Poster Number

A Phase 1, Open-Label, Multicenter Study to Assess the Safety, Tolerability, and Immunogenicity of mRNA-4157 Alone and in Combination in Participants With Solid Tumors

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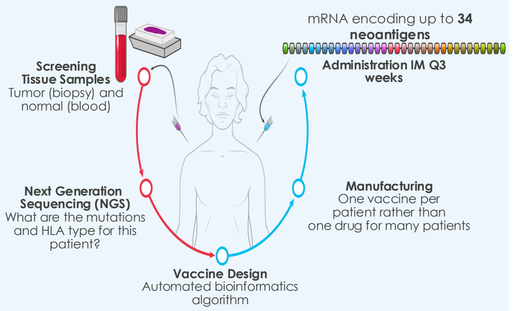
BACKGROUND

- Neoantigens are tumor-specific non-synonymous mutations in proteins that are processed and presented in major histocompatibility complex molecules, driving anti-tumor T-cell responses[1].
- mRNA-4157 is a novel mRNA-based individualized neoantigen therapy that encodes up to 34 patient specific neoantigens mediating anti-tumor T-cell activation[2].
- In the prior dose escalation portion of the mRNA-4157-P101 trial, 1mg IM Q3 w was identified as the recommended dose[3].
- In melanoma, adjuvant mRNA-4157 plus pembrolizumab has demonstrated durable improvements in RFS & DMFS[4].
- Neoantigens have also been seen in less immune-infiltrated, high-risk tumors such as pancreatic adenocarcinoma (PDAC), gastric/GEJ and NSCLC. In fact, long-term survivors demonstrate more neoantigen specific T-cell responses[5,6].
- We hypothesize that in PDAC, gastric/GEJ and NSCLC mRNA-4157 will invigorate neoantigen specific T-cells, potentially delaying recurrence and minimizing micro-metastases, thus affecting patient outcome.
- mRNA-4157-P101 is a single arm study to evaluate safety, tolerability, immunogenicity, ctDNA dynamics, anti-tumor efficacy and exploratory biomarkers of mRNA-4157-based combinations in solid tumors.



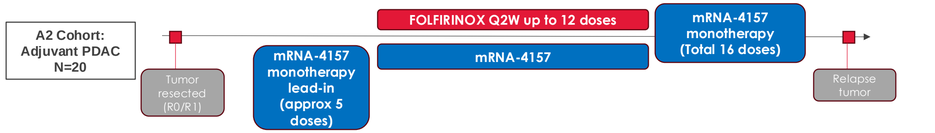
OBJECTIVES

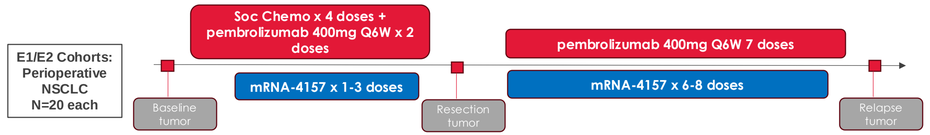
PRIMARY: To determine the safety and tolerability of mRNA-4157-based combinations

SECONDARY: To characterize the preliminary antitumor activity & association of ctDNA to clinical outcomes by mRNA-4157

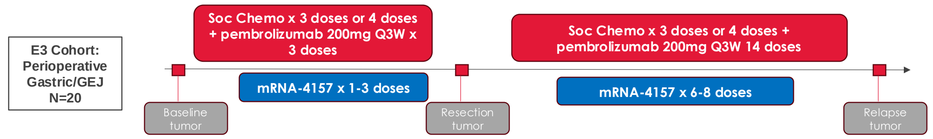
EXPLORATORY: To assess immunogenicity, pharmacokinetics, tumor and blood-based biomarkers

STUDY DESIGN





SoC Chemo: Gemcitabine+ Cisplatin, Carboplatin + Pemetrexed, or Carboplatin + Paclitaxel



SoC Chemo: FLOT (preferred), 5FU + Cisplatin, or Capecitabine + Cisplatin

ELIGIBILITY CRITERIA

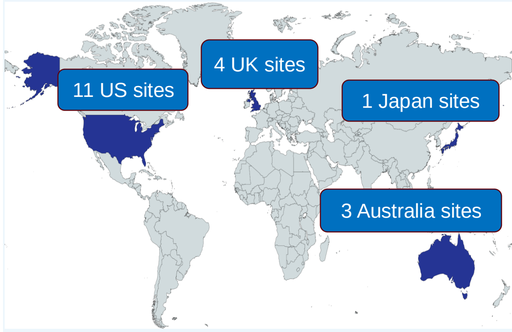
Inclusion	Exclusion
Cohort A2: Non-metastatic, R0/R1 resected PDAC with no evidence of disease Cohort E1: Stage 2-3B (AJCCv8) lung adenocarcinoma Cohort E2: Stage 2-3B (AJCCv8) lung squamous cell carcinoma Cohort E3: locallly advanced, non-metastatic ≥T3 or Node+ gastric or gastroesophageal adenocarcinoma	Treatment with any chemotherapy, immunotherapy, or active investigational agent within 4 weeks of mRNA-4157 treatment start
Measurable disease (RECIST 1.1)	Any CNS metastasis
Suitable for treatment with pembrolizumab (if applicable)	Any steroid or immunosuppressive medication within 7 days of initial mRNA-4157 or Pembrolizumab treatment
Adequate tumor sample available for NGS, for mRNA-4157 manufacture	Active autoimmune condition requiring systemic therapy
ECOG 0 or 1	History of non-infectious pneumonitis requiring steroids, or current pneumonitis
Age ≥18 years	Has solid organ or allogeneic bone marrow transplant
Normal organ and marrow function	History of HIV or active Hepatitis B or C

ASSESSMENTS & ANALYSES

Type	Detail
Tumor imaging	A2: Every 12 weeks from start of treatment. E1, E2, E3: At completion of pre-op therapy, then post-surgery, then every 12 weeks. For those not getting surgery, every 12 weeks from end of pre-op therapy.
Safety	Incidence, nature, and severity of adverse events (including serious AEs and AEs leading to treatment discontinuation) to assess the safety and tolerability of mRNA-4157 with SOC chemotherapy in adjuvant PDAC, and in combination with pembrolizumab and SOC chemotherapy in perioperative NSCLC and gastric/GEJ.
Efficacy	Efficacy follow up for 2 years from start of treatment or until disease relapse, start of non-protocol therapy, death withdrawal of consent or sponsor termination of study that is earliest
Translational analyses	All patients provide both blood and FFPE tumor samples for next-generation sequencing (NGS) enabling mRNA-4157 manufacture. Tumor biomarkers will be analyzed from NGS and imaging analyses from tumor samples. For E1, E2 & E3 cohorts, baseline and post-treatment biopsies will be analyzed for tumor biomarkers and underlying mechanisms of action Serial peripheral immune cells obtained from whole blood or leukapheresis will be tested for immunogenicity using neoantigen peptide pools for all cohorts. For patients with leukapheresis samples, deeper immunophenotyping will be performed to assess immunogenicity contributions. Peripheral T cell receptors and immune cells will be analyzed by NGS. Pharmacokinetics and blood-based biomarkers will also be analyzed. Longitudinal ctDNA levels will be measured from the start of treatment until follow up visits.

CURRENT STATUS

Enrollment is ongoing and as of September 2024 the trial is open in the US, Australia, UK, and Japan.



POSTER QR

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Trial Registration

This study is registered with ClinicalTrials.gov (NCT03313778)

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