

PROVENGE TRIAL A SUCCESS

In the [Fall issue of our newsletter in 2007](#), I commented upon an exciting new approach for the treatment of prostate cancer that harnessed the potential of the immune system. Immunotherapy has been a long sought after goal over the past 40 years as it became understood that cancer cells, somewhat like bacteria and other foreign substances, contained proteins or substances that could be recognized as foreign by the immune system. In the world of infectious diseases, we are well aware that an infection mounts an immune response that overcomes the infectious process, often aided by concurrent treatment with antibiotics. In many cases immunity is established and a subsequent exposure does not produce disease as the immune system has been primed to recognize and eliminate the invader and thereby illness is prevented. Why is the same mechanism not operative with cancer? Actually, in many instances, it probably is Cells that are evolving into a malignant process are recognized and destroyed so cancer does not appear in the host. However cancer does set up a number of protective mechanisms whereby it reduces the effectiveness of the immune system. In addition, the cancer cells still possess a number of characteristics that the immune system does not find inappropriate because they are also part and parcel of the normal cell. Immunotherapy attempts to boost the immune system so it can effectively combat the resident alien called cancer (resident since it originates from cells within the body, alien because it has taken a destructive course to injure and kill the host).

Sipuleucel-T (Provenge®) is such an immune boosting strategy developed to combat prostate cancer. It has proven in several studies to improve survival and, therefore, will again come before the FDA in 2009 for approval Here's how it works: The patient undergoes a process called leukaphoresis whereby over an approximately 3-4 hours white blood cells are extracted from the blood. These cells can be separated so as to identify and harvest the antigen presenting cells (APC), also called dendritic cells. These cells are then exposed to a very powerful immune stimulant that carries prostatic acid phosphatase protein (PAP), thereby programming the antigen presenting cells to recognize PAP. The cells are returned to the patient by intravenous infusion over approximately 30-60 minutes. These antigen presenting cells will engage and educate another group of immune cells, termed T cells so they will seek and destroy any prostate cancer cells in the body which express the PAP antigen. Fortunately most cancer prostate cells do

express PAP and by this methodology, tumors both visible and invisible, can be attacked and eliminated.

A word about the T-cell. This is a specialized cell that has the ability to mobilize the immune system against a foreign invader and which itself is a strong component of any immune destructive process. The body possesses a number of T-cells which have already been educated or programmed against various disease processes and when exposure occurs, they are mobilized to neutralize the foreign invader. However, the body keeps a number of T-cells in reserve at all times for new threats. This is the case with the Provenge® immunotherapy which engages the naïve T-cells and educates them to be on the lookout for any cells containing PAP, namely benign and malignant prostate cells. Fortunately there is no detriment towards the destruction of benign prostate cells and this “side effect” is of no consequence. This may not be the case with other immunotherapies – as an example, with liver cancer the elimination of malignant and benign hepatic liver cells while destroying the cancer would cause excessive side effects and even death if all normal liver cells are destroyed in the process. The prostate is a favorable target because it is not necessary to try to preserve the prostate cells with normal form and function.

The results of this study show that the life of patients receiving immunotherapy can be extended with Provenge® therapy. There are very few side effects and they are easily treated with Tylenol and Benadryl. The therapy is delivered over one month and three sessions and, therefore, is quite convenient and not time consuming. Its extension of life compares very favorably with the current chemotherapeutic with far fewer side effects and a much shorter duration of therapy.

Immunotherapy has held promise for decades, but a clear-cut benefit for the human has never been demonstrated. The Provenge® has brought immunotherapy to reality in the clinical arena. Immunotherapy may now be the fourth modality that can be added to surgery, radiation therapy, and chemotherapy in the multi-pronged effort to control and perhaps cure malignant disease.

FDA approval will probably occur at the end of 2009 and therapy may be available soon thereafter.