

2. NON-TECHNICAL ABSTRACT

Although chemotherapy is considered standard care for patients with metastatic breast cancer, there is no cure for this disease. Patients who have progressed on one chemotherapy agent will often times receive additional chemotherapy agents. One particular chemotherapy agent called docetaxel has activity against metastatic breast cancer. However, it works in less than half the patients with metastatic disease. Thus, new approaches are being examined in the fight against metastatic breast cancer. 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 poxviruses that contain the genes for the tumor proteins. Two of the most commonly found proteins in breast cancer tumor cells are carcinoembryonic antigen (or CEA) and a mucin protein called MUC-1. Vaccinia virus is the vaccine used to prevent smallpox and has been used to produce 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 used to produce the CEA protein. These vaccines have been tested in humans with cancer and appear to be safe after being given to over 600 people in clinical trials. The T-cells also require a second signal to become fully activated, which are provided by specialized immune system proteins called co-stimulatory molecules. There are many co-stimulatory 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 three co-stimulatory molecules (called B7.1, ICAM-1, and LFA-3), called rV-CEA(6D)/TRICOM. A vaccinia virus that produces MUC-1 has also been generated (called rV-MUC-1) and there is some evidence that using two different proteins may improve the responses to a vaccine approach. In addition, a new fowlpox virus was also made with the human CEA and three co-stimulatory molecule genes, and called rF-CEA(6D)/TRICOM. Animal studies and at least two 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. In a recent clinical trial, men with prostate

cancer were given both the vaccine and docetaxel without any significant toxicity. Furthermore, immunologic responses to the vaccine were not diminished with the combination of therapy. The goal of this study is to determine if combining docetaxel with this vaccine can improve the time to progression of metastatic breast cancer compared to docetaxel therapy alone.