306 **EVALUATION OF AB-101, AN ALLOGENEIC CORD BLOOD-DERIVED NATURAL KILLER (NK) CELL THERAPY, AS AN ADCC ENHANCER IN HEMATOLOGIC AND SOLID TUMORS**

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Background AB-101 is a non-engineered, allogeneic, off-the-shelf, cryopreserved cord blood-derived natural killer (NK)-cell therapy in development as a cancer therapeutic. A highly scaled manufacturing process enables production of 1000s of doses from a single donor cord blood unit (CBU). AB-101 has been optimized for combination with monoclonal antibodies (mAbs) to enhance antibody-dependent cellular cytotoxicity (ADCC) and anti-tumor responses through selection of key attributes in the CBU. These include a KIR-B haplotype and natural high-affinity variant of CD16 (158V/V polymorphism), which are associated with improved anti-tumor activity and ADCC enhancement. Administration of AB-101 to patients in combination with mAbs has the potential to enhance the ADCC response thereby increasing anti-tumor activity. Here we present preclinical data to support development of AB-101 in combination with mAbs as an ADCC enhancer in hematologic malignancies and solid tumor indications.

Methods AB-101 was expanded utilizing a proprietary engineered feeder-cell line. In vitro characterization of AB-101 included evaluation of the purity and expression of cell surface markers by flow cytometry. In vitro ADCC assays were performed at various effector to target ratios against hematologic (Raji, ARH-77) and solid tumor (MDA-MB-468) cell lines in the presence of approved therapeutic antibodies. In addition, AB-101 efficacy was assessed in vivo in established hematologic (Raji) and ovarian (SKOV-3) xenograft models.

Results AB-101 was ≥95% CD3-CD56+ with ≥80% CD56+CD16+ and high expression of NK activating receptors such as NKG2D, NKp30, NKp44 and DNAM-1 was observed. Cytotoxicity assays were used to demonstrate the ADCC mechanism of activity in combination with approved therapeutic antibodies. In the Raji cell line, when AB-101 was combined with rituximab, ~ 90% of target cell lysis was observed vs ~ 79% with AB-101 alone. Similar cell killing activity was observed against ARH-77 and MDA-MB-468 cell lines in combination with obinutuzumab and cetuximab, respectively. In addition, in vivo efficacy of AB-101 and AB-101 in combination with rituximab demonstrated enhanced median survival in the Raji xenograft model and AB-101 in combination with trastuzumab led to enhanced survival in the SKOV-3 xenograft model.

Conclusions Data presented suggests that AB-101 is a pure and readily expandable NK cell product that has the potential to be effective in combination with mAbs to treat both hematologic and solid tumors without the need for engineering. AB-101 is currently in a Ph1 clinical trial to evaluate the safety and anti-tumor activity alone and in combination with rituximab in patients with relapsed or refractory NHL (ClinicalTrials.gov: NCT04673617).

Ethics Approval All animal work was conducted under reviewed IACUC protocol and with approval of an IACUC committee at each center where the studies took place.

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