Pancreatic cancer remains one of the deadliest cancers despite immunotherapy breakthroughs. We hypothesized that patients with poor outcomes may have tumors enriched in neo-epitopes activating regulatory T cells (Tregs).

Whole exome sequencing data derived from 13 pancreatic cancer patients with available HLA I and II typing and treated with GVAX, an autologous cancer vaccine engineered to secrete the stimulatory GM-CSF cytokine, was analyzed with Ancer, an in silico neo-epitope identification platform. Distinctive features of Ancer are its ability to accurately predict HLA II ligands and to identify tolerated or Treg epitopes. Using Ancer, we estimated the ratio of effector versus regulatory neo-epitope content for each patient.

Median disease-free survival (DFS) time of patients with high effector content (25 months) was over four times greater than in patients whose ratio shifted towards high regulatory content (6 months). Analysis of the same patients using their tumor mutational burden (TMB) did not yield conclusive results. In contrast, patients with high TMB had a similar median DFS time (17 months) than patients with low TMB (14 months).

While no statistically significant conclusions were obtained due to the low number of patients in our study, our results suggest that higher regulatory neo-epitope content for each patient is associated with shorter DFS. Follow-up studies involving larger cohorts of patients are ongoing.

Immunosuppression

- Poor outcome in pancreatic cancer patients with higher proportions of regulatory T cell neo-epitopes

We used Ancer™ to analyze the mutanome of 13 GVAX-treated pancreatic cancer patients.

**Neo-epitope composition:**

- The ratio of regulatory T cell neo-epitopes (Treg) to effector T cell neo-epitopes (Teff) was compared to a TMB predictor.
- Patients with a high ratio of Treg to Teff neo-epitopes had a worse outcome.

**References and Acknowledgments**

1) Moise L. et al., Hum Vaccin Immunother. 2015;11(9):2312-21.
2) Liu R. et al., Hum Vaccin Immunother. 2015 11:9, 2241-2252

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