CB-012, an allogeneic anti-CLL-1 CAR-T cell therapy engineered with next-generation CRISPR technology to resist both the immunosuppressive tumor microenvironment and immune cell-mediated rejection, for patients with relapsed or refractory acute myeloid leukemia

Background
CB-012 is an allogeneic anti-CLL-1 CAR-T cell therapy in development for evaluation in relapsed or refractory acute myeloid leukemia (r/r AML). CB-012 is engineered with a next-generation CRISPR genome-editing technology to leverage both checkpoint disruption and immune cloaking to improve CAR-T cell antitumor activity. CLL-1 is a compelling therapeutic target as it is highly expressed on AML tumor cells and leukemic stem cells, but not expressed on hematopoietic stem cells. It has also been established as a target in the HLA-DR5 and HLA-DR14, CLL-1 expressing target cells. CB-012 CAR-T cells were engineered with immune cloaking and checkpoint disruption strategies employed to manufacture and armor CB-012 CAR-T cells which lead to production and secretion of PD-L1-specific antibodies to neutralize PD-L1 expression, and 4-1BB:CD40 agonists to increase CAR-T cell functionality.

CB-012 demonstrates potent antitumor activity in xenograft models of AML

CB-012 demonstrates significant antitumor efficacy and prolonged survival in a CLL-1+ patient acute myeloid leukemia (AML) xenograft model. AML cells were intravenously injected into NOD-SCID mice, which lead to effective lysis of CB-012 CAR-T cells or triple cytokines were given intravenously on day 21. CB-012 CAR-T cell therapy significantly prolonged survival when compared to control CAR-T cells or triple cytokines (***, p < 0.0001) Mb. Kaplan-Meier survival plot represents percent survival per each group. Median survival for the control group was 17 days (Day 81), and a single injection of vehicle or CB-012, or control CAR-T (5 x 109 cells, p = 0.004) at 5 days post single dose (4 of 5 CB-012 edits, 138 days (p = 0.0002)).

CB-012 checkpoint disruption armoring enhances antitumor activity in PD-L1-expressing xenograft model

CB-012 demonstrated significant antitumor efficacy and prolonged survival when compared to vehicle and control CAR-T cells in a CLL-1+ patient AML xenograft model. CB-012 CAR-T cells were engineered with immune cloaking and checkpoint disruption strategies to enhance the antitumor activity of CAR-T cells in the PD-L1-expressing xenograft model. CB-012 CAR-T cells were engineered with immune cloaking and checkpoint disruption strategies to enhance the antitumor activity of CAR-T cells in the PD-L1-expressing xenograft model.