

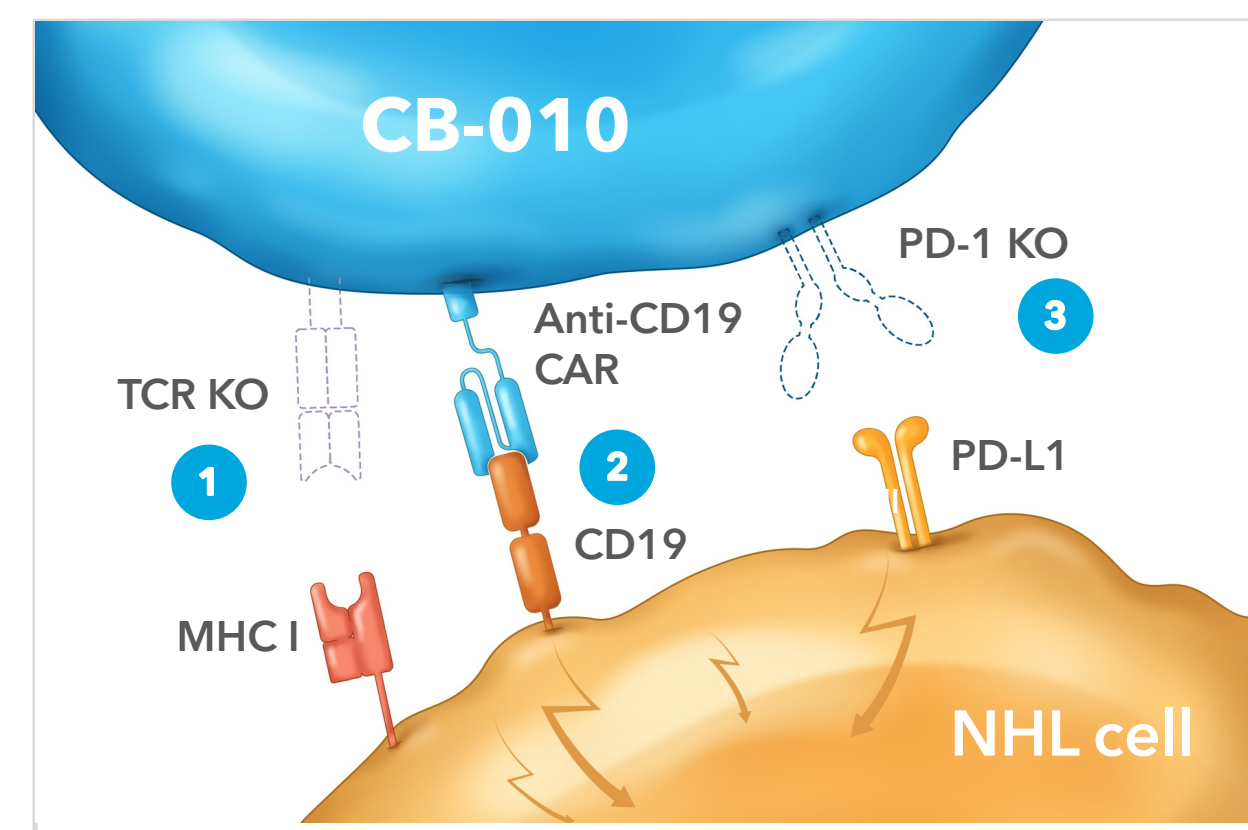
Durable complete response achieved in a relapsed/refractory diffuse large B cell lymphoma (DLBCL) patient treated with a CRISPR-edited allogeneic anti-CD19 CAR-T cell therapy with a PD-1 knockout: Case report from the CB-010 ANTLER trial

Elizabeth Brem¹, Lauren Pinter-Brown¹, Christina Kirk¹, Emiri Matsuda¹, Blake Johnson¹, Ashley Hammad², Donna Mastey², Shally Chung², Kalin Bird², Ben Thompson², Guy Lederger², Franco Davi², Ashraf Garrett², Elizabeth Garner², Enrique Zudaire², Steven Kanner², Tonia Nesheiwat², Socorro Portella², Syed Rizvi², Susan O'Brien¹

¹University of California Irvine, Irvine, CA ²Caribou Biosciences, Inc., Berkeley, CA

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

Key attributes	CB-010	Conventional allogeneic anti-CD19 CAR-Ts
Cas9 chrDNA editing for enhanced genomic integrity	✓	✗
• Reduced off-target editing and genomic rearrangements	✓	✗
1 TRAC gene knockout (KO)	✓	Varies
• Eliminates TCR expression, reduces GvHD risk	✓	Varies
2 Anti-CD19 CAR site-specific insertion into TRAC locus	✓	Varies
• Eliminates random integration, targets tumor antigen	✓	Varies
3 PD-1 KO for enhanced antitumor activity	✓	✗
• Potentially better therapeutic index via initial tumor debulking	✓	✗



Program: CB-010
Healthy donor leukapheresis-derived T cells
Tumor antigen: CD19
Indication: r/r B cell non-Hodgkin lymphoma (B-NHL)
Status: Ongoing Phase 1 trial enrolling 2L LBCL patients in dose expansion

CB-010 CAR construct uses an 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

CB-010 ANTLER Phase 1 trial design

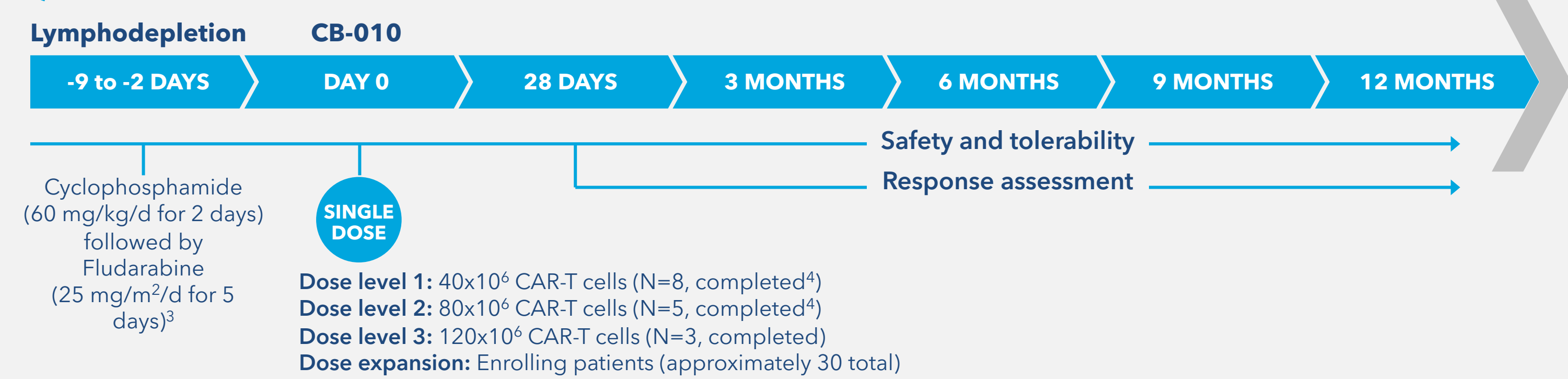
Part A: 3+3 dose escalation - completed (N=16)

- Eligibility: aggressive r/r B-NHL¹ with ≥2 prior lines of chemoimmunotherapy or primary refractory
- Exclusion: prior CD19-targeted therapy

Part B: dose expansion - enrolling

- Eligibility: 2nd line LBCL²
- Exclusion: prior CD19-targeted therapy
- Objective: tumor response, RP2D

r/r B-NHL



NCT04637763

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 NOS, HGBL, PMBCL, tFL, tMZL

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

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Patient case presentation

Patient demographics

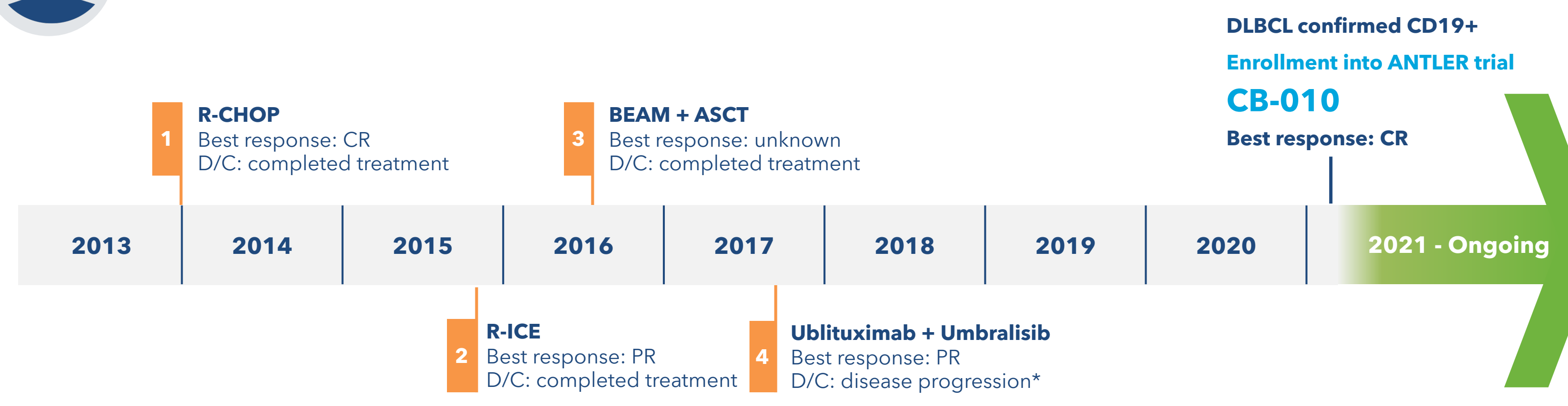
Age	Sex	Race	Ethnicity	Height	Weight	BMI	BSA
68	Male	Not reported	Hispanic or Latino	172.7 cm	129.5 kg	43.4 kg/m ²	2.49 m ²

Medical history and disease characteristics

Tumor subtype	DLBCL (GCB)	Relevant past medical history: • Type II diabetes • Obesity • Hypertension • Aortic stenosis, non-rheumatic	DLBCL confirmed per local pathology report, CD19+ at diagnosis and at the time of enrollment in ANTLER trial
Stage	III		
Years since diagnosis	9 (Sep 2013)		
Prior lines anti-cancer therapy	4		

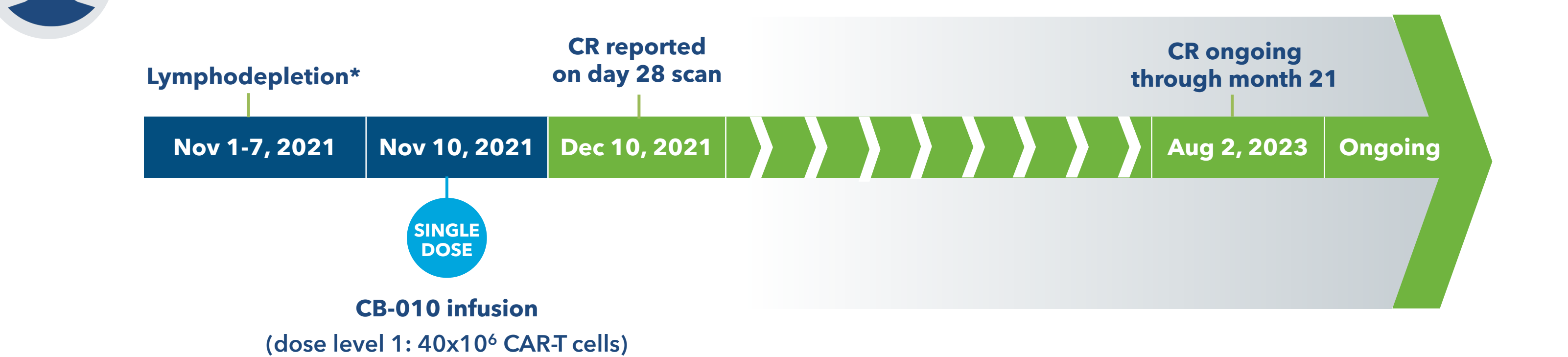
BMI: body mass index, BSA: body surface area, CD: cluster of differentiation; GCB: germinal center B-cell-like

4 prior lines of systemic anti-cancer therapy



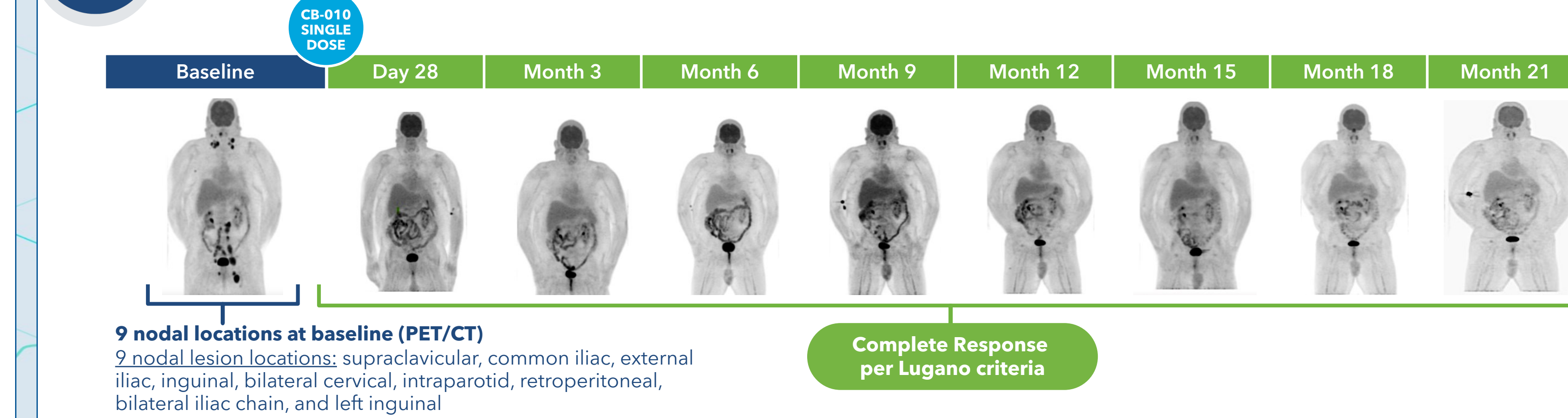
* Disease progression on Ublituximab + Umbralisib occurred in June 2021 prior to ANTLER enrollment

Patient timeline on ANTLER trial



* Cyclophosphamide (60 mg/kg/d for 2 days) followed by Fludarabine (25 mg/m²/d for 5 days)

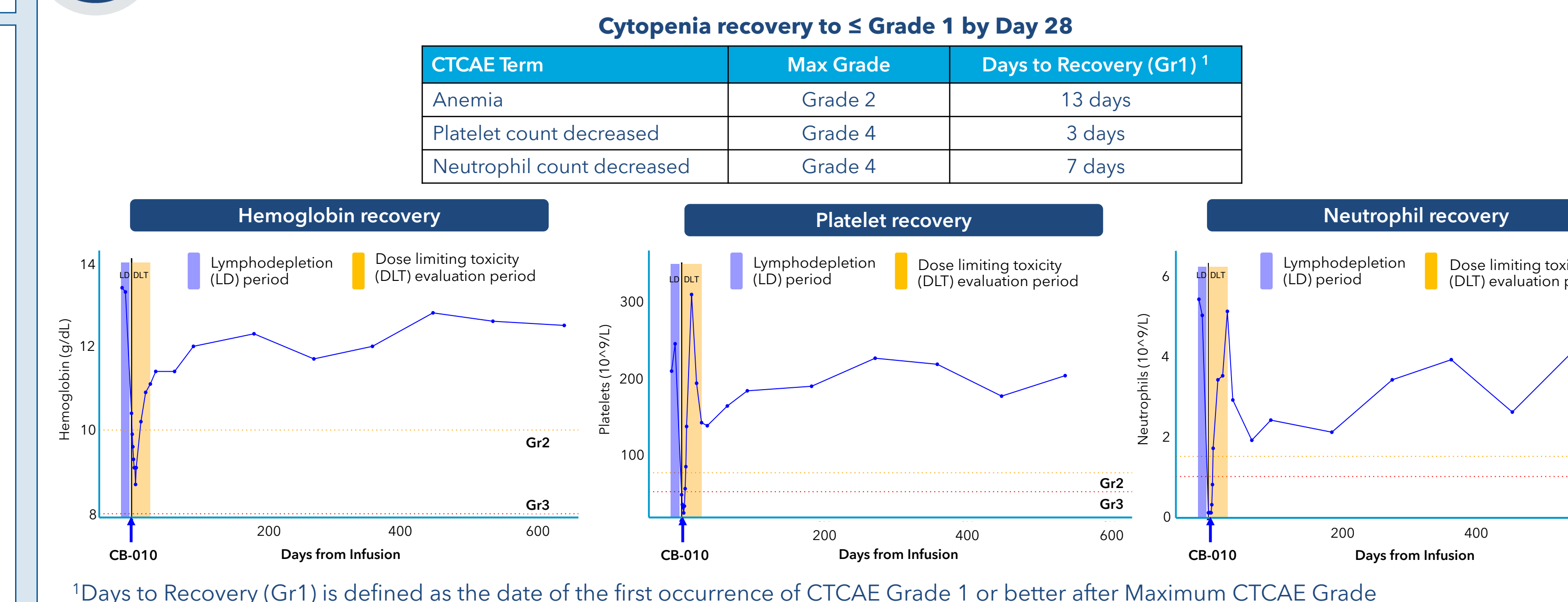
PET/CT scans: ongoing CR through month 21



CR: complete response, CT: computed tomography, PET: positron emission tomography

CB-010 has a generally well-tolerated safety profile

No GvHD, CRS, ICANS, prolonged cytopenias or infections observed in this patient



CB-010: ANTLER Phase 1 trial summary

- CB-010 is the first allogeneic CD19-directed CAR-T cell therapy in the clinic with a PD-1 knockout, a genome-editing strategy designed to enhance antitumor activity by limiting premature CAR-T cell exhaustion
- As previously reported, patients enrolled in the dose escalation portion of the ANTLER trial achieved a 94% ORR, 69% CR rate and a 44% CR rate at ≥ 6 months and CB-010 demonstrated a generally well tolerated safety profile (N =16)
 - ▶ Durable CRs observed with the longest ongoing CR through month 24
 - ▶ PR to CR conversions observed in 3 patients with LBCL
- In this case report, a heavily pretreated DLBCL patient received CB-010 (40 x 10⁶ CAR-T cells) and no GvHD, CRS, ICANS, prolonged cytopenias, or infections were observed with ongoing CR through month 21
- Enrollment of 2L LBCL patients is ongoing in dose expansion

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

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