A First-in-Human Phase 1, Multicenter, Open-label Trial of CB-010, a Next-Generation CRISPR-Edited Allogeneic Anti-CD19 CART Cell Therapy with a PD-1 Knockout, in Patients with Relapsed/Refractory B cell Non-Hodgkin Lymphoma (ANTLER Trial)

CB-010 includes a PD-1 KO designed to improve persistence of antitumor activity
- CB-010 is an allogeneic anti-CD19 CART cell therapy with a 4-1BB costimulatory domain that is derived from healthy donor T cells
- A next-generation CRISPR-Cas9 (chRDNA) technology developed at Caribou that significantly reduces off-target editing was implemented to generate 3 genome edits in the manufacture of CB-010

ANTLER trial design
- Part A: 3+3 dose escalation to determine safety, MTD, and RP2D
- Part B: dose expansion to determine tumor response

ANTLER key trial endpoints
Primary Endpoints:
- Dose Escalation (Part A):
  - Incidence of AEs and SAEs, incidence of AEs defined as DLT
- Dose Expansion (Part B):
  - Objective response rate (CR+PR)
Secondary Endpoints:
- Dose Escalation (Part A):
  - Objective response rate (CR+PR), duration of response, disease control rate, best objective response
  - Progression-free survival, overall survival
- Dose Expansion (Part B):
  - Duration of response, disease control rate, progression-free survival, overall survival
  - Incidence of AEs and SAEs

Note:
- tCTAE ≤ 0 and CRS, ICANS, GvHD grading criteria
- TCT assessment period is 128 days after CB-010 infusion

ANTLER key inclusion criteria
- Age 18 or older at the time of informed consent
- ECOG performance status of 0 or 1
- Measurable disease as per Lugano 2014 criteria
- Multiple subtypes of B-NHL: DLBCL, HGBL, tFL, PMBCL, MCL, FL*, and MZL*
- ≥ 2 prior lines of systemic chemotherapy
- Note: ≥ 1 prior line of chemotherapy for primary refractory disease

ANTLER key exclusion criteria
- Prior therapy with an anti-CD19 targeted agent
- Active or chronic GVHD requiring therapy
- Clinically significant active infection
- Note: Patients receiving IV antibiotics or having received IV antibiotics within 5 days

ANTLER trial summary
- Allogeneic CART cell therapy is an investigational treatment that may address the unmet needs of r/r B-NHL patients with aggressive disease
- CB-010 is a next-generation CRISPR-edited allogeneic CD19-directed CART cell therapy with a PD-1 KO that is being evaluated in the ANTLER trial
- ANTLER is a phase 1 first-in-human trial investigating the safety and efficacy of CB-010 as a single infusion in patients with r/r B-NHL patients at clinical sites across the United States
- Multiple subtypes of B-NHL patients who are eligible for enrollment in the ANTLER trial: DLBCL, HGBL, tFL, PMBCL, MCL, FL*, and MZL*

Patient enrollment is ongoing in the dose escalation phase of the ANTLER trial

Patient enrollment is ongoing in the dose escalation phase of the ANTLER trial

- Aggressively behaving FL and MZL

References

Abbreviations
- ABR: adverse event
- B-NHL: B-cell non-Hodgkin lymphoma
- CAR: chimeric antigen receptor
- CAR T cell: CAR T cell
- CD: cluster of differentiation
- chRDNA: designed for DNA
- CNS: central nervous system
- CR: complete response
- CT: complete tumor response
- CTCAE: Common Terminology Criteria for Adverse Events
- CRISPR: clustered regularly interspaced short palindromic repeats
- CSLBCC: clinical study of liobece-101 T cell CART
- DLT: dose limiting toxicity
- DLT: dose-limiting toxicity
- ECOC: Eastern Cooperative Oncology Group
- HGBL: high-grade B-cell lymphoma
- HGBL: high-grade B-cell lymphoma
- ICANS: immune effector cell-associated neurotoxicity syndrome
- ICANS: immune effector cell-associated neurotoxicity syndrome
- MCL: mantle cell lymphoma
- MZL: marginal zone lymphoma
- NCT: National Cancer Institute
- NHL: non-Hodgkin lymphoma
- NMD: National Medical Date
- NRC: National Research Council
- NR: not reported
- PD, primary disease
- Pts: patients
- RP2D: recommended Phase 2 dose
- RP2D: recommended Phase 2 dose
- SAE: serious adverse event
- SAE: serious adverse event
- SAE: serious adverse event
- SAE: serious adverse event