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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

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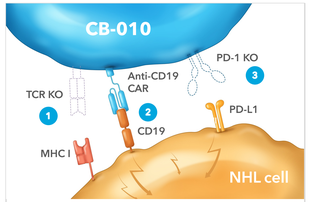
CB-010 has a PD-1 KO designed to reduce T cell exhaustion

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		
2 **Anti-CD19 CAR site-specific insertion into *TRAC* locus**	✓	Varies
• Eliminates random integration, targets tumor antigen		
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-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

r/r B-NHL

Dose level 1: 40x10⁶ CAR-T cells (N=8, completed[4])
Dose level 2: 80x10⁶ CAR-T cells (N=5, completed[4])
Dose level 3: 120x10⁶ CAR-T cells (N=3, completed)
Dose expansion: Enrolling patients (approximately 30 total)

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

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/m²	2.49 m²

Medical history and disease characteristics

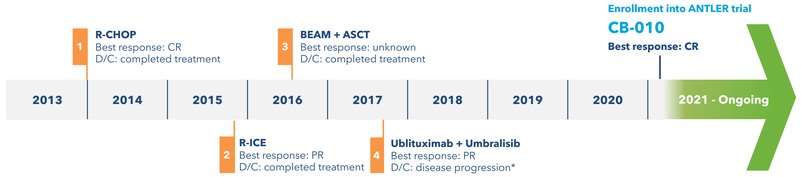
Tumor subtype	**DLBCL (GCB)**
Stage	**III**
Years since diagnosis	**9 (Sep 2013)**
Prior lines anti-cancer therapy	**4**

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

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

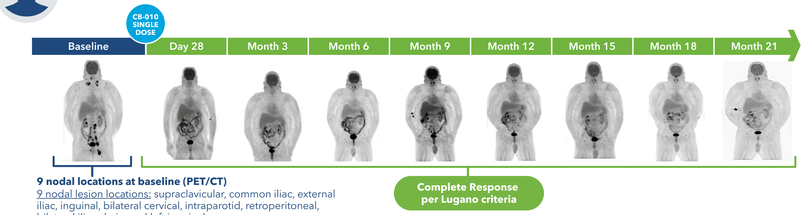


* Disease progression on Ublituximab + Umbralisib occurred in June 2021 prior to ANTLER enrollment

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



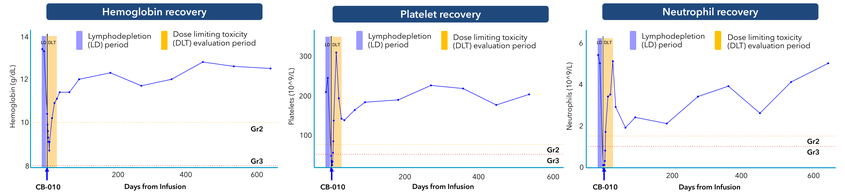
CR: complete response, CT: computed tomography, PET: positron emission tomography

CB-010 has a generally well-tolerated safety profile

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

Cytopenia recovery to ≤ Grade 1 by Day 28

CTCAE Term	Max Grade	Days to Recovery (Gr1) [1]
Anemia	Grade 2	13 days
Platelet count decreased	Grade 4	3 days
Neutrophil count decreased	Grade 4	7 days



[1]Days to Recovery (Gr1) is defined as the date of the first occurrence of CTCAE Grade 1 or better after Maximum CTCAE Grade

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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