

2. NON-TECHNICAL ABSTRACT

There is no effective treatment for patients with pancreatic cancers that cannot be removed by an operation or that have spread outside the pancreas. The ability for vaccines to stimulate an immune response against cancer cells depends on the activity of specific T cells, which can recognize a particular protein, or antigen, found on the tumor cells. These T cells can be generated by immunization with pox viruses that contain the genes for the tumor proteins. Two of the most commonly found proteins in pancreatic tumor cells are CEA and MUC-1. Vaccinia virus is the vaccine used to prevent smallpox and has been modified to express both CEA and MUC-1 previously. Fowlpox virus is a virus that infects birds but does not cause disease in humans and has also been modified to express both the CEA and MUC-1 proteins. These vaccines have been tested in humans with cancer and are well tolerated. The T cells also require a second signal to become fully activated, which are provided by specialized immune system proteins called costimulatory molecules. There are many costimulatory molecules that have been discovered and can be used to help activate T cells. A new vaccine has been developed using vaccinia virus to express CEA and MUC-1 and three costimulatory molecules (B7.1, ICAM-1, and LFA-3 or TRICOM, which stands for TRIad of COstimulatory Molecules), called PANVAC-V. In addition, a new fowlpox virus recombinant pox was also made with the human CEA and MUC-1 and three costimulatory molecule genes, and called PANVAC-F. Animal studies and human clinical trials have suggested that the use of two different vaccines, such as vaccinia followed by fowlpox virus, are better than using a single virus vaccine. Granulocyte-macrophage colony stimulating factor (GM-CSF) is a protein of the immune system that is approved for use in humans to increase the number of white blood cells and has also shown some promise as an anti-cancer agent, especially when used in combination with vaccines. The goal of this study is to determine whether PANVAC-VF in combination with GM-CSF is safe and can stimulate an immune response against CEA and MUC-1 on the pancreatic tumor cells, resulting in an increase in life expectancy in patients receiving the vaccine.