A Phase 1, Open-Label, Multicenter Study to Assess the Safety, Tolerability, and Immunogenicity of mRNA-4157 Alone in Subjects With Resected Solid Tumors and in Combination With Pembrolizumab in Subjects With Unresectable Solid Tumors (Keynote-603)

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Background

The aim of the keypoint is to demonstrate the safety, tolerability, and immunogenicity of mRNA-4157 when administered alone or in combination with pembrolizumab in patients with unresectable solid tumors. The study also aimed to assess the efficacy of this treatment in terms of clinical response and overall survival.

Design

This is a Phase 1, open-label, multicenter study with three parts: Part A (monotherapy), Part B (combination therapy), and Part C (combination therapy).


Part B (Combination Therapy): mRNA-4157 + pembrolizumab in patients with unresectable solid tumors.

Part C (Combination Therapy): mRNA-4157 + pembrolizumab in patients with unresectable solid tumors.

Clinical Data

- **Response rates:**
  - CPI naïve HPV(-) HNSCC: 0%
  - CPI naïve MSS CRC: 0%

- **Safety profile:**
  - Most common side effects include:
    - Injection site reactions
    - Nausea
    - Fatigue
    - Myalgia

Personalized cancer vaccine process

- **Screening:**
  - Blood samples are analyzed using algorithms based on whole exome and RNA sequencing of tumor and normal tissue.

- **Individually designed and manufactured for each patient:**
  - Vaccines are made to target neoantigens.

- **Encapsulated in a novel lipid nanoparticle and delivered intramuscularly:**
  - Ensures a controlled delivery of the vaccine.

Study design

- **Dose escalation:**
  - Dose levels (0.04-1 mg)

- **Dose expansion:**
  - 1 mg

- **Part A:** mRNA-4157 monotherapy (n=16)

- **Part B:** mRNA-4157 + pembrolizumab (n=78)

- **Part C:** mRNA-4157 + pembrolizumab (n=17)

Biomarker Data

- **PD-L1 expression:**
  - Assessed in tumor samples.

- **TMB levels:**
  - Measured in tumor samples.

Conclusions

- **Efficacy:**
  - The overall response rate (ORR) to mRNA-4157 and pembrolizumab combination in CPI naïve HPV(-) HNSCC patients was 0%.

- **Safety:**
  - The most common side effects were similar to those observed in previous studies.

- **Immunogenicity:**
  - The study showed promising immune responses.

- **Future directions:**
  - Further investigation is needed to explore the potential of mRNA-4157 in combination with pembrolizumab for treating HPV(-) HNSCC.

References:


