Clinical trials in-progress

SAFETY, TOLERABILITY, AND IMMUNOGENICITY OF mRNA-4157 IN COMBINATION WITH PEMBROLIZUMAB IN SUBJECTS WITH UNRESECTABLE SOLID TUMORS (KEYNOTE-603): AN UPDATE

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Background T-cell targeting of mutation-derived epitopes (neo-antigens) has shown to drive anti-tumor responses. Immunizing patients against such neoantigens in combination with a checkpoint inhibitor (CPI) may elicit greater anti-tumor responses than CPI alone. Mutations are rarely shared between patients, thus requiring a personalized approach to vaccine design. mRNA-4157 is a lipid encapsulated mRNA based personalized cancer vaccine encoding neoantigens selected using a proprietary algorithm to induce neoantigen specific T cells and associated anti-tumor responses. This report includes updates from the mRNA-4157 Phase1(P1) study. The initial data was presented for two cycles before the first dose of mRNA-4157 and within 12 weeks of last dose (with no intervening RECIST v1.1 after at least 12 weeks of treatment on pembrolizumab). 10 cycles (Q3W) of mRNA-4157 by intramuscular injection at 9 months (Q3W) of mRNA-4157 by intramuscular injection at 65 patients (MSI-h) or TMB-High cancers. Expansion cohorts includes patients with CPI-naive MSS-CRC and HPV-negative HNSCC patients with advanced/metastatic solid tumors.

Methods This study evaluates the safety and efficacy of mRNA-4157 as monotherapy in patients with resected solid tumors (Part A) and in combination with pembrolizumab in patients with advanced/metastatic solid tumors (Parts B). The selected solid tumors in Part A-B includes melanoma, bladder carcinoma, HPV-negative (HPV-neg) HNSCC, NSCLC, SCLC, MSI-High (MSI-h), or TMB-High cancers. Expansion cohorts includes patients with CPI-naive MSS-CRC and HPV-negative HNSCC (Part C) and with resected melanoma (Part D). Patients receive up to 9 cycles (Q3W) of mRNA-4157 by intramuscular injection at up to 1 mg alone (Part A) or in combination with pembrolizumab (200 mg IV Q3W, Parts B-D). Pembrolizumab is administered for two cycles before the first dose of mRNA-4157 and may continue after 9 cycles of combination. Endpoints include safety, tolerability, efficacy and biomarker assessments.

Results 79 patients received mRNA-4157: 16 as monotherapy and 63 in combination with pembrolizumab. Only low grade and reversible treatment related AEs were reported. 14/16 Part A patients (3 melanoma, 11 NSCLC, 2 MSI-h CRC) remained disease free on study. 28 patients in Part B (6 bladder, 2 HNSCC, 3 melanoma, 10 NSCLC, 2 SCLC, 4 MSI-h tumor, 1 TMB-h tumor), 27 patients in Part C (10 HNSCC and 17 MSS-CRC), and 8 patients with resected melanoma (Part D) received combination. 3 CR (1 HNSCC, 1 MSI-h CRC and 1 MSI-h prostate), and 8 PR (1 bladder, 4 HNSCC, 2 SCLC and 1 MSI-h endometrial) were observed with combination. Of 10 CPI-naive HPV-neg HNSCC patients, the response rate was 50% (1CR, 4PR, 4SD) mPFS 9.8months, which compared favorably to published rates of ~14.6% mPFS 2.0months for pembrolizumab monotherapy. 2, 3 Bio-marker assessments including immune gene expression profiling will be presented.

Conclusions mRNA-4157 has an acceptable safety profile along with observed clinical responses in combination with pembrolizumab. Preliminary efficacy analysis from CPI-naïve relapsed/refractory HPV-neg HNSCC cohort suggests activity of this combination. Study is ongoing.

Clinical trials in-progress

DURABLE RESPONSES AND IMMUNE ACTIVATION WITH INTRATUMORAL ELECTROPORATION OF PIL-12 PLUS PEMBROLIZUMAB IN ACTIVELY PROGRESSING ANTI-PD-1 REFRACTORY ADVANCED MELANOMA: KEYNOTE 695 INTERIM DATA

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Background Electroporated plasmid IL-12 (TAVO or tavokinogene telseplasmid) is a novel pro-inflammatory intratumoral therapy with substantial single agent activity in melanoma, which has been shown to synergize with anti-PD-1 antibodies in patients predicted as non-responders to anti-PD-1. 1, 2 Interim data from patients with stage III/IV melanoma actively progressing on anti-PD-1 antibody are presented herein.

Methods Patients with confirmed disease progression by RECIST v1.1 after at least 12 weeks of treatment on pembrolizumab or nivolumab (or combination checkpoint blockade) and within 12 weeks of last dose (with no intervening