Pancreatic cancer vaccine trial demonstrates potential of precision medicine approach to mRNA vaccines

The age of mRNA vaccines was ushered in by the Covid-19 pandemic, but that was only the beginning. The new generation of mRNA vaccines is targeting everything from cancer to malaria, and the applications of mRNA technology go beyond vaccines. In a recent clinical trial report, Rojas et.al used a precision medicine approach to generate mRNA vaccines customized to individual patients.

Pancreatic ductal adenocarcinoma (PDAC) is a highly lethal form of cancer, with a survival rate of only 12%. However, a new study has discovered a potential breakthrough in the form of a personalized vaccine that targets specific mutations in cancer cells. The vaccine, called autogene cevumeran, is based on uridine mRNA–lipoplex nanoparticles and is designed to stimulate the patient's immune system to recognize and attack the cancer cells.

Cancer vaccines are based on the observation that cancer cells often express mutated proteins called "neoantigens" on their surface. These neoantigens are not found in healthy cells, making them a tempting target for vaccine development. Unfortunately, each patient's cancer expresses a unique combination of neoantigens, which makes it difficult to design a vaccine that works for all patients. In this new study, researchers analyzed tumor biopsy samples to create a neoantigen profile for each patient. This profile was then used to generate an mRNA vaccine customized for those individuals.

In a phase I clinical trial, researchers tested the effectiveness of autogene cevumeran in combination with other treatments. The trial involved 16 patients who received a combination of the vaccine and an anti-PD-L1 immunotherapy called atezolizumab. PD-L1 is a protein that inhibits immune responses. Researchers hoped that blocking it would allow a more robust immune response to the vaccine. Following this, 15 of the patients received a modified chemotherapy regimen known as mfolfirinox.

The results were promising. The autogene cevumeran vaccine was well-tolerated and successfully induced a strong immune response in eight out of 16 patients. In fact, half of these patients developed immune responses against multiple vaccine targets. Using a new tracking method, the researchers found that the vaccine-expanded T cells, which are immune cells responsible for fighting cancer, made up a significant portion (up to 10%) of the patient's total blood T cell count. Furthermore, these T cells could recognize and attack the cancer cells.

At the 18-month follow-up, patients who had a robust immune response to the vaccine showed significantly longer periods of recurrence-free survival compared to those who did not respond well to the vaccine. In other words, patients with vaccine-expanded T cells had a lower likelihood of cancer returning. This correlation held true even after accounting for differences in the overall immune fitness of the patients.

The researchers also noted that the immune response generated by the vaccine did not interfere with the patient's ability to respond to other vaccines, such as the one for SARS-CoV-2 (the virus causing COVID-19). This suggests that the autogene cevumeran vaccine can be used in combination with other vaccines without compromising their effectiveness.

Further research is needed to confirm these results and determine the long-term effects of this treatment approach. However, this study represents an important step forward in the development of personalized cancer vaccines and offers new possibilities for improving patient outcomes in pancreatic cancer treatment.