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DEEP AND DURABLE RESPONSE IN A PATIENT WITH PRIMARY REFRACTORY DLBCL TREATED WITH CB-010, A CRISPR-EDITED ALLOGENEIC ANTI-CD19 CAR-T CELL THERAPY WITH A PD-1 KNOCKOUT (ANTLER TRIAL)

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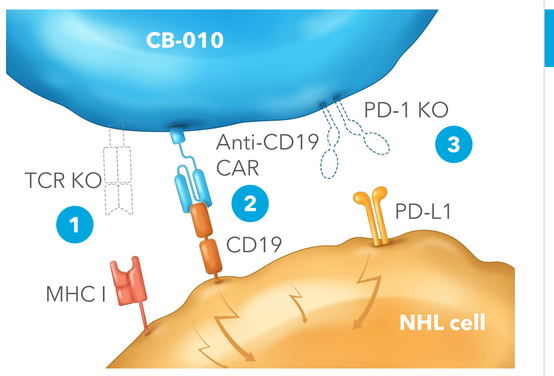
CB-010 has a PD-1 KO designed to reduce CAR-T cell exhaustion



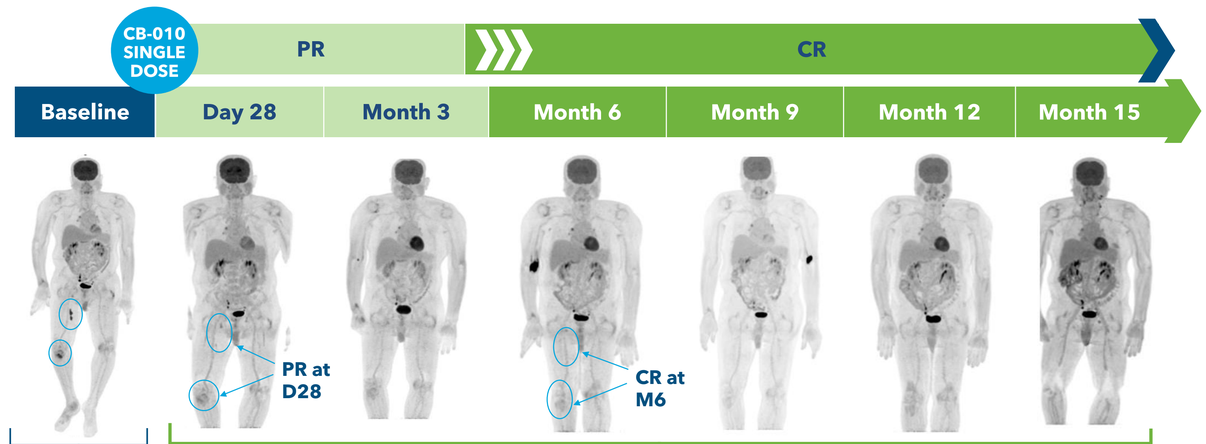
Armored with 3 genome edits

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[a]
- Cas9 chRDNA editing for **reduced off-target editing** and enhanced genomic integrity
- **Anti-CD19** scFv FMC63 with a 4-1BB costimulatory domain

[a] To Caribou's knowledge.

PR to CR conversion at month 6 with ongoing CR through month 15



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

CB-010 ANTLER Phase 1 trial design

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

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

r/r B-NHL

Lymphodepletion | **CB-010**

-9 to -3 DAYS | DAY 0 | 28 DAYS | 3 MONTHS | 6 MONTHS | 9 MONTHS | 12 MONTHS

Safety and tolerability

Response assessment

Cyclophosphamide (60 mg/kg/d for 2 days) followed by fludarabine (25 mg/m²/d for 5 days)[c]

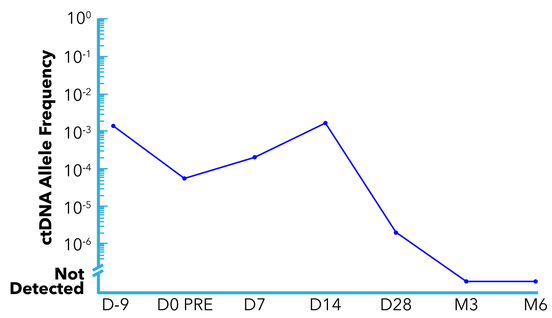
SINGLE DOSE

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

NCT04637763
[a] Subtypes include: DLBCL, HGBL, tFL, PMBCL, FL, MZL, MCL (Note, FL subtype is aggressively behaving, with POD24 (high risk))
[b] LBCL subtypes include: DLBCL NOS, HGBL, PMBCL, tFL, tMZL
[c] Clin Cancer Res. 2011 July 1; 17(13): 4550–4557. doi:10.1158/1078-0432.CCR-11-0116
[d] Includes 2 backfill patients at dose level 1 and 2 backfill patients at dose level 2

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

Patient case presentation

Patient demographics

Age	Sex	Race	Ethnicity	Height	Weight	BMI	BSA
66	Male	Asian	Not Hispanic or Latino	162.6 cm	73.2 kg	28.5 kg/m²	1.79 m²

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

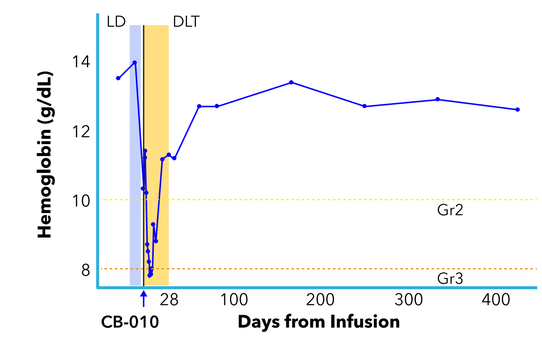
Relevant past medical history:
- Hyperglycemia
- Hypertension
- Gastroesophageal reflux
- Hyperlipidemia
- Anemia
- Thrombocytopenia

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

CB-010 has a generally well-tolerated safety profile

No GvHD, ICANS, or infections observed in this patient

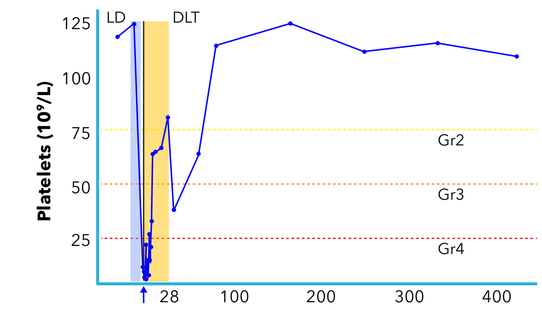
Hemoglobin recovery



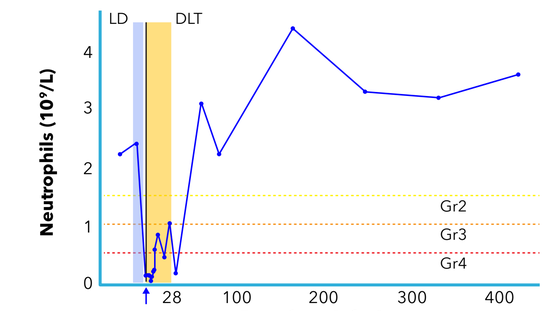
Lymphodepletion (LD) period

Dose-limiting toxicity (DLT) evaluation period

Platelet recovery



Neutrophil recovery



Patient timeline on ANTLER trial

[a] Cyclophosphamide (60 mg/kg/d for 2 days) followed by fludarabine (25 mg/m²/d for 5 days)

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)
  - ➢ Two patients have completed the 24-month study period with an ongoing CR
- In this case report, a patient with primary refractory DLBCL received CB-010 (80x10⁶ CAR-T cells), and **no GvHD, ICANS, or infections were observed**
- PET-CT imaging showed a PR at both 28 days and 3 months after CB-010 infusion, which converted to a CR at 6 months
  - ➢ The patient continues to have an **ongoing CR through month 15** and is clinically doing well
- Robust CAR-T cell expansion was observed at day 10 with ctDNA **undetectable by month 3**
- Enrollment of 2nd line 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

ABBREVIATIONS
BMI: body mass index; B-NHL: B cell non-Hodgkin lymphoma; BSA: body surface area; CAR: chimeric antigen receptor; CD: cluster of differentiation; chRDNA: CRISPR hybrid RNA-DNA; CR: complete response; CRISPR: clustered regularly interspaced short palindromic repeats; ctDNA: circulating tumor DNA; DLBCL: diffuse large B cell lymphoma; DLT: dose-limiting toxicity; FL: follicular lymphoma; GvHD: graft-versus-host disease; HGBL: high-grade B cell lymphoma; ICANS: immune effector cell-associated neurotoxicity syndrome; KO: knockout: LBCL: large B cell lymphoma; LD: lymphodepletion; MCL: mantle cell lymphoma; MHC: major histocompatibility complex; MZL: marginal zone lymphoma; NOS: not otherwise specified; ORR: overall response rate; PD-1: programmed cell death protein 1; PMBCL: primary mediastinal large B cell lymphoma; POD24: progression of disease within 24 months of initiating systemic therapy; PR: partial response; R-CHOP: rituximab + cyclophosphamide, doxorubicin, vincristine, and prednisone; RP2D: recommended Phase 2 dose; r/r: relapsed/refractory; scFv: single-chain variable fragment; TCR: T cell receptor; tFL: transformed follicular lymphoma; tMZL: transformed marginal zone lymphoma; *TRAC*: T cell receptor alpha constant.

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