GI-4000 VACCINE AS ADJUVANT CONSOLIDATION THERAPY IS IMMUNOGENIC FOLLOWING DEFINITIVE TREATMENT IN PATIENTS WITH STAGE III+ ADENOCARCINOMA OF THE LUNG WITH KRAS MUTATIONS


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Background

The efficacy of GI-4000, a yeast-based adjuvant therapy, in subjects with stages III+ NSCLC has been previously reported. GI-4000 is immunogenic in targeting mutated KRAS and in enhancing the immune response to tumor antigens. In this study, we evaluate the immunogenicity and safety of GI-4000 in subjects with KRAS-mutant NSCLC who have completed definitive treatment with curative intent. GI-4000 was also evaluated in comparison to standard of care.
Active immunotherapy with yeast-based Tarmogens

Tarmogens are whole, heat-killed recombinant Saccharomyces cerevisiae yeast modified to express one or more protein targets that stimulate the immune system against diseased cells. The target antigens are markers of diseased cells and can be conserved viral proteins, mutated proteins unique to cancer cells, or proteins over-expressed in cancer. To create a new Tarmogen, DNA encoding target protein antigens is engineered into a yeast expression plasmid. The heat-inactivated yeast, with the target protein inside, is administered as the final expressed in cancer. To create a new Tarmogen, DNA encoding target protein antigens is engineered into a plasmid. The heat-inactivated yeast is administered as the final expression vector.

The primary endpoint was vaccine-induced T cell responses documented by interferon-γ ELISpot assay in peripheral blood mononuclear cells (PBMCs) stimulated with KRAS peptide pools from the specific mutation present in the patient's tumor. The primary endpoint was vaccine-induced T cell responses documented by interferon-γ ELISpot assay in peripheral blood mononuclear cells (PBMCs) stimulated with KRAS peptide pools from the specific mutation present in the patient's tumor. The primary endpoint was vaccine-induced T cell responses documented by interferon-γ ELISpot assay in peripheral blood mononuclear cells (PBMCs) stimulated with KRAS peptide pools from the specific mutation present in the patient's tumor. The primary endpoint was vaccine-induced T cell responses documented by interferon-γ ELISpot assay in peripheral blood mononuclear cells (PBMCs) stimulated with KRAS peptide pools from the specific mutation present in the patient's tumor. The primary endpoint was vaccine-induced T cell responses documented by interferon-γ ELISpot assay in peripheral blood mononuclear cells (PBMCs) stimulated with KRAS peptide pools from the specific mutation present in the patient's tumor. The primary endpoint was vaccine-induced T cell responses documented by interferon-γ ELISpot assay in peripheral blood mononuclear cells (PBMCs) stimulated with KRAS peptide pools from the specific mutation present in the patient's tumor. The primary endpoint was vaccine-induced T cell responses documented by interferon-γ ELISpot assay in peripheral blood mononuclear cells (PBMCs) stimulated with KRAS peptide pools from the specific mutation present in the patient's tumor. The primary endpoint was vaccine-induced T cell responses documented by interferon-γ ELISpot assay in peripheral blood mononuclear cells (PBMCs) stimulated with KRAS peptide pools from the specific mutation present in the patient's tumor.

Conclusions: MBBCC's program of re vivo testing of lung adenocarcinoma resection specimens permits the identification of patients for KRAS specific therapy. GI-4000 is immunogenic in targeting mutated KRAS and is an adjuvant "consolidation" therapy in patients with stage III adenocarcinoma of the lung with KRAS mutations. GI-4000 vaccine as adjuvant consolidation therapy is immunogenic following definitive treatment in patients with stage I-III adenocarcinoma of the lung with KRAS mutations.


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Background: All patients at MSKCC with lung adenocarcinoma undergo re vivo testing for EGFR and KRAS mutations at the time of surgical resection. KRAS mutations occur in 10% of resected lung adenocarcinomas at MSKCC from 2006–2009. GI-4000 is a recombinant yeast-based vaccine with a sequence engineered to express one of 4 mutated KRAS oncoproteins.

Methods: GI-4000 was administered as adjuvant therapy to patients with stage I-III lung adenocarcinomas and GI-4000 was given for 6 weekly doses. In stage I/II patients, 6 monthly doses, then every 3 months for up to 3 years. The primary endpoint was vaccine-induced T cell responses documented by interferon-γ ELISpot assay in peripheral blood mononuclear cells (PBMCs) stimulated ex vivo with KRAS peptide pools from the specific mutation present in their tumor.

Results: 24 subjects were enrolled. Women = 17, Stage I/A = 10, II/B = 4, III = 8, median age 67 (range 50–80), GI-4000 (n=3), G12C (n=4), G12V (n=3), median # of doses per subject = 9 (range 1–16). To date, there have been no serious adverse events related to GI-4000. 17/24 patients had adequate immune sampling to be analyzed by ELISpot assay. GI-4000 was given for 3 weekly doses, then 6 monthly doses, then every 3 months for up to 3 years. The primary endpoint was vaccine-induced T cell responses documented by interferon-γ ELISpot assay in peripheral blood mononuclear cells (PBMCs) stimulated ex vivo with KRAS peptide pools from the specific mutation present in their tumor. 8/17 (47%) of the patients developed an immune response to GI-4000 vaccine as adjuvant consolidation therapy is immunogenic following definitive treatment in patients with stage I-III adenocarcinoma of the lung with KRAS mutations. GI-4000 vaccine as adjuvant consolidation therapy is immunogenic following definitive treatment in patients with stage I-III adenocarcinoma of the lung with KRAS mutations. GI-4000 vaccine as adjuvant consolidation therapy is immunogenic following definitive treatment in patients with stage I-III adenocarcinoma of the lung with KRAS mutations. GI-4000 vaccine as adjuvant consolidation therapy is immunogenic following definitive treatment in patients with stage I-III adenocarcinoma of the lung with KRAS mutations. GI-4000 vaccine as adjuvant consolidation therapy is immunogenic following definitive treatment in patients with stage I-III adenocarcinoma of the lung with KRAS mutations.