Abstract
A number of tumors express activating, transforming mutations at codons 12 and 61 of the \textit{N-ras} oncogene. We report on a Phase I trial of Tarmogens, a class of genetically engineered \textit{S. cerevisiae} immunogens with patient-specific custom mutant peptides, that are simple to manufacture, yet elicit potent CTL immune responses against cells expressing target antigens.

They are not neutralized by the host immune system upon repeated administration, do not require a tumor-specific custom vaccine and are suitable for adoptive immunotherapy. A variety of solid tumors have key mutations in genes that govern the production of proteins involved in cell division. A limited number of mutations in the \textit{n-ras} oncogene are expressed in many solid tumors including colorectal, pancreatic, ovarian and non-small cell lung cancers as well as malignant melanoma. These mutations result in constitutive Ras activation, leading to uncontrolled cell proliferation.

The Phase I Tarmogen trial involved 67 patients with advanced colorectal, pancreatic or non-small cell lung cancer, who had failed at least first line chemotherapy and other conventional treatment modalities.

Conclusions: Tarmogens generate mutation-specific cellular responses with an acceptable safety profile. The development of antigen-specific immune responses in patients is measured by \textit{in vitro} assays.\textit{Saccharomyces cerevisiae} (\textit{S. cerevisiae}) yeast engineered to express one or more target protein antigens to express mutated Ras proteins induce protective cellular immunity as well as complete remission of established, metastatic tumors in mice (Lu et al. 2004 Can Res 64, 5084).

METHODS

Conclusions:

- Treatment received
- 87 patients have been consented, of whom 37 had product-related mutations in their tumors. Twelve patients have been treated. Of the 7 patients that completed dosing in the 0.1 YU cohort, all have shown mutation-specific treatment-related T cell responses by proliferation and cytokine assays. No treatment-related serious adverse events have occurred and possibly treatment-related adverse events have been mild and infrequent.

- Fatigue was the most common possibly-related adverse event in the first two cohorts.
- A total of 9 adverse events were seen in the first two dose cohorts; all were mild in nature.
- 67 patients consented (36 colorectal, 15 NSCLC, 16 pancreatic).
- 10 patients completed dosing in the 0.1 YU cohort and have shown mutation-specific T cell responses to the mutant epitope.
- All three products are manufactured and released separately, based on a single IND.

- 67 patients have been consented, of whom 37 had product-related mutations in their tumors. Twelve patients have been treated. Of the 7 patients that completed dosing in the 0.1 YU cohort, all have shown mutation-specific treatment-related T cell responses by proliferation and cytokine assays. No treatment-related serious adverse events have occurred and possibly treatment-related adverse events have been mild and infrequent.

- Fatigue was the most common possibly-related adverse event in the first two cohorts.
- A total of 9 adverse events were seen in the first two dose cohorts; all were mild in nature.
- 67 patients consented (36 colorectal, 15 NSCLC, 16 pancreatic).
- 10 patients completed dosing in the 0.1 YU cohort and have shown mutation-specific T cell responses to the mutant epitope.
- All three products are manufactured and released separately, based on a single IND.

- 67 patients have been consented, of whom 37 had product-related mutations in their tumors. Twelve patients have been treated. Of the 7 patients that completed dosing in the 0.1 YU cohort, all have shown mutation-specific treatment-related T cell responses by proliferation and cytokine assays. No treatment-related serious adverse events have occurred and possibly treatment-related adverse events have been mild and infrequent.

- Fatigue was the most common possibly-related adverse event in the first two cohorts.
- A total of 9 adverse events were seen in the first two dose cohorts; all were mild in nature.
- 67 patients consented (36 colorectal, 15 NSCLC, 16 pancreatic).
- 10 patients completed dosing in the 0.1 YU cohort and have shown mutation-specific T cell responses to the mutant epitope.
- All three products are manufactured and released separately, based on a single IND.

- 67 patients have been consented, of whom 37 had product-related mutations in their tumors. Twelve patients have been treated. Of the 7 patients that completed dosing in the 0.1 YU cohort, all have shown mutation-specific treatment-related T cell responses by proliferation and cytokine assays. No treatment-related serious adverse events have occurred and possibly treatment-related adverse events have been mild and infrequent.

- Fatigue was the most common possibly-related adverse event in the first two cohorts.
- A total of 9 adverse events were seen in the first two dose cohorts; all were mild in nature.
- 67 patients consented (36 colorectal, 15 NSCLC, 16 pancreatic).
- 10 patients completed dosing in the 0.1 YU cohort and have shown mutation-specific T cell responses to the mutant epitope.
- All three products are manufactured and released separately, based on a single IND.

- 67 patients have been consented, of whom 37 had product-related mutations in their tumors. Twelve patients have been treated. Of the 7 patients that completed dosing in the 0.1 YU cohort, all have shown mutation-specific treatment-related T cell responses by proliferation and cytokine assays. No treatment-related serious adverse events have occurred and possibly treatment-related adverse events have been mild and infrequent.

- Fatigue was the most common possibly-related adverse event in the first two cohorts.
- A total of 9 adverse events were seen in the first two dose cohorts; all were mild in nature.
- 67 patients consented (36 colorectal, 15 NSCLC, 16 pancreatic).
- 10 patients completed dosing in the 0.1 YU cohort and have shown mutation-specific T cell responses to the mutant epitope.
- All three products are manufactured and released separately, based on a single IND.

- 67 patients have been consented, of whom 37 had product-related mutations in their tumors. Twelve patients have been treated. Of the 7 patients that completed dosing in the 0.1 YU cohort, all have shown mutation-specific treatment-related T cell responses by proliferation and cytokine assays. No treatment-related serious adverse events have occurred and possibly treatment-related adverse events have been mild and infrequent.

- Fatigue was the most common possibly-related adverse event in the first two cohorts.
- A total of 9 adverse events were seen in the first two dose cohorts; all were mild in nature.
- 67 patients consented (36 colorectal, 15 NSCLC, 16 pancreatic).
- 10 patients completed dosing in the 0.1 YU cohort and have shown mutation-specific T cell responses to the mutant epitope.
- All three products are manufactured and released separately, based on a single IND.