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Informing Patients About Options, Advancing Lung Cancer Research

November 2009

# New Directions

## Call to Action to Help Advance Research

At July's World Conference on Lung Cancer in San Francisco, CA, researchers agreed that there is a need to improve and expand lung cancer research, to find new drugs that are safer and more effective, and to increase the understanding of how to personalize treatments. We are learning more about how tailoring treatments to the individual will dramatically improve treatment effectiveness. But detection and treatment options will not advance without clinical research.

How can you help advance this research? Consider participating in a clinical trial *as soon as you are diagnosed or at any point after* and learn how your treatment might be personalized to your particular situation. Or, if your loved one has lung cancer, encourage them to explore their clinical trial options. Lung Cancer Alliance led the way in empowering patients by creating the first lung cancer clinical trial matching service. We have joined with five other lung cancer groups\* to reach even more patients. By calling **1-800-698-0931**, you can learn about clinical trials that might potentially be an option for you or your loved one at any point in the cancer process. You will also find out how your doctors can learn about treatments that target the unique characteristics of the tumor.

We hope this newsletter inspires you to call and take action, to learn more about treatment options, and to be a part of the process that will improve early detection and treatment options for everyone affected by lung cancer. It won't happen without you. ■

\*Call to Action Participants: CancerCare, Uniting Against Lung Cancer, Lungevity, Respiratory Health Association of Metropolitan Chicago, National Lung Cancer Partnership.

## 2009 Research Highlights

### Early Stage NSCLC

#### No Significant Difference Found in Survival between Chemotherapy before/after Surgery or Surgery Alone

In early stage NSCLC there is high risk of relapse even if the tumor is completely removed. The Spanish NATCH phase III trial explored whether chemotherapy before or after surgery using carboplatin and paclitaxel (Taxol®) could improve disease-free survival (DFS) compared to surgery alone for NSCLC patients. Patients with early stage NSCLC who had not yet received treatment with any chemotherapy were placed into one of three groups. Group one had surgery only. Group two had chemotherapy then surgery. Group three had surgery then chemotherapy. The results showed no significant difference in DFS between any of the groups. This is a small study and most patients had stage I disease (already considered least likely to benefit from chemotherapy). However, because there seemed to be a small positive advantage in patients receiving chemotherapy before surgery compared to other groups, more study is needed. *NCT00913705*

### Advanced Stage NSCLC

#### Biomarker Analysis Helps Determine Patients Who May Benefit from Erlotinib (Tarceva®) Maintenance Therapy Following First-Line Chemotherapy

Erlotinib is a targeted drug approved for NSCLC treatment after the first treatment fails. The phase III SATURN study looked at whether patients with advanced NSCLC whose cancer was stable after initial chemotherapy would benefit from erlotinib as maintenance therapy. Patients in the study had advanced NSCLC but showed no disease progression after their first chemotherapy. They were given either erlotinib alone or a placebo. Tissue was collected from all patients to test if a specific mutation was present. Researchers concluded that adding erlotinib lowers the risk of cancer progression after successful initial chemotherapy. The analysis of the tumor tissue confirmed that the most benefit was seen in patients who had a mutation in the epidermal growth factor receptor (EGFR), the mutation erlotinib is known to target. *NCT00556712*

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## Definitions

### Statistical Significance

When the results of a study are “statistically significant” it means that there is a greater likelihood that the difference reported is real and not due to chance.

### Endpoint

In a clinical trial, an endpoint is an outcome that can be measured to tell how well a treatment works.

### Disease-Free Survival (DFS)

The length of time after treatment during which a patient survives with no sign of disease.

### Progression-Free Survival (PFS)

The length of time during and after treatment in which the cancer does not get worse (progress).

### Biomarker (molecular marker, signature molecule)

Biological molecules are the basis for all human cells. A biomarker is a biological molecule, found in blood, other bodily fluids or tissue, which is a sign of a normal or abnormal process or of a condition or disease.

### EGFR

Epidermal growth factor receptor is a protein receptor that exists on cell surfaces and controls numerous cell activities, such as cell growth and division. 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.

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### Addition of Vandetanib (Zactima®) to Docetaxel (Taxotere®) Improves Quality of Life

The phase III ZODIAC trial studied the benefits of adding vandetanib to docetaxel as second-line treatment for patients with advanced NSCLC. Vandetanib is an oral drug that specifically targets cancer cells. The study recruited patients throughout Europe, North America, South America, and Asia Pacific. Patients were divided into two groups: one received docetaxel alone and the other received docetaxel plus vandetanib. The group receiving vandetanib had less disease progression and better response to chemotherapy than the group receiving docetaxel alone. The more notable outcome was that the group receiving vandetanib experienced a longer period of time before symptoms got worse. This resulted in improved quality of life. The drug combination also proved to be safe with no unexpected side effects. Vandetanib is the first oral targeted therapy to show a benefit as a second-line therapy for advanced NSCLC patients when combined with chemotherapy. *NCT00312377*

### Adding Erlotinib (Tarceva®) to Bevacizumab (Avastin®) after Treatment with Chemotherapy Plus Bevacizumab Improves PFS

Combining bevacizumab and chemotherapy improves survival for NSCLC patients. Giving erlotinib alone also improves survival for those patients. A new study suggests that giving these two drugs together helps even more. The ATLAS study evaluated bevacizumab combined with erlotinib versus bevacizumab alone, after initial treatment with bevacizumab plus a platinum-based chemotherapy combination, in patients with advanced NSCLC. Those not experiencing disease progression or major side effects received bevacizumab plus erlotinib or bevacizumab alone (plus placebo). The trial ended early because bevacizumab plus erlotinib showed clear improvement in progression-free survival (PFS) compared to the other group. Because of this positive development, patients who were in the group receiving placebo were given the option of adding erlotinib to their treatment. The combination was considered as safe as using either drug alone. Researchers concluded that adding erlotinib to bevacizumab after treatment with chemotherapy and bevacizumab improves the PFS of patients with locally advanced, recurrent, or metastatic NSCLC. *NCT00257608*

### Maintenance pemetrexed (Alimta®) may delay disease progression after initial chemotherapy

Pemetrexed is an approved treatment for patients with advanced NSCLC whose cancer progressed after initial treatment. A recent phase III trial studied the benefits of maintenance pemetrexed therapy in patients with advanced NSCLC. This study tested the drug in patients whose disease had not progressed to see if the addition of pemetrexed would delay progression. Patients received either pemetrexed or placebo after initial chemotherapy. The results showed that those who took pemetrexed had more time to disease progression and had longer overall survival compared to those receiving the placebo. These positive results, along with the fact that pemetrexed is easy to give and generally has fewer side effects than other chemotherapies, could impact the treatment of patients with advanced NSCLC whose cancer has not progressed after initial treatment. *NCT00102804*

### Patients with EGFR Mutations Show High Levels of Response to New Targeted Therapy, BIBW 2992 (Tovok®) after Failure of One Line of Chemotherapy

Lung cancers with EGFR mutations have been associated with positive responses to treatment with drugs such as erlotinib and gefitinib, which block those mutations from occurring. Although many patients who have EGFR mutations respond to those treatments at first, eventually the tumor becomes resistant and the drugs stop working. Current research is exploring the next generation of these drugs, which may be effective once the first drugs stop working. A phase II study has begun to analyze one new drug, BIBW 2992, in patients with NSCLC and EGFR mutations who have seen disease progression after one line of chemotherapy. Preliminary data has shown that nearly two-thirds of these patients had a partial response to BIBW 2992 and one-third of patients showed stable disease. BIBW 2992 is an oral drug and was tolerated fairly well with the most common side effects being the same as in other drugs of this type, including diarrhea and skin-related disorders. An international phase III trial has started that will study BIBW 2992 as an initial treatment for NSCLC patients that have tested positive for EGFR mutations. *NCT00525148*

To learn about open clinical trials that you qualify for, call 800.698.0931.

It may also be useful to take any studies of interest to your doctor to discuss.

### **Preliminary Study Results Show That Biomarkers Linked to Angiogenesis May Predict Response to Bevacizumab (Avastin®) and Carboplatin/Paclitaxel (Taxol®)**

The phase III study, ECOG 4599, showed that advanced NSCLC patients treated with bevacizumab and carboplatin/paclitaxel lived longer than those treated with carboplatin/paclitaxel alone. As a follow-up to these results, researchers studied the blood of some of these patients in an effort to identify markers that may predict the success of the bevacizumab and carboplatin/paclitaxel treatment. Similar studies in advanced breast and colorectal cancers showed that biomarkers can be detected that predict response to specific treatments. Early results from this study suggest that certain markers related to the angiogenesis pathway (the pathway responsible for new blood vessel growth) may predict which advanced NSCLC patients will respond to treatment with bevacizumab and carboplatin/paclitaxel. *NCT00021060*

### **Small Cell Lung Cancer**

#### **Antibody Shows Promise in Detecting Small Cell Lung Cancer (SCLC) in Serum Test, May Lead to Treatment Targeting for SCLC in the Future**

Recent results from a pilot study showed that an antibody called ICT-109 was able to significantly confirm small cell lung cancer (SCLC) cells in blood samples of patients already diagnosed with lung cancer. The antibody binds to a protein that has been shown to be present in higher levels in SCLC. These results mean progress in the development of a simple blood test that could detect SCLC. The reliable and early detection of lung cancer in general would be critical to delivering effective treatments, but because SCLC tends to be a more aggressive form of lung cancer, finding it as early as possible is even more critical for these patients. Researchers are now looking at the possibility that ICT-109 may have use as a delivery system to send a chemical with cancer killing properties to the cancer. This may prove to be an effective treatment strategy for SCLC in the future.

### **Biomarker Testing**

#### **NSCLC Patients with High Levels of Free Insulin Growth Factor in Blood May Respond Better to Chemotherapy and Targeted Therapy, Figitumumab (CP-751871)**

To identify patients who may benefit from specific treatments, researchers analyzed blood samples of NSCLC patients in a phase II study of the drug figitumumab plus carboplatin and paclitaxel. Figitumumab is a targeted therapy that blocks the activity of the insulin growth factor pathway, one route that, when mutated, can lead to the uncontrolled growth of cancer cells. Researchers looked at the levels of free insulin growth factor (fIGF) molecules in the blood. The study found that, when there are high levels of fIGF-1 in the blood, the patient has increased response to chemotherapy, as well as to figitumumab. In the group with high fIGF-1, PFS was longer when these patients received figitumumab plus carboplatin and paclitaxel than those who only received carboplatin and paclitaxel. In the group of patients with low blood levels of fIGF-1, there was no significant effect of figitumumab. These results suggest that determining the levels of fIGF-1 in the blood before treatment may help identify patients who respond best to figitumumab. *NCT00147537*

### **Prevention**

#### **Hormone Therapy (Estrogen Plus Progestin) Use in Postmenopausal Women May Increase Risk of Death from Non-Small Cell Lung Cancer (NSCLC)**

Research suggests a link between sex hormones and lung cancer, but to date studies have shown mixed results. A study by the Women's Health Initiative provides further insight. This randomized trial of two commonly used hormones (conjugated equine estrogen plus medroxyprogesterone acetate) was conducted in 16,608 postmenopausal women; half received hormone therapy and half received placebo. Researchers analyzed results to look at lung cancer incidence and mortality. After nearly six years in the trial and over two years of additional follow-up, the number of NSCLC cases and deaths from the disease were the same between groups. There was, however, a trend for more NSCLC diagnoses in the group receiving hormone therapy that was not significant at first. After five years, however, there hormone therapy, and those patients were also more likely to die from NSCLC than those on placebo. The findings indicate that hormone therapy for more than five years significantly increases risk of death from NSCLC. This risk was further increased in current smokers and suggests that current smokers should try to quit or consider this risk before beginning or continuing hormone therapy. ■

### **Maintenance Therapy**

Therapy given to help keep cancer from coming back after initial successful initial treatment. Maintenance therapy may include treatment with drugs, vaccines, or antibodies (a proteins in the immune system) that kill cancer cells.

### **Placebo**

An inactive substance or treatment that looks the same as, and is given the same way as, an active drug or treatment being tested. The effects of the active drug or treatment are compared to the effects of the placebo.

### **Randomized Trial**

Trial design in which participants are assigned by chance to a treatment group.

### **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:

Timing is everything! Clinical trials are available at all stages of lung cancer, but only enroll patients at certain times. It is important to understand what studies you are eligible for each time you make a treatment decision.

### 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 a particular time, but the only way to decide is to learn about available studies and to explore at each window of opportunity. ■

## Staging Guidelines for Non-Small Cell Lung Cancer Change in 2009

The International Association for the Study of Lung Cancer (IASLC) announced important changes to the way non-small cell lung cancer is staged in 2009. The changes provide greater understanding of how non-small cell lung cancer should be staged, and were the result of the examination of a much larger and more international database of cases.

Understanding the stage (or extent) of lung cancer is important in determining what treatment options are available and can help patients better understand the reasons for those options.

For information on current non-small cell lung cancer staging guidelines, go to the Lung Cancer Alliance website at [www.lungcanceralliance.org](http://www.lungcanceralliance.org) or call the toll-free information line at 1.800.298.2436. ■

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