AN OBSERVATIONAL CLINICAL STUDY WITH RAS PEPTIDE VACCINE TG01 EVALUATING IMMUNE RESPONSE, SAFETY AND OVERALL SURVIVAL IN PATIENTS WITH NON-RESECTABLE Pancreatic Cancer

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BACKGROUND
 TG01 is the first injectable antigen-specific cancer immunotherapy (ASCI) targeted to treat patients with KRAS mutations. TG01 consists of a mixture of synthetic peptides representing the 13 oncogenic mutations in KRAS. Oncogenic mutations in KRAS drive cell growth and malignant transformation and is found in more than 85% of pancreatic adenocarcinomas. Clinical efficacy of peptide cancer vaccines has generally been poor due to the short length of the peptide, which are only able to activate MHC class I restricted CD8+ cytotoxic T-cells. The TG01 peptides are 17 amino acids long and designed to activate both CD8+ cytotoxic T-cells as well as MHC class II CD4+ helper T-cells which is necessary to sustain the T-cell response.2-4 TG01 induces mutant-RAS (mtRAS) specific T-cell responses which are enhanced by co-administration of GM-CSF (recombinant granulocyte-macrophage colony-stimulating factor).

METHODS
 25 treatment naïve non-resectable pancreatic cancer patients were administered TG01/GM-CSF at week 1, 2, 3, 4, 6, 10 (= treatment period) followed, after a three-months pause, by a booster period of one weekly administration for four weeks. Figure 1. The patients were followed up for up to 12 months from the first TG01/GM-CSF administration. In this study, DTH immune response was recorded in 56% (14 of 25) of the patients included in the phase I/II trial with 4 RAS peptides and who showed an immune response (DTH and/or mtRAS specific T-cell response).3 Treatment period was identical across the two studies. Both studies show increased survival for the immune responders versus the non-responders, and compares favorably with untreated patients where median survival is ~ 3.7 months.4 A randomized controlled trial is required.

RESULTS
 The patients’ characteristics are outlined in Table 1. Fourteen out of 25 patients (56%) recorded at least one positive DTH reaction by week 10. Table 2. Most patients recorded the first positive DTH reaction at week 3 or 4 of the 14 immune responders reported 2 or more positive DTH reactions throughout the treatment period.

DISCUSSION
 In this study, DTH immune response was recorded in 56% (14 of 25) of the non-resectable pancreatic cancer patients. The result correspond with data from phase I/II studies with another antigen-specific cancer immunotherapy consisting of 4 RAS peptides, where 58% (13 of 60) of the non-resectable pancreatic cancer patients showed mtRAS specific T-cell responses.1 Fourteen out of 25 patients (56%) recorded at least one positive DTH reaction by week 10, Table 2. Most patients recorded the first positive DTH reaction at week 3 or 4 of the 14 immune responders reported 2 or more positive DTH reactions throughout the treatment period. The patients’ characteristics are outlined in Table 1. Fourteen out of 25 patients (56%) recorded at least one positive DTH reaction by week 10. Table 2. Most patients recorded the first positive DTH reaction at week 3 or 4 of the 14 immune responders reported 2 or more positive DTH reactions throughout the treatment period.1

REFERENCES