

A PHASE 1/2, OPEN-LABEL, DOSE-ESCALATION, SAFETY AND TOLERABILITY STUDY OF NC762 IN SUBJECTS WITH ADVANCED OR METASTATIC SOLID TUMORS

<http://dx.doi.org/10.1136/jitc-2022-SITC2022.0748>

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Background NC762 is a humanized IgG1κ monoclonal antibody that targets human B7-H4 (B7 homolog 4), a transmembrane protein, associated with the B7 family of molecules known for their immunomodulatory functions. While limited expression is observed on healthy tissue, B7-H4 is commonly expressed by several tumor types including ovarian, lung, renal, melanoma, prostate, pancreatic, and breast cancers and is often correlated with poor clinical outcome. Given differential expression of B7-H4 in healthy and cancerous tissue, B7-H4 presents itself as an attractive candidate for a targeted therapeutic monoclonal antibody (mAb) for oncology.

Preclinical data demonstrated that binding of NC762 to tumors expressing B7-H4 results in inhibition of tumor growth in vivo. The inhibitory effect on tumor growth is not dependent upon T cells and does not appear to be a predominant antibody-dependent cellular cytotoxicity (ADCC) mechanism. However, NC762 has been Fc engineered to enhance binding to CD16a and does demonstrate increased anti-tumor activity in the presence of NK cells.

Methods This is a multi-center, first in human, phase 1/2, open-label, single-armed study to determine the safety and tolerability, MTD, and pharmacologically active dose for NC762, as well as to assess preliminary efficacy, and explore predictive and pharmacodynamic biomarkers in subjects with advanced or metastatic solid tumors. The 3+3 dose escalation design in 5 cohorts is to establish recommended phase 2 dose (RP2D) (NCT04875806). Phase 1b and 2 study will select for patients expressing B7-H4+ in specific tumor types including ovarian.

Results As of 07/20/2022, a total of 14 patients (Median age 69; 5F, 9M) with 5 tumor types, have been enrolled, treated, and completed the DLT period. Median line of prior therapies was six. NC762 (up to 10mg/kg), was well tolerated, with no safety concerns, no infusion-related toxicities, nor any reported DLT. Clinical benefit is seen from the lowest dose cohorts with a few stable diseases beyond six months. PK and potential pharmacodynamic biomarkers continue to be evaluated as the phase 1 study continues to enroll and will be presented.

Conclusions Preliminary evaluation of NC762 in subjects with advanced or metastatic solid tumors appears to be safe and well-tolerated. Further evaluation will be performed with the final cohort at 20mg/kg and simultaneous expansion of 10mg/kg in B7-H4+ advanced solid tumors to confirm these initial findings.

Trial Registration NCT04875806

Ethics Approval This study has been approved by the IRB of all the participating institutions, and all participants have given informed consent before taking part in the study.

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.