

The Latest Cancer Treatments

What's New? We Continue to Move Forward Fast

by *N. Simon Tchekmedyian, M.D., F.A.C.P.*

*Medical Director, Pacific Shores Medical Group
Clinical Professor of Medicine, UCLA School of Medicine*

Since our October 2003 summary on cancer treatments, two novel cancer drugs, Avastin™ and Erbitux®, which were being reviewed by the FDA at the time, have been approved for clinical use. We will review these and other developments.

Avastin™ is an angiogenesis inhibitor, a medication that blocks the formation and growth of new blood vessels that feed cancer cells. These blood vessels are essential for cancer cells to thrive, grow and spread. Indeed, the blood vessels bring nutrients to the cancer cells and provide avenues for the cancer cells to travel to other sites, such as the liver, the lungs, the bones, or even the brain. Scientists have been working for a very long time to find methods to selectively block these tumor-feeding blood vessels, and over 300 substances have been studied. Finally, Avastin™, which is a monoclonal antibody, has been found to be effective. A monoclonal antibody is a protein made by the immune system, and it has a very specific target to which it binds. In this case, Avastin™, targets, binds to, and neutralizes the vascular endothelial growth factor, a protein involved in the promotion of cancer blood vessel growth.

It was quite an exciting time for our team, as we participated in the Avastin™ clinical trials that led to the approval of Avastin™ as a therapeutic option for colon cancer patients. Importantly, the addition of Avastin™ to standard chemotherapy for colorectal cancer prolonged the length of patients' lives. Studies are now testing whether Avastin™ will be helpful in other cancer types. Avastin™ is given intravenously as an infusion and side effects have included either blood clots or bleeding. Efforts are also underway to try to block cancer blood vessels with new oral medications.

Erbitux® is also a monoclonal antibody that is given intravenously. Erbitux® targets the epidermal growth factor receptor, a protein that fosters the growth and cancerous behavior of malignant cells. #27, Pg. 5 Erbitux® can be effective in advanced colorectal cancer. Its typical side effect is a persistent skin rash that looks like acne. Erbitux® and other similar experimental antibodies are now being tested for treatment of lung cancer and head and neck cancer.

An intriguing recent finding came out of a study performed in Israel where the use of "statins," drugs used very frequently to reduce the level of cholesterol, was associated with a 46% reduction in the risk of colorectal cancer. The mechanism of this effect is unknown, and additional studies are being planned to further determine the potential preventive and therapeutic role of these medications.

A major finding was that an oral chemotherapy agent, temozolomide, increased the survival of patients with glioblastoma multiforme, the most serious type of primary brain cancer. Temozolomide was given after surgery together with radiation therapy, and was given for an additional six-month period after completion of radiation. When used in this fashion, it improved the probability of being alive at two years compared to the use of radiation alone. The medication is now a new standard in the treatment of this very serious brain tumor.

We also had good news in the prostate cancer front. Two separate studies demonstrated that chemotherapy based on Taxotere™, an intravenous chemotherapy drug, prolongs the lives of patients with advanced prostate cancer.

Our team at Pacific Shores Medical Group, together with many colleagues presented the results of a clinical trial with the use of a new investigational chemotherapy agent, epothilone, for the treatment of prostate cancer at the annual meeting of the American Society of Clinical Oncology (ASCO 2004). #45, Pg. 5 Epothilone was generally well tolerated and active in patients with prostate cancer, and additional studies are ongoing.

In addition to looking for new therapies, we need to improve on the existing ones. As an example, Taxol®, an effective drug in multiple cancers including breast cancer, was recently found to be more effective when given on a once-a-week schedule. Indeed, in a study performed in

patients with advanced breast cancer, Taxol® was more effective when given once a week as compared to being given every three weeks. Taxol® can be associated with allergic reactions, and therefore multiple medications must be given, to prevent such reactions. A new Taxol® preparation, known as Abraxane™, is being tested. Initial tests suggest that this experimental preparation, because of its constitution, is not associated with allergic reactions and may be easier to administer.

Patients with breast cancer very often wonder what their risk of cancer recurrence is after they have been cancer free for five years. A recent study followed 1,400 patients who had been cancer free for five years. The study's goal was to determine their rate of cancer recurrence over the following 10 years. Interestingly, the outlook depended on the initial stage of their breast cancer. For stage I patients, the risk of the cancer coming back was less than 10%. However, for stage II patients it was about 20%, and for stage III patients it was about 30%. This data may help doctors to counsel and monitor patients after the first five years of a breast cancer diagnosis.

Breast cancer continues to be a major research focus. Estrogen can stimulate breast cancer cells, particularly those that are found to be estrogen-receptor positive on testing. We now have many methods to lower the effects of estrogen on cancer cells in pre- and postmenopausal patients. In the premenopausal patients, we can suppress ovarian production of estrogen with injections, we can remove the ovaries, or we can use tamoxifen, which prevents the action of estrogen on the cancer cells. In the postmenopausal patients we can also utilize drugs called aromatase inhibitors, which prevent estrogen production from sources other than the ovaries. Aromatase inhibitors are effective not only in advanced breast cancer, but also in early breast cancer, to prevent recurrences after initial surgery. Because they lower the estrogen levels, they can lead to osteoporosis; therefore research is focusing on the prevention of osteoporosis in these patients. The aromatase inhibitors, however, are less of a concern with regard to blood clots and endometrial cancer, which are potential risks when tamoxifen is used. Aromatase inhibitors can cause joint stiffness, and doctors and patients need to carefully individualize a treatment program based on all medical aspects involved. For breast cancer patients with HER-2 positive tumors, the medication Herceptin® is now being tested to determine whether it could improve the cure rate when used either before or after initial breast cancer surgery. #28, Pg. 5

Research is also ongoing to determine the role of magnetic resonance imaging (MRI) in the detection and diagnosis of breast cancer. MRI is being utilized predominantly as a diagnostic method in patients at high risk for breast cancer because of personal or family history. It can also be used to assess the extent of cancer in the breast and, in certain instances, in the evaluation of breast implants.

Studies continue with the antibody rituximab, which has been very effective for patients with non-Hodgkin's malignant lymphoma. Rituximab is finding additional roles, such as in the treatment of certain autoimmune conditions including a type of anemia. #7, 9, Pg. 4 These are conditions where the immune system turns against normal tissues. Thus, research into new cancer treatments has provided a turning point for the control of other serious but non-cancerous diseases.

Recurrences after surgery for non-small-cell lung cancer are very frequent even in early stages of the disease. Two major studies presented at ASCO 2004 revealed that the use of chemotherapy after surgery for relatively early stage lung cancer prevents recurrences and is associated with a significant improvement in the probability of surviving the disease.

Alimta®, a new chemotherapy drug, was recently approved by the FDA for treatment of mesothelioma, a cancer of the lining of the lungs associated with history of asbestos exposure, and for treatment of lung cancer. It is given intravenously every three weeks, and requires the administration of vitamin B-12 and folic acid to reduce potential side effects. It is a new option for the treatment of lung cancer and a welcomed new treatment for mesothelioma, a disease that can be very refractory to therapies.

Gleevec™, a major breakthrough in the treatment of chronic myelogenous

