



Highlights from the 2008 Annual Meeting of the American Society of Clinical Oncology

Upper Digestive System Cancers

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A combination of chemotherapies placed directly into the abdomen seems to help people with metastatic stomach cancer go a longer time without their cancer returning.

Sorafenib Plus Chemotherapy for Metastatic Stomach Cancer (p 123)

Adding sorafenib, an effective treatment for metastatic liver and kidney cancers, to standard chemotherapy may help shrink tumors in people who have metastatic stomach cancer.

Cancer can affect several different parts of the upper digestive system, including the pancreas, liver, and stomach.

Each year, approximately 38,000 adults in the United States are diagnosed with pancreatic cancer. Because pancreatic cancer often does not cause specific symptoms early in its development, it may not be detected until the cancer has metastasized—spread beyond the pancreas to other areas of the body (such as the liver or lungs) or into surrounding tissues such as blood vessels.

Doctors diagnose liver cancer in approximately 21,000 Americans each year. The liver is the largest internal organ in the body and is vital to digestion, removing wastes from the body and producing blood-clotting substances, among other important functions. The most common form of metastatic liver cancer, which we discuss in this chapter, is called hepatocellular

carcinoma. New medications are now available to treat it.

Stomach cancer is diagnosed in nearly 22,000 Americans each year. Infection with *Helicobacter pylori* (*H. pylori*), a type of bacteria, seems to be a major cause of stomach cancer. Most people diagnosed with stomach cancer are in their late 60s or older.

Pancreatic Cancer

CHEMOTHERAPY AFTER SURGERY FOR EARLY-STAGE PANCREATIC CANCER

People who have early-stage pancreatic cancer (in which the tumor is confined to the pancreas) are usually treated with surgery to completely remove the tumor. However, the risk of the tumor returning is high. In the past, these patients received no additional treatment after surgery. It appears that the chemotherapy gemcitabine (Gemzar) given after surgery may lower the risk of the cancer returning and help patients live longer.

Gemcitabine has been the standard treatment for metastatic pancreatic cancer that cannot be surgically removed. Researchers wanted to learn whether this medication might also benefit people with early-stage pancreatic cancer.

More than 350 people took part in a clinical trial called CONKO-001. They were divided into two groups. One group received treatment with gemcitabine after surgery; the other group had no additional treatment after surgery. After three years, nearly 40 percent of those people who received gemcitabine survived; of those who did not take the drug, only about 20 percent survived. Of those who received gemcitabine, nearly 25 percent stayed cancer free after three years. Of those who did not receive the drug, less than 10 percent were cancer free after three years.

After five years, more than twice as many people in this clinical trial who were treated with gemcitabine survived than patients in the study who did not receive the drug (21 percent versus nine percent). In addition, after five years, more than 15 percent

of those who received gemcitabine remained cancer free. In comparison, about five percent of those who did not take the medication remained cancer free.

Studies are ongoing to compare gemcitabine alone and in combination with targeted treatments such as erlotinib (Tarceva) or with radiation in people who have undergone successful surgery for their pancreatic cancer. Unlike chemotherapy, targeted treatments attack specific molecules and cell mechanisms thought to be important for cancer cell survival and growth. This specific targeting helps to spare healthy tissues and causes less severe side effects.



GEMCITABINE WITH RADIATION FOR LOCALLY ADVANCED PANCREATIC CANCER

Locally advanced pancreatic cancer refers to tumors that have not spread beyond the pancreas. But these tumors cannot be treated with surgery because they have grown into or attached themselves to vital organs. Researchers from the Eastern Cooperative Oncology Group (ECOG) continue to search for better ways to treat people with locally advanced pancreatic cancer. In a recent ECOG-sponsored clinical trial, they turned to radiation to learn whether it might make gemcitabine an even more effective option for people with this type of cancer.

Nearly 75 people took part in the clinical trial. Approximately half received gemcitabine for six weeks. The other half received gemcitabine for six weeks plus radiation, given five days a week for six weeks.

Six months after the treatments were completed, there did not appear to be a difference between the two groups in

terms of how many people survived. However, 12 months after treatment, 50 percent of those in the group that received radiation plus gemcitabine were still alive, compared with about 30 percent of those in the group that received gemcitabine alone.

Eighteen months after treatment, about 30 percent of those in the radiation-plus-gemcitabine group survived, compared with about 10 percent of those in the gemcitabine-alone group. This trend was seen 24 months after treatment as well.

According to researchers, the results from this and other recent clinical trials suggest that people with locally advanced pancreatic cancer should consider beginning treatment with chemotherapy and continue taking chemotherapy for three or four months. Then, if their cancer has not spread from the pancreas to other parts of the body (that is, become metastatic), they should consider undergoing radiation treatments along with their chemotherapy.

Further study of this combined treatment approach is needed to learn which people with pancreatic cancer would benefit most from it. Researchers say that the clinical trial did confirm the value of including radiation in the treatment of locally advanced pancreatic cancer.

OXALIPLATIN IN COMBINATION TREATMENT FOR METASTATIC PANCREATIC CANCER

For nearly 10 years, gemcitabine has been the standard first-line (initial) treatment for people with metastatic pancreatic cancer that cannot be treated with surgery. But when the cancer no longer responds to gemcitabine, other options must be considered as second-line treatments. Doctors have disagreed on what is the best second-line treatment for pancreatic cancer. In the CONKO-003 clinical trial, two combination treatments were studied in approximately 160 people who had metastatic pancreatic cancer that no longer responded to gemcitabine.

About 75 patients were treated with OFF, a combination of three anti-cancer drugs: oxaliplatin (Eloxatin), folinic acid, and 5-fluorouracil (5-FU). The others were treated with FF, which consists of just the two drugs folinic acid and 5-FU.

People in the OFF group went longer before their cancer began to grow again compared with those in the FF group (13 weeks versus nine weeks). Those in the OFF group also survived twice as long as those in the FF group (26 weeks versus 13 weeks).

Even though this clinical trial included a small number of participants, researchers are encouraged by the results of the three-drug OFF combination.

BEVACIZUMAB IN COMBINATION TREATMENT FOR METASTATIC PANCREATIC CANCER

Another study, known as the AVITA clinical trial, focused on the targeted treatment bevacizumab (Avastin) in people with metastatic pancreatic cancer. Bevacizumab has been approved by the U.S. Food and Drug Administration (FDA) for use with chemotherapy in people who have metastatic colorectal, lung, or breast cancer. It has increased survival for adults with metastatic colorectal cancer, and researchers hoped that it could offer the same benefit to adults with metastatic pancreatic cancer.

More than 600 people with metastatic pancreatic cancer took part in AVITA. None of the participants had been previously treated with chemotherapy. About half of the group received a combination of erlotinib and gemcitabine, which has been shown previously to increase survival in those with metastatic pancreatic cancer. The other half received these two medications plus bevacizumab.

The three-drug treatment including bevacizumab did not improve survival beyond that achieved with gemcitabine plus erlotinib. Although this clinical trial did not produce a significantly better way to treat people with metastatic pancreatic cancer, it did confirm the results of previous studies of erlotinib and gemcitabine.

Liver Cancer

SORAFENIB FOR METASTATIC LIVER CANCER

In November 2007, the FDA approved the targeted treatment sorafenib (Nexavar) for hepatocellular carcinoma—the most common type of liver cancer—that cannot be removed surgically. The approval was based on a clinical trial known as SHARP, which included more than 600 people in the Americas, Europe, Australia, and New Zealand. The SHARP trial showed that sorafenib increased survival for people with metastatic liver cancer. It's the first medication to do so.

The results of the SHARP trial are supported by the findings of another clinical trial conducted by researchers at the National Taiwan University Hospital in Taipei. Metastatic liver cancer is much more common and more severe in Asian countries, so the Taiwanese researchers studied sorafenib in nearly 225 people with metastatic hepatocellular carcinoma who had not received prior chemotherapy. Two thirds of the patients in their clinical trial received sorafenib, and the other third received a placebo (a look-alike medication containing no active ingredient).

Sorafenib improved survival by almost 50 percent: on average, those treated with sorafenib survived more than six months after treatment, whereas those who received a placebo survived just over four months. In addition, sorafenib lengthened the amount of time patients went without their cancer growing. The tumor shrank or did not grow in 35 percent of those treated with sorafenib, compared with about 15 percent of those taking a placebo.

These positive results confirmed the survival advantage of



sorafenib. What makes these findings more impressive is the fact that people in the Taiwanese clinical trial were in poorer health and had more metastases than the people who participated in the SHARP clinical trial.

Stomach Cancer

CHEMOTHERAPY FOR METASTATIC STOMACH CANCER

In the search for more effective treatments for people with metastatic stomach cancer, several combinations of different chemotherapies have been studied. One promising treatment plan, known as iceMFP, was studied by researchers from the Asan Medical Center in Seoul, South Korea.

More than 500 people with metastatic stomach cancer took part in a clinical trial of this new chemotherapy plan. IceMFP consists of cisplatin (Platinol and others) and mitomycin (Mutamycin and others) given early on in treatment, plus doxifluridine and cisplatin given over a longer term. (Doxifluridine is not approved by the FDA for use in the United States.)

Approximately half of the people in the clinical trial were treated with iceMFP, and the others were treated with mitomycin and doxifluridine only. All of these people also had surgery to remove their tumor. All of the medications were placed directly into patients' abdomens using an approach called intraperitoneal chemotherapy. In this procedure, anti-cancer drugs are put into the abdomen through a thin tube. The surgeon makes a small incision to insert the tube. The idea behind this type of treatment is that it places a higher concentration of the medications near the tumor, more than can be delivered by injecting them into the bloodstream.

About three and a half years after treatment, more people in the group treated with iceMFP had not experienced a return of their cancer, compared with those in the group that received only mitomycin and doxifluridine (60 percent versus

50 percent). Also, more than 70 percent of those treated with iceMFP survived, compared with nearly 60 percent of those in the mitomycin-doxifluridine group.

Further studies of this encouraging treatment approach are needed to confirm these early results.

SORAFENIB PLUS CHEMOTHERAPY FOR METASTATIC STOMACH CANCER

Another promising treatment option for people with metastatic stomach cancer is being studied in an ECOG-sponsored clinical trial known as E5203. In this clinical trial, a combination of a newer medication with two standard anti-cancer drugs was given to 44 people with metastatic or locally advanced stomach cancer that could not be treated with surgery.

Because sorafenib has shrunk kidney and liver tumors in many people who have already tried other treatments that did not work, researchers hoped that it might be able to do the same thing for people with stomach tumors that have resisted treatment. Adding sorafenib to two standard medications for stomach cancer—docetaxel (Taxotere) and cisplatin—shrank tumors in many of the clinical trial participants.

Tumors shrank significantly in about 40 percent of the people treated with the three-drug combination of sorafenib, docetaxel, and cisplatin. By comparison, they shrank significantly in only 25 percent of those who had received only the standard treatment of docetaxel and cisplatin.

Researchers found these results so encouraging that a larger clinical trial of this chemotherapy combination is likely.

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.