



*A Report From the American Society of Clinical Oncology 2007 Annual Meeting*

## Upper Digestive System Cancers

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**C**ancer can affect several different parts of the gastrointestinal system, including the stomach, the esophagus (the tube through which food passes on its way to the stomach), the pancreas (a large gland that helps in digestion and produces insulin), and the liver. All of these cancers are more common in men than in women.

Doctors diagnose stomach cancer in more than 21,000 Americans each year. As with other cancers, most people with stomach cancer are older, above age 72. People who eat a diet high in smoked, salted, or pickled foods may be at increased risk for stomach cancer. On the other hand, eating fresh fruits and vegetables may protect against this disease.

Each year more than 15,500 Americans are diagnosed with esophageal cancer. Most of those who develop esophageal cancer are over the age of 60. This type of cancer is linked to tobacco use, heavy alcohol use, and irritation from gastric reflux—the back-up of stomach acid. People who have had other head and neck cancers also have an increased chance of developing esophageal cancer.

More than 37,000 Americans are diagnosed with pancreatic cancer each year, and it is one of the most challenging cancers to treat. Most pancreatic cancers occur in people over the age of 60. The risk for developing pancreatic cancer triples if a parent or sibling had the disease. Also, a family history of colon or ovarian cancer increases the risk of pancreatic cancer, as does a history of tobacco use or diabetes.

Every year in the United States, approximately 19,000 people are diagnosed with **hepatocellular cancer**, the most common type of liver cancer. This type of cancer is a major problem worldwide and is strongly associated with chronic infection with the hepatitis B virus or the hepatitis C virus. **Vaccines** can prevent infection with hepatitis B, and researchers are now working to develop a vaccine to prevent hepatitis C infection.

## What's New, What's Important

- Combination chemotherapy with 5-fluorouracil and cisplatin (Platinol) given before surgery is an effective treatment for people with cancer of the stomach and lower esophagus. This treatment prolongs their lives compared with surgery alone.
- S-1, a drug widely used in Japan but not yet approved in the United States, seems to be one of the most promising chemotherapies used alone or in combination for people with advanced stomach cancer.
- Sorafenib (Nexavar), a drug taken by mouth, is the first medication to prolong the lives of people with advanced liver cancer. It may now become the new standard of care for this cancer.

At this year's meeting of the American Society of Clinical Oncology, researchers reported some promising new advances for these gastrointestinal cancers.

## Stomach and Esophageal Cancers

### CHEMOTHERAPY BEFORE SURGERY FOR CANCER OF THE STOMACH AND LOWER ESOPHAGUS

The combination of two chemotherapies—5-fluorouracil (5-FU) and cisplatin (Platinol)—is called FP. It's one of the most effective treatments for cancer of the stomach and lower esophagus (the tube through which food passes on its way to the stomach). Researchers believed that using this combination before surgery might prolong the lives of people with this type of cancer. The findings of a French clinical trial seem to indicate that they were right.

Between 1995 and 2003, researchers at about 25 centers throughout France studied nearly 225 people with cancer of the lower esophagus and stomach. Approximately half of the

patients were treated with surgery alone, and the other half were treated with FP four to six weeks before surgery.

Nearly six years after treatment, almost 40 percent of the group that received FP chemotherapy before surgery was still alive, compared with about 25 percent of the surgery-only group. Also, patients given chemotherapy before surgery went longer without their cancer returning than those only treated with surgery.

Researchers concluded that FP chemotherapy given before surgery is an effective treatment for people with cancer of the stomach and lower esophagus, prolonging their lives compared with those who receive surgery alone. This conclusion is consistent with other recent findings suggesting that chemotherapy is a useful addition to surgery in cancers of the stomach and esophagus that can be removed.

### CHEMOTHERAPY FOR ADVANCED STOMACH CANCER

To learn which are more effective, several combinations of different chemotherapies have been studied in people with advanced stomach cancer. According to the findings of two Japanese clinical trials, the most promising medications seem to be cisplatin, irinotecan (Camptosar), and a drug called S-1 which is used widely in Japan for advanced stomach cancer but has not yet been approved in the United States. S-1 is a pill taken by mouth.

In the first clinical trial, called SPIRITS, the combination of cisplatin and S-1 was compared with S-1 alone in about 300 people. Three-fourths of the patients had cancer that could not be treated with surgery, and the rest had cancer that had returned. None had been treated previously with chemotherapy for their advanced stomach cancer. Half of the people in the clinical trial were treated with an S-1 pill twice a day. The other half received the same S-1 treatment plus cisplatin.

One year after treatment, more people treated with the combination of drugs were still alive than those treated with just S-1 (54 percent versus 47 percent). The same was true two years after treatment: Survival rates were higher in the group that received both S-1 and cisplatin than in the group that received just S-1 (24 percent versus 15 percent). How effective this combination would be in treating people with similar cancers outside Japan and whether changes in doses might be needed are questions that will have to be answered in further clinical trials.

In the second Japanese clinical trial, researchers studied three different treatments in about 700 people with advanced stomach cancer. The three treatments were 5-fluorouracil (5-FU) alone; a combination of irinotecan and cisplatin; and S-1 alone. As in the first clinical trial, people who took part in this study either had cancer that could not be treated with surgery or cancer that had returned.

The results with the combination treatment and S-1 appeared to be better than those with 5-FU. For example, the time until the cancer grew was about three months with 5-FU, almost five months with the combination, and just over four months with S-1. The survival rate was also lowest with 5-FU (10.8 months, compared with 12.3 months with the combination and 11.4 months with S-1.) Researchers say they are particularly impressed with S-1. The benefits of this medication were seen when it was given alone as well as with cisplatin. However, further clinical trials with S-1 are needed to see whether these Japanese results can be duplicated in people with advanced stomach cancer in the United States.



## Liver Cancer

### SORAFENIB (NEXAVAR): A NEW STANDARD OF CARE FOR LIVER CANCER?

About 40 percent of liver cancers are diagnosed at an advanced **stage**. However, there are no standard treatment options for advanced hepatocellular carcinoma, the most common form of liver cancer. Now, for the first time, there seems to be a promising treatment that should become the new standard of care for this type and stage of cancer.



A new drug called sorafenib (Nexavar) was recently approved for treatment of kidney cancer, and researchers hope that it may also be effective against advanced liver cancer. The international SHARP trial studied more than 600 patients with liver cancer in the Americas, Europe, Australia, and New Zealand. About half of the patients received sorafenib, which is taken by mouth,

and the rest of the patients received a **placebo** (an inactive substance) for six months.

People who received sorafenib lived longer than those who did not receive this drug (11 months versus eight months). Also, the cancer took longer to grow in patients taking sorafenib than in those who took the placebo. The findings from this study were so positive, the study was stopped early so that people taking placebo could be given sorafenib.

Many researchers are calling this study of sorafenib a breakthrough trial because it is the first drug to improve survival for patients with advanced hepatocellular cancer.

## What's New, What's Important

- A new anticancer drug called volociximab appears to offer encouraging results for people with metastatic pancreatic cancer.
- The combination of a new injection called TNFerade with standard chemotherapy and radiation may help people with advanced, inoperable pancreatic cancer live longer.

Sorafenib belongs to a class of drugs known as **targeted treatments**. These drugs zero in on cell mechanisms that supply blood to tumors and promote their growth. Rather than killing all types of cells, as chemotherapy does, targeted treatments attack cancer cells primarily, sparing healthy tissues and causing less severe side effects.

Sorafenib helps stop cancer by blocking **receptors** for vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF). These substances play a critical role in the growth of blood vessels that feed cancer tumors (a process called angiogenesis). Sorafenib also targets another substance, called RAF kinase, which helps signal cancer cells to grow and divide. Researchers believe that these multiple actions are what make the drug so effective at slowing the growth of cancer.

## Pancreatic Cancer

The standard treatment for advanced, inoperable pancreatic cancer is a chemotherapy called gemcitabine (Gemzar). But researchers have been trying to discover whether combining this medication with other drugs will help prolong the lives of patients.

### VOLOCIXIMAB FOR METASTATIC PANCREATIC CANCER

A new anticancer drug called volociximab looks promising for people with **metastatic** pancreatic cancer, according to early

clinical trial findings. Researchers from a number of medical centers in the United States and the United Kingdom have tested volociximab in combination with the chemotherapy gemcitabine.

In the first part of this two-part trial, 20 patients with metastatic pancreatic cancer received volociximab **intravenously** once every two weeks and gemcitabine once a week during a four-week cycle. None of the patients had received prior chemotherapy.

The preliminary results showed that the cancer did not grow in more than 50 percent of the patients and even significantly shrank in one patient. Six months after treatment, the cancer still had not grown in nearly 40 percent of the people who took part in the clinical trial. In addition, 11 months after treatment, more than 30 percent of the people had survived. The most common side effects with volociximab were nausea (experienced by 70 percent of patients), vomiting (by 60 percent), and constipation (by 50 percent).

In the second part of this clinical trial, a higher dose of volociximab given weekly is being tested. The results are expected later in 2007.

### **TNFERADE COMBINED WITH CHEMOTHERAPY AND RADIATION FOR ADVANCED, INOPERABLE PANCREATIC CANCER**

Early results of another combination approach being studied are also encouraging. Researchers from the University of Chicago, the University of California at Irvine, and Baylor College of Medicine in Houston, as well as several other centers in the United States, have focused their attention on a substance called TNFerade, which is given in a series of injections.

The Pancreatic Cancer Clinical Trial is called the PACT study. It includes people who have an advanced, inoperable type of

pancreatic cancer. The first 50 patients in the PACT study were separated into two groups. Group 1 received a combination of five weekly injections of TNFerade in addition to the standard treatment of chemotherapy and radiation. Group 2 received just the standard treatment without TNFerade injections.

People who were treated with the TNFerade combination lived longer than those treated with just chemotherapy and radiation (19 months versus 11 months). In addition, for the first three months after treatment, the size of the tumors decreased more with the TNFerade treatment than with just chemotherapy and radiation. Patients treated with the TNFerade injections did experience mild flu-like symptoms.

The clinical trial is continuing, and the total number of patients expected to be studied is around 300. Researchers are looking forward to learning whether this early positive trend is confirmed.

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**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.