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A PHASE 1B/2, OPEN-LABEL, SAFETY, TOLERABILITY AND EFFICACY STUDY OF NC410 PLUS PEMBROLIZUMAB FOR PARTICIPANTS WITH IMMUNE CHECKPOINT INHIBITOR (ICI) REFRACTORY, OR MSS/MSI-LOW ICI NAÏVE ADVANCED OR METASTATIC SOLID TUMORS

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Background The tumor extracellular matrix (ECM) functions as a physical barrier to immune cell infiltration and acts to directly inhibit immune cells by interacting with the inhibitory receptor, Leukocyte Associated Immunoglobulin-Like Receptor-1 (LAIR-1). Several recent publications on pre-clinical studies have demonstrated this inhibition can be reversed by NC410, a recombinant form of the LAIR-2 protein, a naturally produced soluble decoy that normally functions to compete with LAIR-1 binding. NC410 is composed of LAIR-2 protein fused to a human Fc domain of the immunoglobulin (Ig) subtype IgG1.¹ More recently, in vivo modeling studies demonstrate that treatment with PD(L)-1 blockade in a murine lung model drives enhanced collagen production due to an increase in TGF- β signaling, resulting in resistance to treatment targeting the PD-L1 pathway. Genetically driven overexpression of LAIR-2, in this model was able to overcome resistance, sensitize tumors to PD(L)-1 blockade, reduce tumor growth, and increase local immune cell activation.² Extensive preclinical testing by NextCure and collaborators has demonstrated that the combination of NC410, and anti-PD(L)-1 leads to consistent reduction of tumor burden and enhanced survival in several animal models. A clinical trial of NC410 Phase 1 monotherapy in participants with advanced or metastatic solid tumors is currently on-going. Preliminary clinical and biomarker data has been presented,³ supporting immune activation and mechanism of action proposed for NC410.

Methods This is an open-label, non-randomized, Phase 1b/2 study to determine the safety and tolerability of NC410 when combined with Pembrolizumab. This study will also assess the clinical benefit of combination therapy in participants with advanced unresectable and/or metastatic ICI refractory solid tumors (CRC MSI-H, Gastric including GE junction, Esophageal, Endometrial, and H&N cancer) in Cohort 1, and ICI Naïve, Microsatellite Stable or Microsatellite Instability Low (MSS/MSI-low) solid tumors (CRC, Gastric including GE junction and Ovarian) in Cohort 2. Key eligibility criteria include measurable disease based on RECIST v1.1 and being able to provide tissue samples at screening. Participants will receive pembrolizumab 400 mg on Day 1 of each 42-day cycle. NC410 will be given on Days 1, 15 and Day 29 of each 42-day cycle. Objective response rate (ORR) based on RECIST v1.1 will be the primary endpoint, while duration of response (DoR), disease control rate (DCR), progression-free survival (PFS), and overall survival will be evaluated as secondary endpoints. Several biomarker effects of NC410 in combination with pembrolizumab in peripheral blood and tumor tissue will be assessed.

REFERENCES

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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.

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