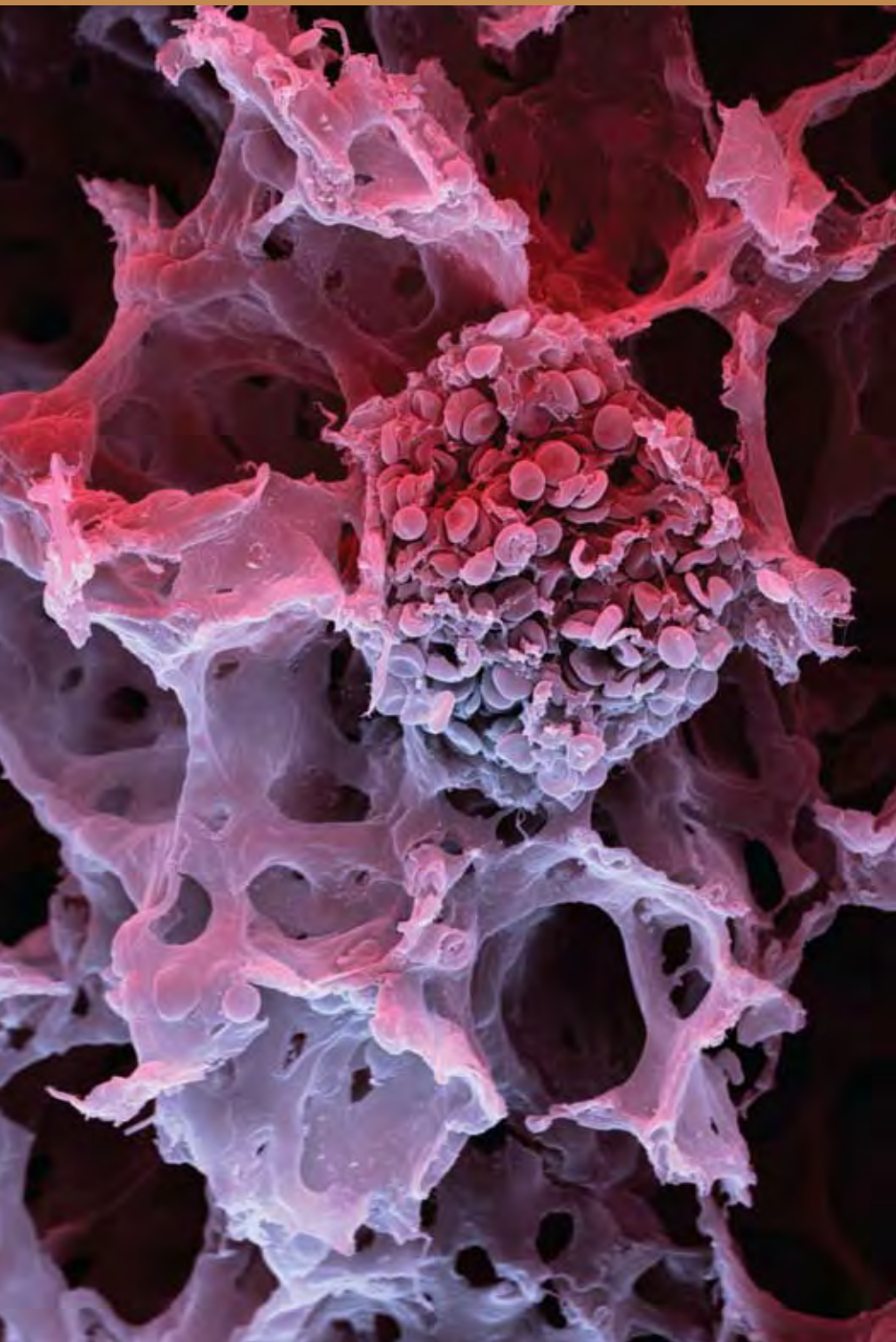

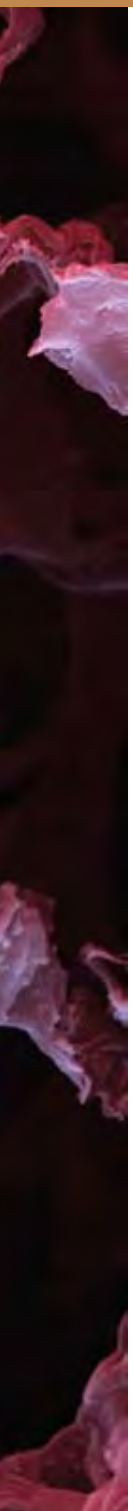

Lung Cancer

Highlights from the 2009 Annual Meeting of the American Society of Clinical Oncology

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◀ Air passages in the lungs

STEFAN DILLER/PHOTO RESEARCHERS, INC.

Lung cancer is the second most common cancer in both men and women. Doctors recommend treatment for lung cancer based on its stage:

- **Early-stage lung cancer** is located only in the lungs and has not spread to any lymph nodes. (Lymph nodes are a linked system of small bean-shaped structures throughout the body that filter out and destroy bacteria and other harmful substances. When cancer spreads to the lymph nodes, it can travel to other parts of the body.)
- **Locally advanced lung caner** is found in the lung and nearby lymph nodes.
- **More advanced lung caner** is found in the lung and in the lymph nodes in the middle of the chest and may be accompanied by fluid in the chest.
- **Metastatic lung cancer** is the most advanced stage of lung cancer. This is when the cancer has spread to a distant part of the body, such as the liver or other organs.

The two main types of lung cancer are small cell lung cancer, which makes up about 15 percent of cases, and non-small cell lung cancer (NSCLC), which accounts for the other 85 percent.

These two types of lung cancer are diagnosed based on how the cells look under a microscope. It is important for doctors to distinguish NSCLC from small cell lung cancer because the two types of cancer are usually treated in different ways.

All of the studies discussed here focus on NSCLC.

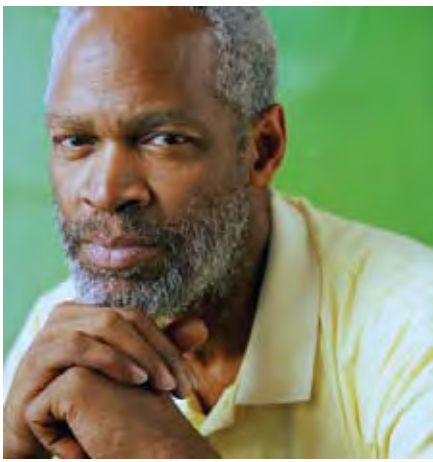
Early-Stage Lung Cancer

PREDICTING RESPONSE TO CHEMOTHERAPY FOR LUNG CANCER

A new test may help identify people who will benefit from chemotherapy for lung cancer.

For people with NSCLC that can be removed surgically, doctors often use chemotherapy after surgery to help prevent the cancer from returning. However, they have been unsure whether this type of chemotherapy—called adjuvant chemotherapy—is best for every patient who has had surgery. Now, according to the results of a recent clinical trial, a new test may help predict which people will benefit most from adjuvant chemotherapy.

The clinical trial measured the amount of two different proteins—called MSH2 and ERCC1—in more than 750 people being treated for NSCLC. Cancer cells use these proteins to repair damage from chemotherapy with cisplatin (Platinol and others), a drug commonly used to treat lung cancer.



Among the patients with *low or undetectable* amounts of MSH2, those who received cisplatin survived about 16 months longer than those who did not get this chemotherapy. So, having little or no MSH2 was an advantage.

Having low levels of MSH2 *and* low levels of ERCC1 was even more of an advantage. Among the people with low levels of both of these proteins, those who received cisplatin survived about 21 months longer than those who did not receive cisplatin.

Having *high* levels of MSH2 was a disadvantage; chemotherapy did not improve survival. Among the patients with high levels of MSH2, those who received cisplatin survived for about nine months less than those who did not receive chemotherapy.

Measuring MSH2 and ERCC1 levels is a test that can be used

to predict which people with NSCLC will benefit from cisplatin chemotherapy. When doctors know who is most likely to benefit from a particular treatment, they can help patients avoid the side effects and costs of an unnecessary treatment.

CHEMOTHERAPY FOR EARLY-STAGE LUNG CANCER

In people with early-stage NSCLC, adjuvant treatment has long-lasting benefits.

For people who have early-stage NSCLC with cancer cells in their lymph nodes, doctors usually recommend adjuvant chemotherapy after surgery. According to the updated results of a clinical trial, the benefits of such treatment, which contains the standard cancer drug cisplatin, may last for years.

Nearly 500 people with early-stage NSCLC took part in the clinical trial. After surgery, about half of the patients received chemotherapy including cisplatin. The others did not receive chemotherapy.

Five years after treatment, more people who were treated with chemotherapy (69 percent) had survived than those who did not receive chemotherapy (54 percent). However, these benefits of treatment were seen only in those whose lung cancer had spread to nearby lymph nodes on the same side of the body. Those whose lung cancer had not spread to the lymph nodes did not appear to benefit from chemotherapy.

Advanced and Metastatic Non-Small Cell Lung Cancer

PEMETREXED AS MAINTENANCE THERAPY FOR ADVANCED NSCLC

A new standard of care seems to extend the lives of people with advanced NSCLC.

Maintenance chemotherapy is a continuation of treatment with one or more drugs after completing chemotherapy, usually with cisplatin or carboplatin (Paraplatin and others). The goal of maintenance chemotherapy is to prevent the cancer from growing or spreading. Especially with the newer targeted treatments, maintenance chemotherapy generally causes less severe side effects than traditional chemotherapy.

Unlike chemotherapy, targeted treatments block specific cell mechanisms that are thought to be important for cancer cell growth. Targeted treatments are meant to spare healthy tissues and cause less severe side effects.

Based on the results of a recent clinical trial, treatment with pemetrexed (Alimta) has been approved by the U. S. Food and Drug Administration as maintenance therapy for advanced NSCLC.

More than 650 people took part in this international clinical trial. These patients had advanced NSCLC that had not grown after four cycles of chemotherapy with a drug like cisplatin or carboplatin. Two-thirds of the patients were treated with pemetrexed.

Those who received pemetrexed survived three to five months longer than those who did not receive the drug. In addition, the benefit of maintenance therapy with pemetrexed was greater in patients who had a subtype of lung cancer called nonsquamous cell NSCLC. Those with the squamous cell subtype of NSCLC do not seem to benefit from the use of pemetrexed.

TARGETED TREATMENT FOR ADVANCED NSCLC

Erlotinib (Tarceva), vandetanib (Zactima), and BIBW 2992 appear to slow the growth and spread of lung cancer.

Four recent clinical trials show that the targeted treatments erlotinib (Tarceva), vandetanib (Zactima), and BIBW 2992 may slow the growth and spread of advanced NSCLC. These drugs target the faulty genes and proteins that contribute to the growth of cancer.

The first clinical trial included more than 750 people who had locally advanced, recurrent, or metastatic NSCLC. One group of patients received a combination of erlotinib and bevacizumab (Avastin), a type of targeted treatment that blocks the formation of a blood supply to nourish the tumor. Another group received bevacizumab plus a placebo (a look-alike pill containing no active ingredient). It took about a month longer for the cancer to continue growing in the first group of patients, who had received both drugs, than in the second group, who had received bevacizumab and a placebo.

Six months after treatment, the drug combination continued to benefit patients who had taken it. In the group that received the combination of erlotinib and bevacizumab, the cancer had not grown in 40 percent of patients. In the group that received bevacizumab and a placebo, the cancer had not grown in fewer than 30 percent of the patients.

Interestingly, people who had never smoked and those who had an Asian or Pacific Island ethnic background seemed to

benefit even more from the combination treatment than the others. More research is needed to find out why.

Another clinical trial on the use of erlotinib as maintenance therapy for people with advanced NSCLC showed similar positive results. Nearly 900 patients whose cancer stopped growing after first-line (first-time) treatment with chemotherapy were included in this clinical trial. About half of the patients received maintenance therapy with erlotinib, and the others did not.

For those who received erlotinib, it took 41 percent longer for their cancer to start to grow and/or spread. People whose cancer had a certain abnormal (or mutated) epidermal growth factor receptor (EGFR) gene did even better (45 percent longer). As in the first study with erlotinib, the outcome was even better in those who were Asian and had never smoked.

Researchers do not yet know whether the fact that erlotinib slows cancer growth means it will also extend the lives of people with advanced NSCLC. However, they believe that this drug is an important step forward in the treatment of lung cancer.

The third study included nearly 1,400 people with advanced NSCLC. In these patients, the cancer had continued to grow after their first-line treatment did not work or stopped working. Some of the patients received second-line treatment with the combination of a standard drug, docetaxel (Taxotere), and a newer drug, vandetanib. The others received docetaxel plus a placebo.

It took longer for the cancer to continue to grow in those who received the two drugs (about 17 weeks) than in those who did not (14 weeks). Although there did not seem to be a difference between the two treatments in terms

of survival, symptoms such as cough, weight loss, and difficulty breathing improved in those who were treated with docetaxel and vandetanib.

Vandetanib works by targeting two receptors in lung cancer. These receptors—EGFR and the vascular endothelial growth factor receptor (VEGFR)—play a key role in the growth of new blood vessels that feed tumors. Although these receptors are targeted separately by other drugs, vandetanib is the first drug to target both receptors.

Finally, in the fourth study, a new medication referred to as BIBW 2992 may slow the growth of advanced lung cancer in people who have a mutated (changed) EGFR gene. In this clinical trial, more than 100 patients with lung cancer and this mutated gene have started once-a-day treatment with BIBW 2992.

So far, 67 people enrolled in the trial have been evaluated. The tumor has shrunk by at least half in more than 60 percent of them. The tumor has neither grown nor shrunk in another 31 percent of the people treated with BIBW 2992.

Researchers are pleased with these early results. BIBW 2992 is being studied further in an international clinical trial, in the hope that it may become an effective option for people with advanced lung cancer who have a mutated EGFR gene.

RADIATION THERAPY TO PREVENT THE SPREAD OF LUNG CANCER TO THE BRAIN

A treatment called prophylactic cranial irradiation may stop lung cancer from spreading to the brain.

People who are treated for locally advanced NSCLC are living longer. However, there is a chance that their cancer may still spread to the brain.

Researchers may have found an effective way to prevent this

spread. It is called prophylactic cranial irradiation (PCI). This treatment delivers radiation to the head to reduce the risk that cancer will spread to the brain.

Approximately 350 people who were treated for locally advanced NSCLC took part in a clinical trial to test PCI. About half of these patients received PCI, and the others did not. Before they joined this clinical trial, these people had already responded to treatment for their lung cancer. With this earlier treatment, their cancers had disappeared, shrunk, or stopped growing.

Cancer spread to the brain in fewer people who had been treated with PCI (about eight percent) than in those who did not receive PCI (about 18 percent). However, PCI did not appear to extend the lives of these patients. Researchers are continuing to study how best to use PCI in people with locally advanced NSCLC.

Please note: *Although the treatments discussed in this chapter are showing promise, most are still in clinical trials—some in earlier phases of research—and may not be available yet to the general public. Your doctor can help guide you as to which new medications could be right for you and whether you are eligible to take part in the clinical trials of these new treatments.*