Abstract Title: A phase 1/2, open-label, dose-escalation, safety and tolerability study of NC410 in subjects with advanced or metastatic solid tumors

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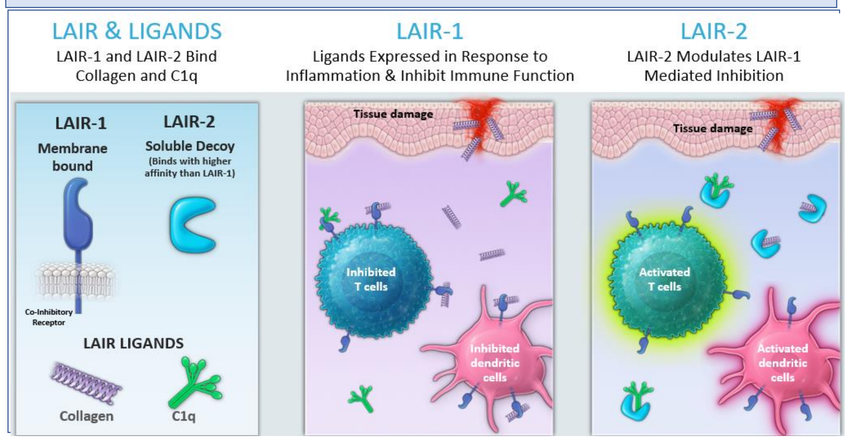
Martin Gutierrez[1], Filip Janku[2], Linjie Tian[3], , Jason Luke[4], Elaine Shum[5], John Shin[6], Ido Weiss[3], Linda Liu[3], Dallas Files[3], Sol Langermann[3], Han Myint[3], Marijo Bilusic[6]

Hackensack University Medical Center[1], Hackensack, NJ; MD Anderson[2], TX; NextCure Inc[3], MD; University of Pittsburg[4], PA; NYU Langone Health Perlmutter Cancer Center[5], New York, NY; National Cancer Institute[6], Bethesda, MD

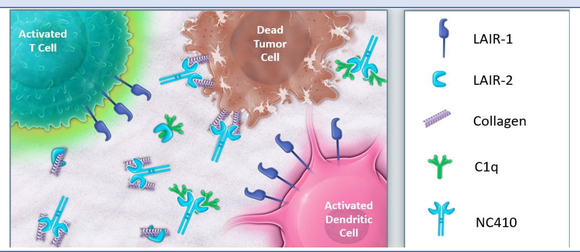
Background

Abnormalities in the extracellular matrix of the tumor microenvironments (TME) support tumor progression, lead to immune dysfunction, and provide targets for cancer therapeutics. Collagens are a primary component of the extracellular matrix. Abnormal levels and dysregulated exposure of collagens for immune cell interactions in the TME have been proposed to disrupt anti-tumor immunity. LAIR-1 is an inhibitory receptor expressed on the cell surface of several immune cell subsets. LAIR-1 binding to collagens inhibits immune cell function. LAIR-2 is a soluble homolog of LAIR-1 that binds to and out competes LAIR-1 binding to collagens and serves as a natural decoy to promote immune function. NC410 is a fusion protein of LAIR-2 fused to human IgG1 Fc domain and acts as a LAIR-1 decoy and induces ECM remodeling to promote immune cell infiltration and function in TME.

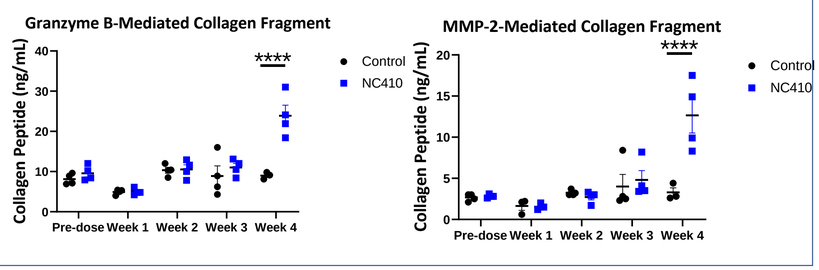
LAIR Patho-Biology



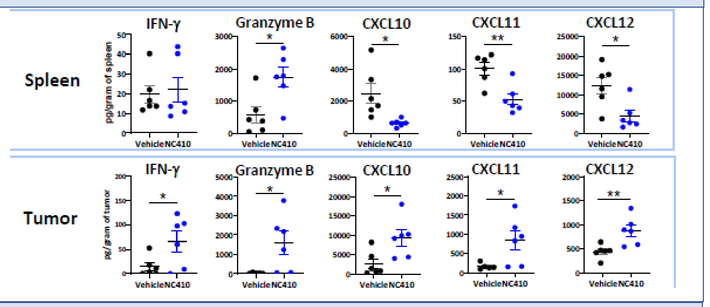
NC410 is a Fusion Protein of LAIR-2 Fused to Human IgG1 Fc Domain: Prevents Immune Suppression & Promotes T cell Function



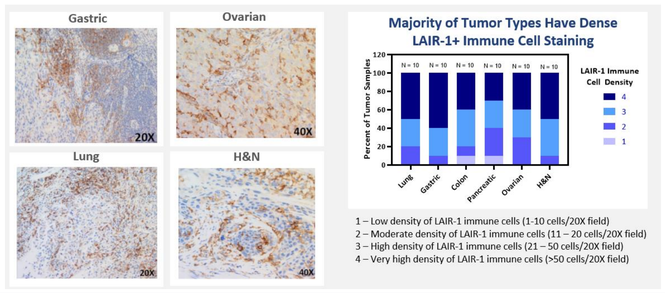
Collagen degradative products indicative of immune activation and ECM remodeling are increased with NC410 treatment



NC410 potentiates local and systemic anti-tumor T cell immunity



LAIR1 Expression in Immune Cells in TME



NC410 Inclusion & Exclusion Criteria

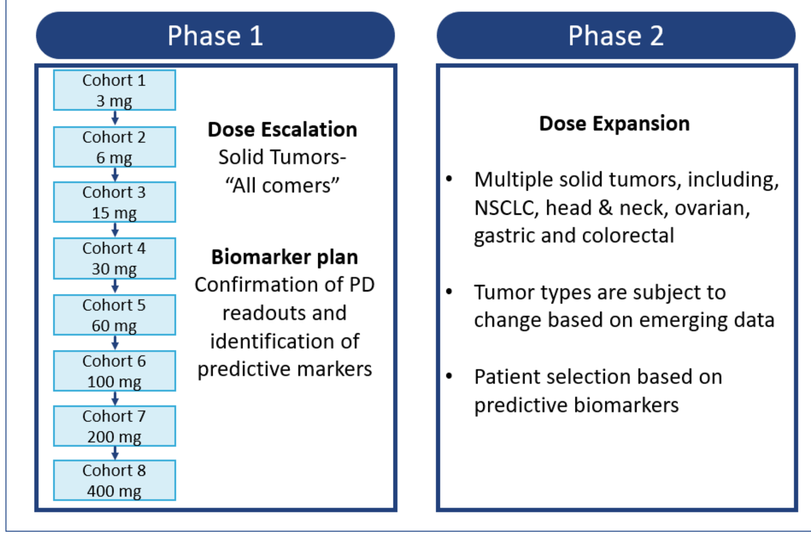
Inclusion Criteria:

- Men and women aged 18 or older.
- ECOG performance status 0 to 1.
- Locally advanced or metastatic disease; locally advanced disease must not be amenable to resection with curative intent.
- Subjects who have disease progression after treatment with available therapies that are known to confer clinical benefit, or who are intolerant to treatment, or who refuse standard treatment. Note: There is no limit to the number of prior treatment regimens.
- Presence of measurable disease based on RECIST v1.1. Tumor lesions situated in a previously irradiated area, or in an area subjected to other locoregional therapy, are not considered measurable unless there has been demonstrated progression in the lesion

Exclusion Criteria:

- Screening laboratory values of:
  - ANC <1.5 × 10^9/L; Platelets < 100 × 10^9/L; Hemoglobin < 9 g/dL or < 5.6 mmol/L
  - Serum creatinine > 1.5 × institutional upper limit of normal (ULN)
  - AST & ALT ≥ 2.5 × ULN; Total bilirubin ≥ 1.5 × ULN; INR > 1.5 × ULN; aPTT > 1.5 × ULN
- Transfusion of blood products (including platelets or red blood cells) or administration of colony-stimulating factors (including GCSF, GMCSF, rEPO within 14 days before the first administration of study drug)
- Receipt of anticancer medications or investigational drugs
- Active autoimmune disease that required systemic treatment in the past
- Known active CNS metastases and/or carcinomatous meningitis.
- Known additional malignancy that is progressing or requires active treatment, or history of other malignancy within 2 years of study entry
- Evidence of active, noninfectious pneumonitis or history of interstitial lung disease.
- History or presence of an abnormal ECG
- Active infection requiring systemic therapy
- Evidence of hepatitis B virus (HBV) or hepatitis C virus (HCV) infection or risk of reactivation; Known history of HIV (HIV 1 or HIV 2 antibodies)

NC410 Study Schema



Outcome Measure

Primary Outcome

1. Number of participants with treatment-emergent adverse events as assessed by CTCAE 5.0
   - Frequency, duration, and severity of treatment-emergent adverse events (AEs)
2. Define a maximum tolerated dose (MTD) or pharmacologically active dose (PAD)
   - A 3 + 3 design will be utilized to determine the MTD of **NC410**

Secondary Outcome

1. Objective response rate (ORR) per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 and modified RECIST (mRECIST) v1.1
2. Duration of Response (DoR) per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 and modified RECIST (mRECIST) v1.1
3. Disease Control Rate (DCR) per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 and modified RECIST (mRECIST) v1.1

Conclusions