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Informing Patients About Options, Advancing Lung Cancer Research

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New Directions

What is a Cancer Vaccine?

The latest in new approaches to cancer treatment involves the use of vaccines to treat lung cancer or decrease risk of recurrence. Most people are familiar with vaccines that are used to prevent common illnesses, such as the flu, measles, and polio. The newest research in cancer vaccines involves triggering the immune system to recognize and attack human cancer cells without harming normal cells. Scientists are able to isolate genetic material from cancer cells and incorporate them into a vaccine that will cause the immune system to recognize and destroy the cancer cells. This is an exciting area of research in lung cancer, and several trials appear to hold great promise.

Summaries of recent clinical trials based on vaccines as well as variations of current standard therapies, targeted therapies and diagnostic tests are listed below. The following information does not include all new findings, but gives a brief overview of some of the major areas of discovery. ■

2008 Research Highlights

Early Detection and Prevention

Blood Test May Help Predict Lung Cancer in Smokers

Early detection may be the best way to improve survival rates for those diagnosed with lung cancer. Researchers in Germany have developed a blood test that uses genetic “fingerprints” to predict lung cancer in smokers. Genetic fingerprinting allows scientists to study an individual’s specific genetic sequence and compare it to other genetic sequences. In this study, researchers identified a particular RNA sequence that was present in individuals with lung cancer, but not in individuals without lung cancer. The researchers then looked for this fingerprint in smokers who had not been diagnosed with cancer, and followed them over two years to see if they developed lung cancer. Approximately 85% of those individuals that were eventually diagnosed with lung cancer over this period had been identified by the RNA fingerprint. The test also showed similar accuracy in correctly classifying those individuals that remained cancer-free. These results have encouraged further development of the predictive blood test and may eventually improve early detection and survival rates among lung cancer patients.

Celecoxib (Celebrex® and Celebra®) May Help Prevent Cancer in Current and Former Smokers

In a randomized study of patients who currently or formerly smoked, lung tissue samples revealed

that an enzyme typically responsible for inflammation and pain, cyclooxygenase-2 (COX-2), may also be responsible for the growth of lung tumors. Only individuals with a 20 pack year history were included in the study. A pack year is defined as a way to measure the amount a person has smoked over a long period of time. It is calculated by multiplying the number of packs of cigarettes smoked per day by the number of years the person has smoked. During the study, those who received high doses of a medicine, celecoxib, that blocks the COX-2 enzyme demonstrated reduced levels of cancerous cell growth in the lung. The treatment was both safe and tolerable and may represent a way to decrease lung cancer risk in current and former smokers.

Gene Sequence Profile May Predict Effect of Chemotherapy in Early Stage NSCLC

A genetic test may be able to predict which early stage NSCLC (non-small cell lung cancer) patients may benefit from chemotherapy after surgery. Researchers used a genetic signature to separate patients into a low risk and a high risk group based on the presence or absence of genetic markers seen in a test of 15 genes. The researchers found that chemotherapy was beneficial to high risk patients, but not to the low risk patients. Further development of such a test may help doctors better identify which patients diagnosed with early stage NSCLC would benefit from post surgical chemotherapy.

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Definitions

Resectable:

A tumor that can be removed by surgery. Sometimes a tumor is not considered resectable. This is because either the surgery could risk damage to vital organs or because the cancer has already made its way into the bloodstream and surgery would not have any benefit to the patient.

Antibody:

A protein in the immune system that identifies and destroys foreign substances, such as bacteria and viruses. Scientists have developed antibodies that recognize **antigens**, which are substances on cancer cells, and the goal of these treatments is to induce an immune response against the cancer cells.

EGFR:

Epidermal growth factor receptor is a protein receptor that exists on cell surfaces and controls numerous cell activities. Certain mutations of this protein can lead to a malfunction of EGFR that causes cancerous cells to rapidly multiply. An EGFR inhibitor is a drug that helps keep this from happening.

Early Stage NSCLC

Study Indicates PET/CT Imaging Is Best to Determine NSCLC Surgical Candidates

Imaging tests done before surgery are critical in determining which patients are candidates for surgery. A type of imaging test that combines positron emission tomography and computed tomography (PET/CT) is able to identify patients with more advanced disease that is not seen in conventional imaging. Staging with PET/CT before surgery, along with imaging tests done to check for spread of the cancer to the brain, more accurately identified patients whose cancer had already spread and spared those patients unnecessary surgeries.

Phase III Study Confirms Benefits of Pre-Operative Gemcitabine (Gemzar®)-Cisplatin in Early Stage NSCLC Patients

A phase III study was initiated to test if three cycles of gemcitabine/cisplatin given before surgery provides a benefit over surgery alone in patients with early stage NSCLC. The outcomes of previous studies (released during enrollment for the current study) indicated that survival outcomes improved significantly when chemotherapy was given prior to surgery. Due to these findings, researchers felt it was unethical to continue the current study because those in the surgery-only group would not receive the added benefit of chemotherapy. The results from the 270 patients who completed the trial before it was stopped further confirmed this benefit.

Advanced Stage NSCLC

Cetuximab (Erbix®) and Cisplatin / Vinorelbine Treatment Shows Higher Survival Rates in Patients with Advanced NSCLC

A phase III study assessed if an antibody that targets EGFR, cetuximab, in combination with chemotherapy agents cisplatin/vinorelbine was safer and more effective than the chemotherapy alone in advanced NSCLC patients. The results demonstrated, on average, that patients treated with cetuximab plus cisplatin/vinorelbine lived longer than those who received cisplatin/vinorelbine alone. Patients receiving Erbix also experienced fewer toxic side effects than other similar drugs. This is the first study to show a survival benefit of an EGFR inhibitor in combination with platinum-based chemotherapy in advanced NSCLC. This is also the first EGFR inhibitor safe for use in squamous cell cancer.

Antibody Used in Combination with Paclitaxel and Carboplatin Shows Benefits in NSCLC Patients

The Insulin-like Growth Factor type 1 Receptor (IGF-1R) is a protein similar to the hormone, insulin. IGF-1R plays a role in a cell's ability to divide, spread and survive. When this protein stops working properly, it has been linked to cancer progression. A phase II study tested an antibody, CP-75,851, that targeted IGF-1R for the treatment of advanced untreated NSCLC. The results showed that almost half of the patients responded favorably to the combination of the antibody with chemotherapy agents paclitaxel and carboplatin, with an even higher response from those with squamous cell carcinoma. Additional enrollment in this trial has continued to show limited side effects and several drastic disease reductions and reversals. Results from this study have led researchers to conclude that the combination of CP-75,851 and paclitaxel and carboplatin treatment shows great promise.

Pemetrexed (Alimta®) Offers Superior Progression-Free Survival in Advanced NSCLC Patients

A phase III trial tested the potential benefit of the chemotherapy pemetrexed in patients with advanced stage NSCLC who had received prior platinum-based chemotherapy and whose cancer was stable. Typically, the best method of care for these patients is to continue follow-up treatment that enhances patient comfort and relieves complications and side effects to maintain patient quality of life. However, the results demonstrated that all of the patients receiving pemetrexed responded favorably to the drug, especially those with types of NSCLC other than squamous cell. There was also a significant decrease in tumor size and less progression of the disease. This study confirms pemetrexed has greater effectiveness in patients with non-squamous cell lung cancer.

Vaccine May Help Late Stage NSCLC Patients Survive Longer

IDM-2101 is a vaccine designed to trigger immune responses that target cancerous cells. In the study, patients with advanced stage or recurrent NSCLC were enrolled. Results revealed there was an increase in overall survival. Almost all of the patients showed some degree of an immune response, which means that the body was more able to recognize cancerous cells in order to respond to them. Overall, the researchers concluded that IDM-2101 may provide a survival benefit for NSCLC patients whose cancer has spread.

IGN101 Vaccine Can Improve Relapse-Free Survival in NSCLC Patients Who Had Surgery

Cell adhesion molecules (CAMs) play a role in how cells function, including their growth, development of specific roles, and death. The epithelial cell adhesion molecule (EpCAM) has been found to be present on cancers that start in epithelial cells, which account for most lung cancers. Epithelial cells line the surfaces of many bodily structures, including the lungs. IGN101 is a cancer vaccine that is directed against EpCAM. The IGN101 vaccine produces EpCAM molecules that trigger an immune response that may fight cancerous cells with repeated injections. Their survival time was compared to another group of patients who did not receive the vaccine. There was no difference in overall relapse free survival between the group that received the vaccine and the group that did not. However, within the group that received the vaccine, the researchers observed that patients with lower numbers of immune cells at the beginning of the study showed improved relapse free survival compared to patients who had higher levels of immune cells. They concluded that early NSCLC patients vaccinated with IGN101 following surgery may benefit if certain types of immune cells are low.

TG4010 Vaccine Used in Combination with Chemotherapy Shows Positive Results in NSCLC Patients

TG4010 is a type of vaccine that contains both IL2—a protein that stimulates the immune system—and the antigen MUC1. Antigens such as MUC1 help generate immune response to target cancerous tumor cells. In this study, advanced stage NSCLC patients received either a combination of the chemotherapies cisplatin and gemcitabine alone or they received the chemotherapies with the TG4010 vaccine. 43% of the patients receiving the vaccine showed a decrease in disease progression compared to 27% of the patients who did not receive the vaccine. Any negative responses related to TG4010 were minor and common in this type of treatment, according to the researchers. The researchers confirmed that the types of immune responses generated by MUC1 antigens were prompted by the TG4010 vaccine. The combination of TG4010 with chemotherapy in NSCLC showed a significantly increased response rate and longer progression free survival, both highly promising findings. This study is still ongoing.

Small Cell Lung Cancer

North American Trial of Irinotecan (Camptosar®) As Treatment for Extensive Stage SCLC Failed to Match Positive Results of Japanese Trial

The role of irinotecan in the treatment of SCLC (small cell lung cancer) remains controversial. Irinotecan works by blocking cancer cells from multiplying and growing. It has been used in combination with other chemotherapy agents such as the platinum-based therapy cisplatin. A similar treatment is one using a combination of etoposide, also known as VP-16® or VePesid®—an enzyme inhibitor that helps fight cancer cell replication—and cisplatin. Although a Japanese study involving patients diagnosed with extensive stage SCLC showed better survival rates for those treated with irinotecan and cisplatin over those treated with etoposide and cisplatin, another small trial did not. This most recent trial was conducted to further understand which treatment is more effective. This large randomized trial did not confirm the positive results of the Japanese study. Results showed that irinotecan and etoposide combined with cisplatin produced about the same overall response rates and survival outcomes. In addition, those taking irinotecan complained of more intestinal upset than those on etoposide. As a result, etoposide plus cisplatin remains the standard of care for extensive stage SCLC for North American patients. The differences found between this study and the Japanese study may be the result of the differences in medications and possible genetic differences between the Japanese and North American populations.

Two Amrubicin Studies Show Benefit in Extensive Stage SCLC

Amrubicin, a drug that makes it difficult for cancer cells to grow, has been approved to treat SCLC and NSCLC in Japan.

When extensive stage SCLC spreads during initial treatment or returns within three months, it is less likely to respond to additional chemotherapy. In this phase II trial, patients with extensive stage SCLC that did not respond to a first chemotherapy treatment of cisplatin or carboplatin were treated with amrubicin. At the time the study data was released, a significant difference in progression-free and overall survival was seen in those who received amrubicin. Researchers conclude that further study is needed but that amrubicin may be an effective treatment for SCLC patients that have not responded well to first-line (initial) chemotherapy.

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Randomized Trial

Trial design in which participants are assigned by chance to a treatment group. The researchers do not know which treatment is better.

Double-Blind Study

A clinical trial design in which neither the participating individuals nor the study staff knows which participants are receiving the experimental drug.

Controlled Trials for Cancer

One group of participants is given standard of care (i.e., the control group), while another group is given a standard treatment plus an experimental drug or therapy.

Primary Research Goals in Clinical Trials:

Phase I

These first studies in people evaluate the safety and dosage of a new drug or treatment.

Phase II

These studies continue to test the safety of the drug, and begin to evaluate how well the new drug works.

Phase III

These studies confirm the effectiveness of the study drug or treatment and compare it to the current standard of care.

When to search:

When are clinical trials looking for volunteers?

1. Just before a biopsy (if the trial involves studying tissue from a tumor).
2. Just prior to the first surgery or radiation treatment ("neo-adjuvant" studies).
3. Immediately after surgery or radiation treatment ("adjuvant" studies).
4. After cancer has recurred, spread (metastasized), or is still growing despite another treatment
 - First-line studies: These studies offer the first treatment given once lung cancer has advanced.
 - Second-line studies: These studies offer the second treatment given once lung cancer has advanced and a first-line therapy has failed.

A clinical trial may not turn out to be a patient's best option at any particular time, but the only way to decide is to learn about available studies and be prepared for each window of opportunity to explore. ■

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Another study of amrubicin also involved patients diagnosed with extensive stage SCLC. This time, the study included those who had shown a positive response to their first treatment with a platinum based chemotherapy but whose cancer had returned more than three months after treatment. In the study, two-thirds of the participants were given amrubicin and the rest were treated with topotecan (Hycamtin), another chemotherapy used to treat SCLC that inhibits cancer cell growth in a different way than amrubicin. At the time the data were released, 40% of those given amrubicin had a positive response (measured by disease response, progression free and overall survival) compared with a 12% positive response in those who received topotecan. The researchers concluded that amrubicin is a better second-line treatment for patients with extensive stage SCLC who had responded well to initial chemotherapy but whose cancer had returned. ■

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