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

Armored with 3 genome edits

1. **TRACT knockdown (KD)**
   - Eliminates TCR expression, reduces GvHD risk

2. **Anti-CD19 CAR site-specific insertion into TRACT 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

CB-010 ANTLETR Phase 1 trial design

Part A: 3+3 dose escalation - completed (N=16)
- **Eligibility**: aged ≤ 66 years, with ≥2 prior lines of chemotherapeutic therapy or primary refractory
- **Exclusion**: prior CD19-directed therapy
- **Lymphodepletion**: Cyclophosphamide (60 mg/kg/d for 2 days) followed by fludarabine (25 mg/m² for 5 days)

Part B: dose expansion - enrolling with blockade of 2nd-tier PD-L1
- **Exclusion**: prior CD19-targeted therapy
- **Objective**: tumor response, RP2D

Patient case presentation

**Patient demographics**

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

**Medical history and disease characteristics**

- **Tumor subtype**: DLBCL
- **Stage at screening**: III
- **Years since diagnosis**: N/A
- **Prior lines anti-cancer therapy**: None

**Relevant past medical history**

- Hyperglycemia
- Gastroesophageal reflux
- Hyperlipidemia
- Aspergillosis
- Thrombocytopenia

**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 KO, genome-editing strategy designed to enhance antitumor activity by limiting potent CAR-T cell exhaustion
- **As previously reported**, patients enrolled in the dose escalation portion of the ANTLER trial achieved a 94% ORR, 69% CR ongoing through month 15
- **Two patients have completed the 24-month study period with ongoing CR**
- **In this 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**

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

**ABBREVIATIONS**

- AML: acute myeloid leukemia
- B-ALL: B-precursor acute lymphoblastic leukemia
- B cell non-Hodgkin lymphoma
- BSA: body surface area
- CAR: chimeric antigen receptor
- CD: cluster of differentiation
- ctDNA: circulating tumor deoxyribonucleic acid
- CR: complete response
- CRISPR: clustered regularly interspaced short palindromic repeats
- DLBCL: diffuse large B-cell lymphoma
- ICANS: immune-mediated adverse neurotoxicity syndrome
- ICER: incremental cost-effectiveness ratio
- ICOS: inducible costimulatory
- LD: lymphodepletion
- MCL: mantle cell lymphoma
- MHC: major histocompatibility complex
- NHL: non-Hodgkin lymphoma
- ORR: overall response rate
- PD: progressive disease
- RP2D: recommended Phase 2 dose
- tMZL: tMZL
- TRAC: T cell receptor alpha constant.