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Meeting Abstract

Genes, vaccines, and immune checkpoints: An all out attack on pancreatic cancer

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Abstract

Pancreatic cancer is the fourth leading cause of cancer deaths in men and women in the United States. Unlike most other cancers, the mortality rates have remained steady over the past 20 years. Surgery is the best hope for cure. However, the 5-year overall survival following surgery is about 25% even with the best adjuvant therapy. For advanced disease, there are few therapies that have been approved with survival advantages that are measured in months.

Immune based therapies are currently undergoing clinical testing in patients with pancreatic cancer. However, it has become clear that the immune system has the ability to recognize cancer through similar mechanisms used to recognize infectious agents. Until recently, it was difficult to identify the specific genes recognized by the immune system that are expressed by most cancers including pancreatic cancer. We have been developing an allogeneic granulocyte-macrophage colony-stimulating factor (GM-CSF) secreting pancreatic tumor vaccine approach for the treatment of patients with pancreatic cancer. Recently completed phase I and II studies demonstrated the bioactivity of this vaccine as measured by elevated post-vaccination serum levels of GM-CSF, post-vaccination eosinophilia that is associated with systemic vaccine-related rashes and vaccine recall reactions, and post-vaccination delayed type hypersensitivity (DTH) reactions to autologous tumor. These responses are most often observed in patients demonstrating prolonged disease-free survival. Analysis of post-vaccination immune responses identified mesothelin as a candidate new target against which both T cell and antibody responses were directed in patients who remain disease-free. Additional clinical trials have been designed to test whether modulation of specific signaling pathways that down-regulate cancer specific T cell responses in tumor bearing hosts can be integrated with vaccination to enhance the overall immune response. The preclinical studies driving these trials, the study outcomes, and the immune analyses of these trials will be discussed.

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