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 study aimed to evaluate the safety, tolerability, and immune response of mRNA-4157 alone or in combination with pembrolizumab in patients with advanced solid tumors. Two dose escalation cohorts were included:

- **Cohort A**: 13 adjuvant patients treated with mRNA-4157 alone.
- **Cohort B**: 10 patients treated with mRNA-4157 in combination with pembrolizumab.

The study design consisted of a screening and cohort enrollment phase, followed by a treatment and assessment period. Clinical outcomes were evaluated based on tumor response, immune-related adverse events (irAEs), and immune-related biomarkers.

**Key Findings**

- **Cohort A**,
  - **13 patients** received mRNA-4157 monotherapy.
  - **10 patients** experienced a 4-week treatment cycle, while 3 received 5 cycles.

- **Cohort B**,
  - **23 patients** received mRNA-4157 in combination with pembrolizumab.
  - **19 patients** were treated with pembrolizumab as monotherapy.

**Clinical Outcomes**

- **Tumor Response**:
  - **9 patients** (69.2%) in Cohort A showed stable disease.
  - **14 patients** (60.9%) in Cohort B achieved tumor response.

- **Immune Biomarkers**:
  - **Increased expression of PD-L1 and PD-L2** was observed in treated patients.
  - **Enhanced vaccine antigen expression** was noted.

**Safety**

- **Adverse Events** included:
  - **irAEs** such as elevation of GGT and thrombocytopenia.
  - **irAEs** were manageable and did not lead to treatment discontinuation.

**Conclusions**

- **mRNA-4157** appears well-tolerated and safe at all dose levels, with minimal adverse events.
- **No mRNA-4157 related grade 3/4 AE or SAEs were reported**.
- **Clinical responses** were observed in 4 out of 20 patients treated with mRNA-4157/pembrolizumab combination.

**Study Summary**

This study aimed to assess the safety, tolerability, and immune response of mRNA-4157 alone or in combination with pembrolizumab in patients with advanced solid tumors. The study design included a screening and cohort enrollment phase, followed by a treatment and assessment period. The main findings were:

- **Cohort A**:
  - 13 patients received mRNA-4157 monotherapy.
  - 10 patients showed stable disease.

- **Cohort B**:
  - 23 patients received mRNA-4157 in combination with pembrolizumab.
  - 14 patients achieved tumor response.

**Safety**:

- Adverse events were manageable and did not lead to treatment discontinuation.

This study provides valuable insights into the potential of mRNA-4157 for treating advanced solid tumors, highlighting the need for further evaluation in clinical practice.