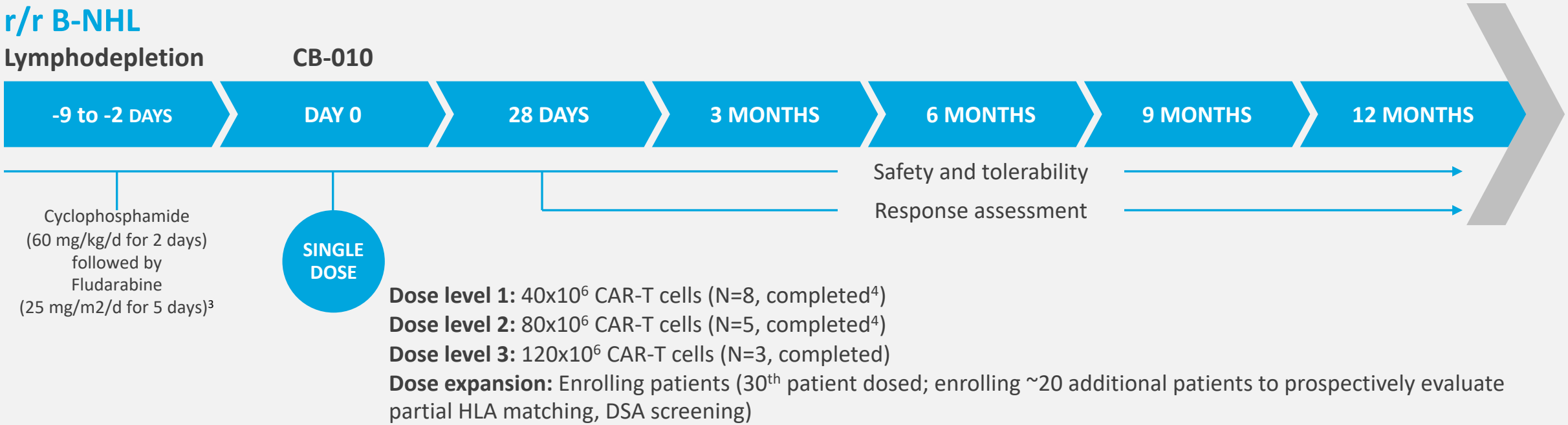
CAR: chimeric antigen receptor; KO: knockout; CD: cluster of differentiation; chRDNA: CRISPR hybrid RNA-DNA; CRISPR: clustered regularly interspaced short palindromic repeats; PD-1: programmed cell death protein 1; TCR: T cell receptor; *TRAC*: T cell receptor alpha constant; scFv: single-chain variable fragment

[1] To Caribou's knowledge.

CB-010 ANTLER Phase 1 trial:
Dose escalation complete and enrolling 2L LBCL patients in dose expansion

Part A: 3+3 dose escalation – completed (N=16)
- Eligibility: aggressive r/r B-NHL[1] with ≥2 prior lines of chemoimmunotherapy or primary refractory
- Exclusion: prior CD19-targeted therapy

Part B: dose expansion – enrolling
- Eligibility: 2nd line LBCL[2]
- Exclusion: prior CD19-targeted therapy
- Objective: tumor response, RP2D



Dose level 1: 40x10^6 CAR-T cells (N=8, completed[4])
Dose level 2: 80x10^6 CAR-T cells (N=5, completed[4])
Dose level 3: 120x10^6 CAR-T cells (N=3, completed)
Dose expansion: Enrolling patients (30th patient dosed; enrolling ~20 additional patients to prospectively evaluate partial HLA matching, DSA screening)

NCT04637763
DSA: donor specific antibody; HLA: human leukocyte antigen
[1] Subtypes include: DLBCL, HGBL, tFL, PMBCL, FL, MZL, MCL (Note, FL subtype is aggressively behaving, with POD24 (high risk))
[2] LBCL subtypes include: DLBCL, HGBL, PMBCL, tFL
[3] Clin Cancer Res. 2011 July 1; 17(13): 4550–4557. doi:10.1158/1078-0432.CCR-11-0116
[4] Includes 2 backfill patients at dose level 1 and 2 backfill patients at dose level 2

ANTLER dose escalation: baseline and disease characteristics

Characteristics	Total (N=16)
Median age, years (range)	66 (55-82)
Male, n (%)	14 (88)
ECOG performance status, n (%)	
0	6 (38)
1	10 (62)
Time since first diagnosis, years	
Median (range)	2.4 (0.2-16.4)
Non-Hodgkin lymphoma subtype, n (%)	
LBCL	10 (63)
DLBCL	7 (44)
HGBL	2 (13)
PMBCL	1 (6)
Other B-NHL	6 (38)
MCL	3 (19)
FL[1]	2 (13)
MZL	1 (6)
$CD19^+$ disease, n (%)	16 (100)
Prior systemic therapies, median number (range)[2]	2 (1-8)

DLBCL: diffuse large B cell lymphoma; FL: follicular lymphoma; HGBL: high-grade B cell lymphoma; MCL: mantle cell lymphoma; MZL: marginal zone lymphoma; PMBCL: primary mediastinal large B cell lymphoma

[1] Aggressively behaving, with POD24 (high risk)

[2] Patients are CD19 CAR-T naïve

CB-010 has generally well-tolerated safety profile (N=16)

No DLTs at dose level 2 or dose level 3, no Grade 3+ CRS, no GvHD observed

AEs of special interest	ANTLER dose escalation (N=16)		
	CRS	ICANS[1]	Infections[2, 3]
Any grade, N (%)	7 (44%)	4 (25%)	7 (44%)
Grade 1	4 (25%)	2 (13%)	2 (13%)
Grade 2	3 (19%)	-	4 (25%)
Grade 3	-	1 (6%)	1 (6%)[3]
Grade 4	-	1 (6%)	-
Median time to onset, days (range)	3.5 (1,7)	7.5 (5,10)	27.0 (0, 279)
Median duration, days (range)	3.0 (1,9)	2.0 (1,34)	14.0 (2,63)

	CRS Gr 3+	ICANS Gr 3+	Infections Gr 3+
CB-010 ANTLER Phase 1	**0%**	**13%**	**6%**
Kymriah Phase 2[4]	23%	15%	41%
Yescarta Phase 1/2[5]	13%	31%	29%
Breyanzi Phase 1[6]	4%	12%	23%

AE: adverse event; CRS: cytokine release syndrome; DLT: dose-limiting toxicity; GvHD: graft-versus-host disease; ICANS: immune effector cell–associated neurotoxicity syndrome; TEAE: treatment-emergent adverse event

[1] Four total events, 2 Grade 1; 2 Grade 3+ at dose level 1, both with complete resolution of symptoms with supportive care.

[2] Infection events reported were on or after CB-010 infusion, with highest grade reported per patient.

[3] Grade 3 cellulitis (right antecubital) occurred after CB-010 infusion and was unrelated to CB-010 per the investigator.

[4] Kymriah: USPI, NCT02445248, Schuster NEJM 2019, N=111

[5] Yescarta: USPI, NCT02348216, N=101

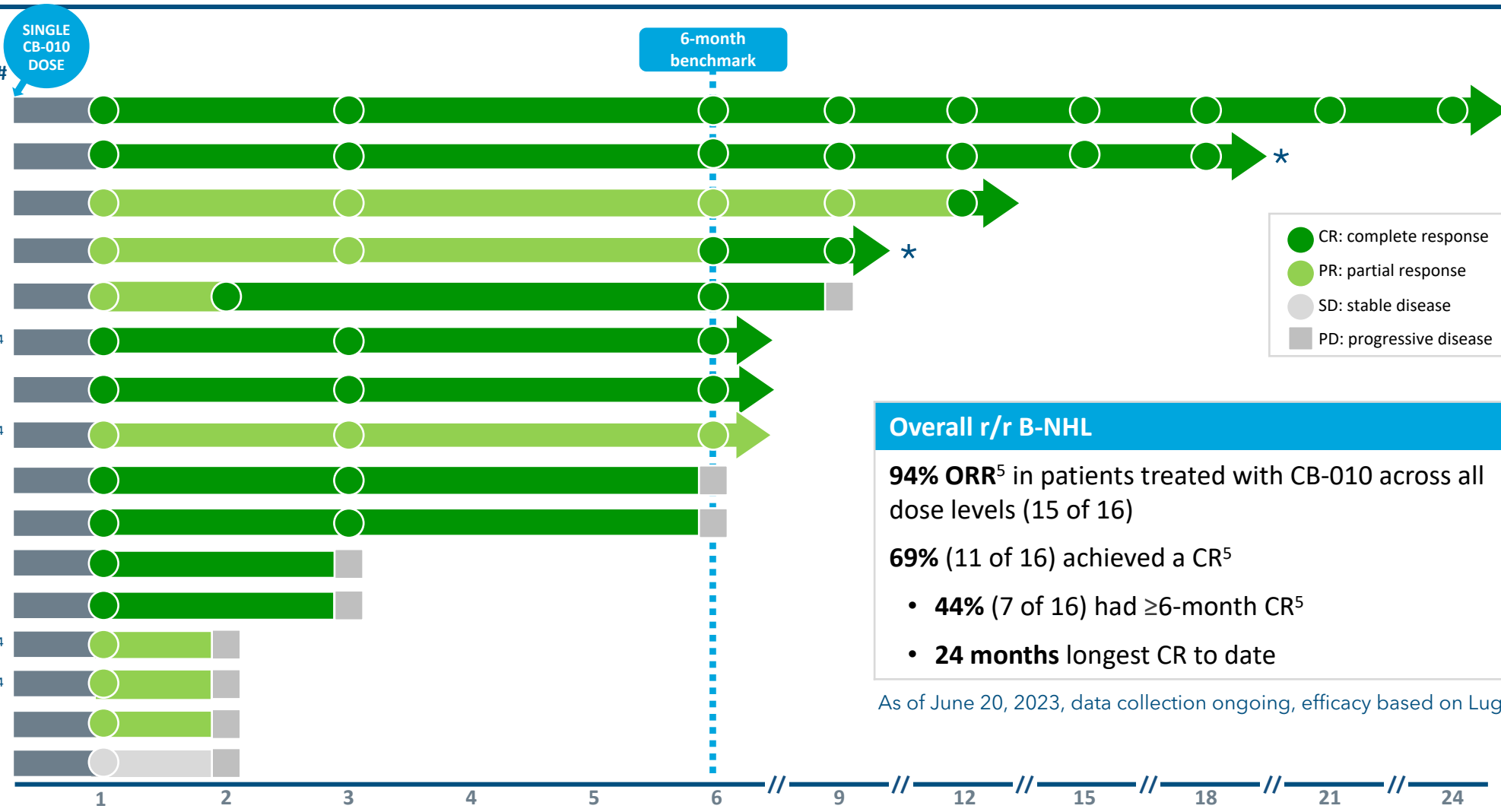
[6] Breyanzi: USPI, NCT02631044, N=192

As of May 4, 2023 data cutoff date

CB-010 ANTLER dose escalation efficacy assessment (N=16)

Overall depth and duration of response

Subtype	Dose	Prior # Rx	Best Resp.	Pt #
FL[1]	40M	8	CR	1
DLBCL	40M	4	CR	4
DLBCL[2]	80M	1	CR	7
DLBCL[2]	80M	1	CR	8
PMBCL[3]	40M	2	CR	5
MCL	40M	2	CR	13[4]
DLBCL	80M	2	CR	9
MZL	80M	4	PR	15[4]
MCL	40M	4	CR	2
FL[1]	40M	2	CR	3
DLBCL	40M	2	CR	6
DLBCL	120M	2	CR	10
HGBL[2]	40M	1	PR	14[4]
MCL	80M	2	PR	16[4]
HGBL[2]	120M	1	PR	12
DLBCL	120M	2	SD	11



Overall r/r B-NHL

94% ORR[5] in patients treated with CB-010 across all dose levels (15 of 16)

69% (11 of 16) achieved a CR[5]

- **44%** (7 of 16) had ≥6-month CR[5]
- **24 months** longest CR to date

As of June 20, 2023, data collection ongoing, efficacy based on Lugano

[1] Aggressively behaving, with POD24 (high risk)
[2] Primary refractory disease
[3] Patient 5's 3-month scan conducted on day 63 post CB-010 as per investigator's discretion
[4] Patients 13-16 are backfill patients at 40M and 80M
[5] Certain patients converted from a CR or PR to PD at various assessment time points as indicated in the chart above
* Update on patient 4 presented at LLM congress (CR ongoing thru month 21) and patient 8 presented at EU CAR-T congress (CR ongoing thru month 15)

Subgroup efficacy profile supports 2L LBCL clinical development

	r/r B-NHL	r/r LBCL[2]	2L LBCL[3]
Endpoints N, (%)	**All patients** (N=16)	**Subgroup** (N=10)	**Subgroup** (N=4)
Overall response rate (ORR)[1]	15 (94%)	9 (90%)	4 (100%)
Complete response (CR) rate[1]	11 (69%)	7 (70%)	2 (50%)
≥6-month CR rate[1]	7 (44%)	5 (50%)	2 (50%)
CR at longest duration to date	24 months	18 months	12 months[4]

[1] Certain patients converted from a CR or partial response (PR) to progressive disease (PD) at various assessment time points.
[2] Subgroup includes patient #4, 5, 6, 7, 8, 9, 10, 11, 12, and 14.
[3] Four primary refractory patients were enrolled in dose escalation. Subgroup includes patient #7, 8, 12, and 14.
[4] Patient #7 had a CR at 12 months, which converted from PR at the prior efficacy assessment.

Patient #8 case report (primary refractory DLBCL patient)

Age	Sex	Race	Ethnicity	Height	Weight	BMI	BSA
66	Male	Asian	Not Hispanic or Latino	162.6 cm	73.2 kg	28.5 kg/m^2	1.79 m^2

Medical history and disease characteristics

Tumor subtype	**DLBCL**
Stage at screening	**IV**
Years since diagnosis	**1 (March 2022)**
Prior lines anti-cancer therapy	**1** **R-CHOP (Mar-Jun 2022)** **Primary refractory** w/ biopsy-confirmed disease progression July 2022

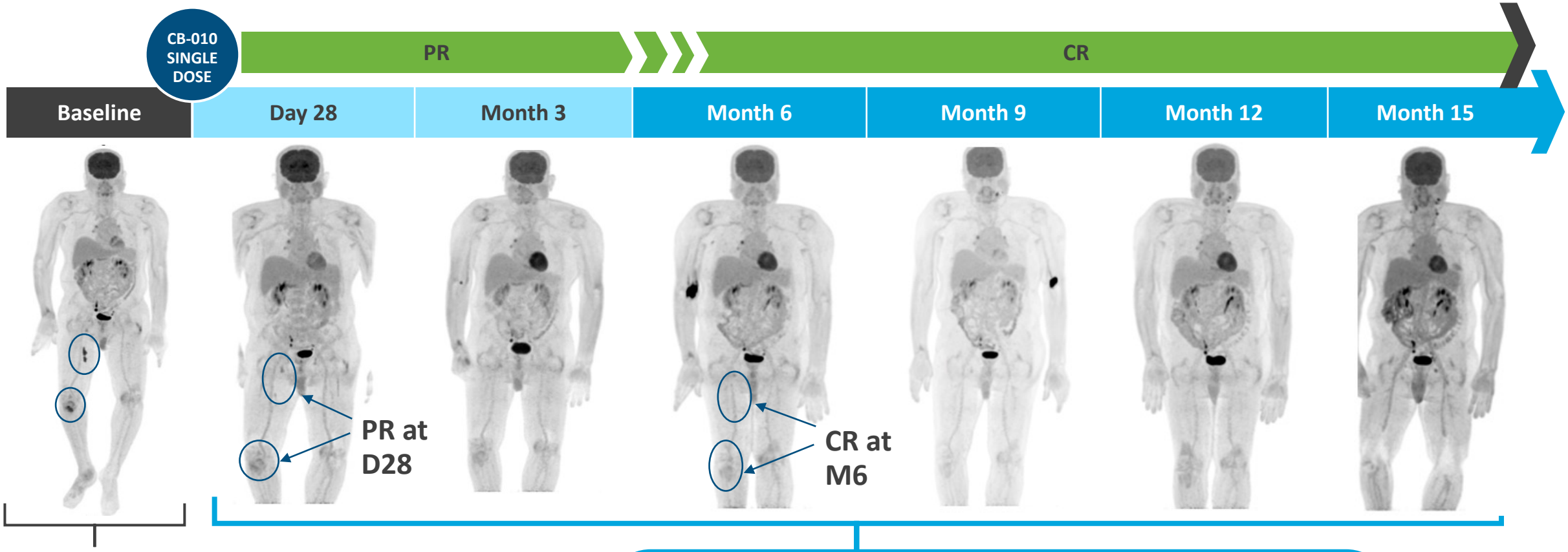
Relevant past medical history:

- Hyperglycemia
- Hypertension
- Gastroesophageal reflux
- Hyperlipidemia
- Anemia
- Thrombocytopenia

DLBCL confirmed per local pathology report, CD19+ at the time of enrollment in ANTLER trial (Sep 2022)

Poster presentation at EHA/EBMT CAR-T meeting (Feb 2024; Valencia, Spain)

Patient #8: PR to CR conversion at month 6 with ongoing CR through month 15 (80M CB-010 dose)



4 EXTRANODAL LOCATIONS AT BASELINE (PET/CT)

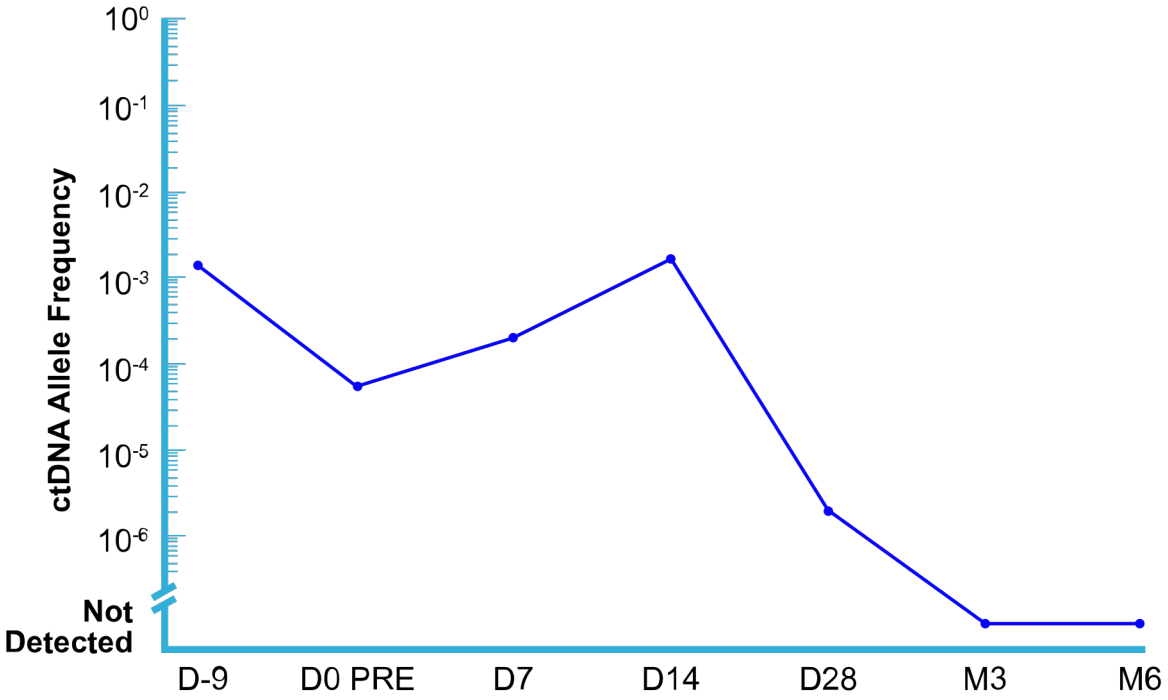
2 target lesions: right upper and mid medial thigh (skin)
2 non-target lesions: right thigh soft tissue, proximal right tibia

PR to CR conversion at month 6 per Lugano criteria

Poster presentation at EHA/EBMT CAR-T meeting (Feb 2024; Valencia, Spain)

Patient #8: Robust CAR-T cell expansion observed at day 10 with ctDNA undetectable by month 3

ctDNA undetectable by month 3



CAR-T cell expansion observed at Day 10 in the peripheral blood

Poster presentation at EHA/EBMT CAR-T meeting (Feb 2024; Valencia, Spain)

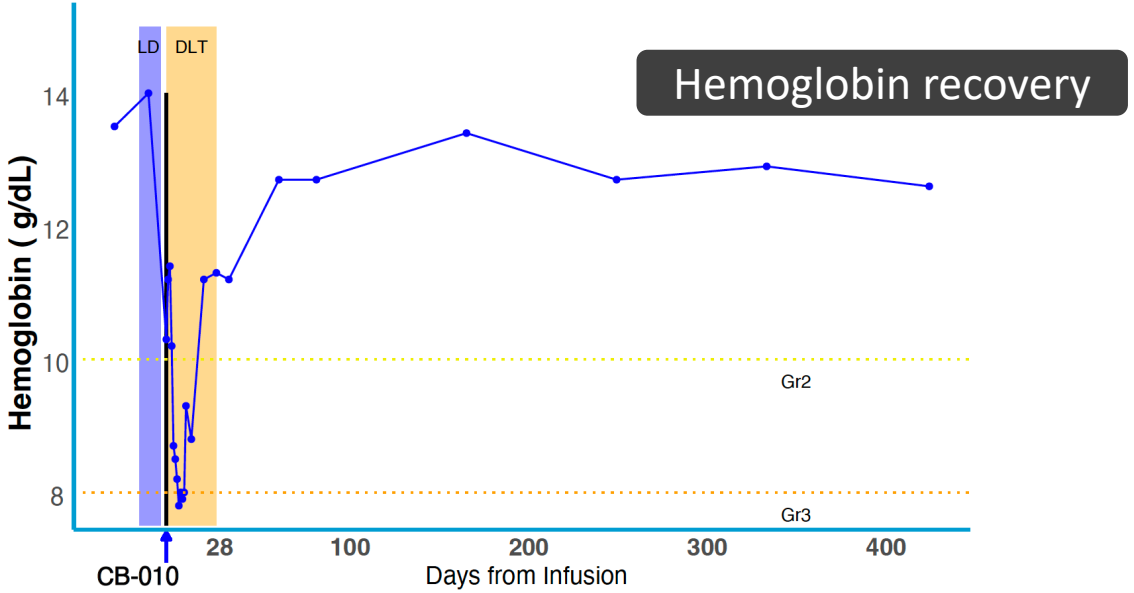
Patient #8: safety and cytopenia recovery

No GvHD, ICANS, or infections observed with Grade 1 CRS days 4-7

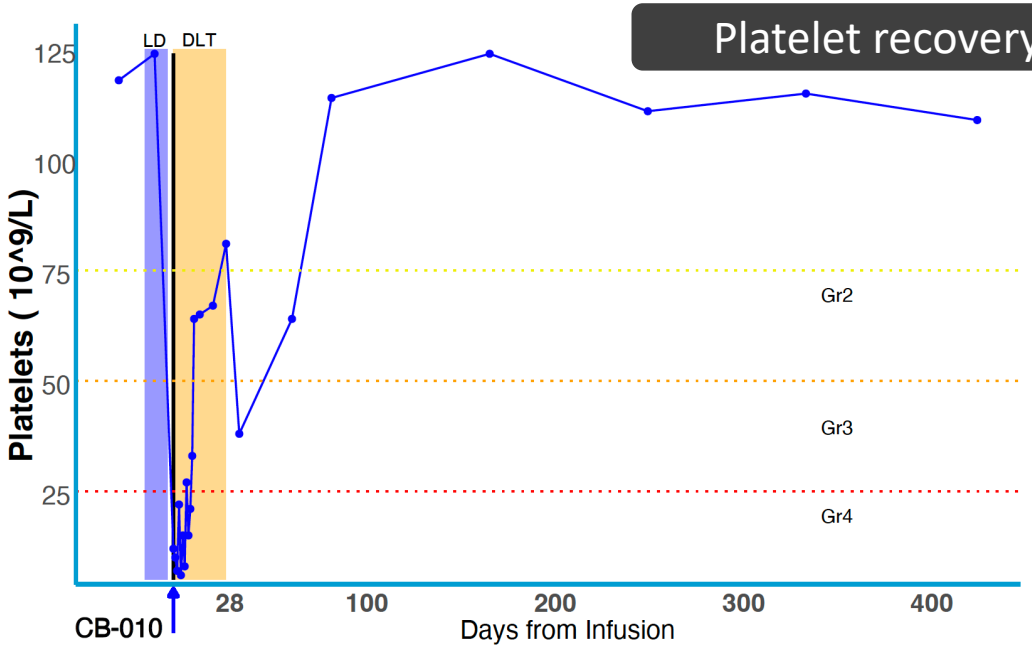
Lymphodepletion (LD) period

Dose-limiting toxicity (DLT) evaluation period

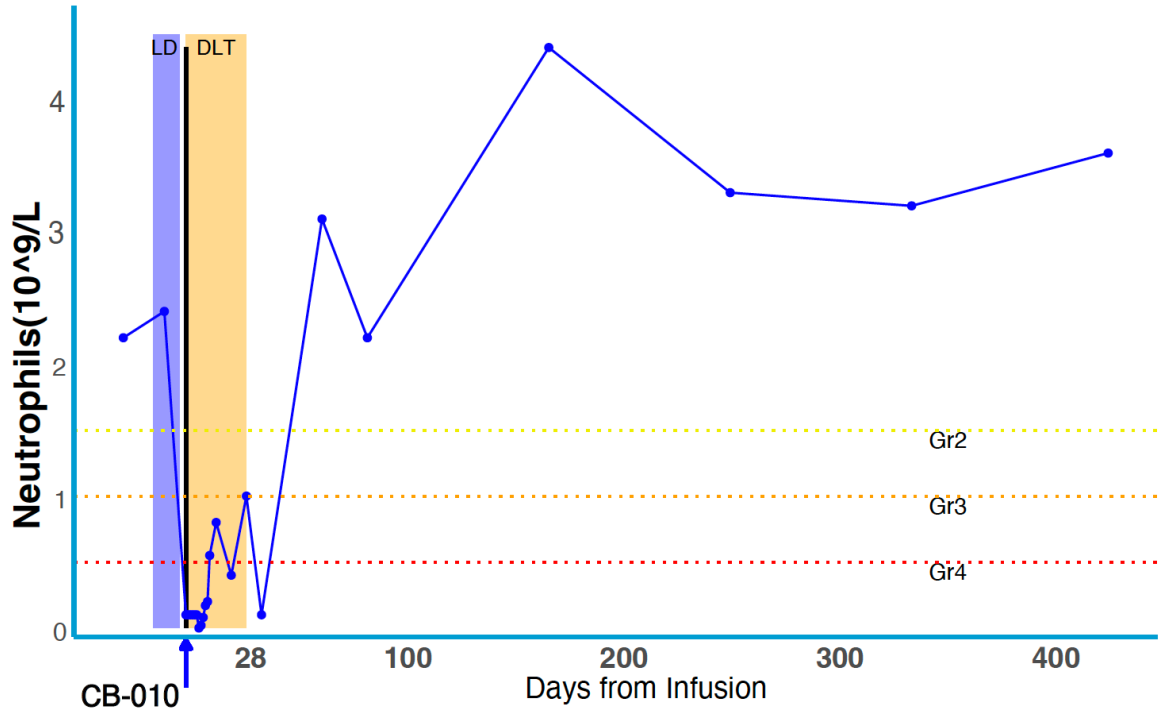
Hemoglobin recovery



Platelet recovery



Neutrophil recovery



Poster presentation at EHA/EBMT CAR-T meeting (Feb 2024; Valencia, Spain)

ANTLER CB-010 summary and next steps

- CB-010, the first allogeneic CD19-directed CAR-T with a PD-1 knockout, demonstrated promising safety and efficacy in patients with r/r B-NHL in dose escalation (N=16)
- **CB-010 was generally well tolerated with adverse events consistent with anti-CD19 CAR-T cells**
  - No GvHD occurred
  - One DLT (Grade 3 ICANS that resolved in ~39 hours) occurred at DL1 (40 x 10^6 CAR-T cells)
  - No DLTs occurred at DL2 (80 x 10^6 CAR-T cells) and DL3 (120 x 10^6 CAR-T cells)
- **94% ORR, 69% CR rate, and 44% CR rate at ≥6 months observed**
- Durable CRs were achieved after a single dose of CB-010
  - Longest duration of response in patient #1, with **ongoing CR through Month 24**
  - PR to CR conversions observed in 3 patients with LBCL
- Enrollment of 2L LBCL patients ongoing in dose expansion with initial dose expansion data to be presented at upcoming medical congress (2Q2024)

CB-010 was granted Regenerative Medicine Advanced Therapy (RMAT), Fast Track, and Orphan Drug designations by the FDA in 2022