

## Advances in Treating Lung Cancer

Survival rates for lung cancer are poor, which is why developing new ways to treat the disease—or prevent it altogether—is so important.

Lung cancer is the most dangerous type of cancer, killing 85% of people within five years of diagnosis. “Lung cancer causes more deaths in women than breast and ovarian cancer combined, and more than three times more deaths in men than prostate cancer,” emphasizes Julie Brahmer, M.D., an assistant professor at Hopkins’s Sidney Kimmel Comprehensive Care Center.

But effective treatments for lung cancer do exist, with those that can extend survival by even a few months representing a significant advance in treatment. Treating lung cancer also can improve quality of life.

Here’s an overview of the newest treatments for lung cancer, along with a look at drugs that are under development to treat or even prevent the disease.

### New Combinations and Agents

Several new chemotherapy regimens for lung cancer have been developed in the last few years, and one drug has been approved.

**New regimens.** About 80% of lung cancers are non-small cell lung cancers. Treatment for this type of cancer usually consists of surgery fol-

lowed by chemotherapy and, sometimes, radiation. In some cases, chemotherapy and radiation are used to shrink the tumor prior to surgery.

The drug cisplatin (Platinol) used to be the standard treatment for non-small cell lung cancer. Now, a second drug—such as gemcitabine (Gemzar), vinorelbine (Navelbine), paclitaxel (Taxol), or docetaxel (Taxotere)—is added to boost cisplatin’s effectiveness. In addition, a less toxic drug called carboplatin (Paraplatin) sometimes is substituted for cisplatin. Like most chemotherapy regimens, these combinations usually cause temporary but severe side effects that may include nausea, vomiting, loss of appetite, hair loss, mouth sores, severe diarrhea, fatigue, and low resistance to infection.

Other regimens for non-small cell lung cancer are also being examined, such as gemcitabine (Gemzar) in combination with vinorelbine (Navelbine) or paclitaxel. Another combination that has shown promise in Japanese trials is uracil and tegafur, neither of which has been approved in the United States. The hope is that these combinations might be just as effective as older combinations, but

less toxic. Also being studied is bevacizumab (Avastin), a drug that was recently approved for treating colon cancer, to see if it can extend survival when added to carboplatin and paclitaxel.

Small cell lung cancer accounts for the remaining 20% of lung cancers. Surgery is ineffective for this type of lung cancer, but chemotherapy and radiation are often used together for limited disease; chemotherapy alone is used for extensive disease.

Cisplatin plus etoposide (VePesid, Etopophos, Toposar) is usually considered the optimal chemotherapy regimen for small cell lung cancer. However, a Japanese study found that substituting irinotecan (Camp-Tosar) for etoposide improved survival from 9.4 months to 12.8 months among people with metastatic disease (cancer that has spread beyond the lungs). Three randomized controlled trials are under way to test this finding. Researchers are also examining gemcitabine, paclitaxel, vinorelbine, and topotecan (Hycamtin) in combination with cisplatin for use in small cell lung cancer.

**Gefitinib (Iressa).** A new option for people with non-small cell lung

arguing that these levels of radon do not pose a significant risk and that attention should be focused on finding the homes with the highest levels. Recently, researchers estimated that reducing radon levels in all homes with readings higher than 4 pCi/L would result in 2% to 4% fewer lung cancer deaths.

To determine whether radon levels are high in your area, call your local EPA office. Taking a radon measurement in an individual house is the only way to definitively know the radon level, and several inexpensive kits are available in most hardware stores. Etched-track or electret detectors are good choices; the best of these kits take measurements over at least a three-month period.

cancer that doesn't respond to conventional chemotherapy is gefitinib, which was approved in 2003. In one study of 142 people whose tumors didn't respond to two or more types of chemotherapy, 11% had a response to gefitinib. This response lasted for at least seven months in half the people. It is unknown whether this response will translate into fewer cancer-related symptoms or longer survival. Unfortunately, attempts to boost the effectiveness of standard chemotherapy by adding gefitinib have been disappointing.

Gefitinib is taken by mouth and usually produces only minor side effects, such as diarrhea, rash, acne, and dry skin. It can also cause nausea and vomiting. Although it has several mechanisms of action, one of the ways in which it works is by blocking the activity of a tumor protein called epidermal growth factor (EGFR).

Researchers are studying other EGFR inhibitors for the treatment of non-small cell lung cancer, including erlotinib (Tarceva) and the monoclonal antibody cetuximab (Erbix).

#### Novel Approaches

Two innovative approaches being tested for lung cancer treatment are vaccination and gene therapy.

**Vaccination.** The GVAX lung

cancer vaccine is made from a patient's own tumor cells. These cells are genetically modified to secrete a hormone that stimulates the immune system to attack the tumor. In a study of 33 people with advanced non-small cell lung cancer who received the vaccine, 3 (9%) went into complete remission that lasted about a year and a half. Half the patients lived for at least a year, which is longer than the six or seven months seen in other studies with docetaxel. Two 75-person trials with the vaccine are currently being conducted.

**Gene therapy.** Researchers at M.D. Anderson Cancer Center and the University of Texas Southwestern have identified three tumor-suppressor genes that reduce human lung cancer growth in mice. They are hoping that by injecting the genes into a patient's lung tumor, cancer cells will die or grow more slowly.

#### Lung Cancer Prevention

Taking a medication to reduce the risk of cancer is a relatively new approach to cancer management. A number of agents are being tested to see if they can reduce the risk of lung cancer in people at high risk (mainly smokers and people who smoked for many years before quitting).

**9-cis-retinoic acid.** In a 2003

study of 177 former smokers, 9-cis-retinoic acid repaired some of the lung damage caused by smoking. This raises the possibility that 9-cis-retinoic acid, a substance related to vitamin A, might reduce the risk of lung cancer in former smokers.

**Anethole dithiolethione (ADT).** A recent Canadian study looked at the use of ADT, a drug used to treat dry mouth, in 101 current and former smokers with irregular growths in their lungs. Compared with a placebo, ADT halved the risk of developing new growths and progression of existing growths.

**Cyclooxygenase inhibitors.** A growing body of evidence indicates that the cyclooxygenase-2 (COX-2) enzyme plays a key role in lung cancer. Clinical trials are examining whether drugs that inhibit this enzyme, for example celecoxib (Celebrex), can reduce the risk of lung cancer in high-risk patients or enhance the effectiveness of chemotherapy regimens.

**Other agents.** Hopkins researchers are currently studying a drug called iloprost and a tea made from broccoli sprout extract in people at high risk for lung cancer, says Dr. Brahmer. To find out about more ongoing clinical trials, visit [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (national) or [www.hopkinskimmelcancercenter.org/clinicaltrials/index.cfm](http://www.hopkinskimmelcancercenter.org/clinicaltrials/index.cfm) (Hopkins only).

The label on the kit should say that it meets EPA requirements or is certified by the state. A state-certified contractor or one who has passed the EPA Radon Contractor Proficiency Program should be used if it is necessary to reduce radon levels in a home.

**Dietary measures.** Since damage of DNA by free radicals is considered one of the causes of many types of cancer, it was hoped that antioxidant supplements or an increased intake of antioxidant-rich foods might reduce the risk of lung cancer. A Scandinavian study, however, found that beta-carotene supplements increased the risk of lung cancer in cigarette smokers. Currently, no dietary measures are known to diminish the risk of lung cancer.