



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

Kidney Cancer

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Nearly 52,000 Americans are diagnosed with kidney cancer each year. African-Americans have a slightly higher rate of kidney cancer than whites. A family history of kidney cancer, high blood pressure, smoking, obesity, and kidney disease can all raise the risk of getting this type of cancer. It's about twice as common in men as in women. This year, researchers have reported a number of important steps forward in the fight against kidney cancer.

Advanced Kidney Cancer

BEVACIZUMAB (AVASTIN) WITH INTERFERON ALFA (INTRON A, ROFERON-A)

In a clinical trial conducted by French researchers at more than 100 centers in nearly 20 countries, two well-known drugs were combined and given to patients with **metastatic** kidney cancer. One of the drugs was interferon alfa (Intron A, Roferon-A), which belongs to a class of drugs called **cytokines**. These drugs increase the body's natural ability to fight cancer and help shrink cancer that has spread beyond its original site. The other drug was bevacizumab (Avastin), which belongs to a newer class of medications called **targeted treatments**. Rather than killing both healthy and unhealthy cells, as chemotherapy does, targeted treatments primarily attack cancer cells, sparing healthy tissues and causing less severe side effects. In 2004, the U.S. Food and Drug Administration (FDA) approved bevacizumab for **first-line** treatment of advanced colorectal cancer.

The study included more than 600 patients who had surgery to remove a kidney. More than 300 patients took interferon alfa plus bevacizumab for one year. The others received interferon alfa plus a **placebo** (an inactive substance).

The overall response rate (a measure of a treatment's ability to slow or stop the growth of cancer) was better in the patients who received the combination of interferon alfa and

What's New, What's Important

- Combining interferon alfa (Intron A, Roferon-A) and bevacizumab (Avastin) may offer an effective alternative to current treatments for patients with advanced kidney cancer.
- In people with advanced kidney cancer, sorafenib (Nexavar) seems to prolong the time it takes for their cancer to start growing.
- Sunitinib (Sutent) is the new standard for first-line treatment of advanced kidney cancer. Researchers can use certain risk factors to help predict the length of time until the cancer grows with this drug.
- A new anti-cancer drug called volociximab may help people with metastatic kidney cancer go longer without their cancer growing.
- Early clinical trial results show that pazopanib, a new drug that targets specific areas of cancer cells while sparing healthy tissues, may be useful against advanced kidney cancer.
- The combination of pegylated glutaminase and norleucine—substances that reduce the levels of a compound which tumors seem to thrive on—may prove to be useful for treating people with kidney cancers that resist other options.

bevacizumab than in those who did not (31 percent versus 13 percent). In the group that received the combination of drugs, it took 10 months before the cancer started growing again. It took only five months for the cancer to start growing again in the group that received interferon alfa and a placebo.

Further clinical trials involving interferon, bevacizumab, and others, alone and in combination, are being conducted to find the safest and most effective treatment.

SORAFENIB (NEXAVAR)

In December 2005, the FDA approved sorafenib (Nexavar) for treatment of advanced kidney cancer. Studies have shown

that the drug shrinks kidney tumors in many people who have already tried other treatments that did not work. According to the final results of a new clinical trial, sorafenib also seems to prolong the time it takes for patients' cancer to start growing again.

Researchers from nearly 20 countries reported the final results of the TARGET clinical trial, which included more than 900 people with advanced kidney cancer. All patients had received one previous type of treatment that was not effective. Half of the people received sorafenib for almost a year (40 weeks), and the other half received a placebo.

People who were treated with sorafenib showed an improvement in the average time they went without their cancer growing, compared with those who received a placebo (five-and-a-half months versus nearly three months). Researchers were so impressed with the results that more than 200 people in the placebo group were switched to treatment with sorafenib. People who were treated with sorafenib lived longer after the start of treatment than did those who received the placebo: nearly 18 months versus a little longer than 15 months.

Sorafenib helps stop cancer by blocking **receptors** for **vascular endothelial growth factor (VEGF)** and platelet-derived growth factor (PDGF)—substances that play a critical role in the growth of blood vessels that feed cancer tumors. Doctors may use levels of VEGF to predict how a patient will respond to treatment. In the TARGET clinical trial, for instance, sorafenib seemed to be a bit more effective in people who had high blood VEGF levels at the start of treatment.



SUNITINIB (SUTENT)

Last year, preliminary findings from a large international clinical trial showed that sunitinib (Sutent) appeared to be better than interferon alfa as a first treatment for advanced kidney cancer. Updated results reported by researchers at Memorial Sloan-Kettering Cancer Center (MSKCC) in New York City confirm these early findings. The New York researchers concluded that sunitinib is the new standard for first-line treatment of metastatic renal cell cancer, a form of kidney cancer.

This clinical trial—the first of its kind to study sunitinib as a first-line treatment for advanced kidney cancer—involved 750 people. Most of them had been treated with surgery to remove their original kidney tumor, but none had received any other treatment. Half of the clinical trial participants were given the standard drug interferon alfa. The other half were given sunitinib, which is an oral drug that works by cutting off the blood supply of cancer cells and blocking their ability to grow.

More than 30 percent of the people treated with sunitinib responded to the drug. This response lasted for an average of 11 months. In contrast, only 6 percent responded to treatment with interferon alfa, a response that lasted an average of five months.

Risk factors, including the number of **metastases** and time from diagnosis to treatment, have been used for years to predict results in people being treated for kidney cancer with cytokines, of which interferon is one. Now that sunitinib has essentially replaced cytokines for first-line treatment of kidney cancer, researchers wanted to know whether these risk factors can also predict the outcome of newer targeted drugs like sunitinib.

The researchers at MSKCC found that the number of risk factors patients had did indeed predict how long it would take their cancer to grow when taking sunitinib. When patients were grouped using the risk factors, the time until the cancer grew was about 15 months for those with no risk factors, about 11 months for those with one risk factor, and eight months for those with two or more risk factors.

On the Horizon

VOLOCIXIMAB

Researchers from medical centers in the United States and the United Kingdom have studied a new anti-cancer drug called volociximab and are encouraged by the early results.

The 40 people enrolled in this clinical trial had metastatic kidney cancer. Nearly half of them had received at least two other treatments before joining this study. Also, 38 of the patients had had surgery to remove a kidney. They received volociximab **intravenously** every two weeks for up to two years.

In 31 patients, the cancer did not grow. In one person the cancer even shrank significantly. Six months after treatment, nearly 80 percent of the people who took part in the clinical trial were still alive. More than two years after treatment, nearly 70 percent were still alive. The most frequent side effect of treatment with volociximab was mild tiredness (experienced by about 65 percent of patients on the drug). Higher doses of this promising drug are being tested as well.

PAZOPANIB

It's certainly important to continue the search for new kidney cancer treatments. Surgery is an effective treatment for some patients with early-**stage** disease, but many others will have a recurrence (return of cancer) after surgery. When first diagnosed, many patients already have advanced kidney cancer. And because kidney cancer generally resists standard chemotherapy, new treatments are needed.

Researchers are studying a new drug called pazopanib for use in many different tumor types, including kidney and ovarian cancers. A targeted treatment, pazopanib helps stop cancer by blocking substances called growth factors that promote the growth and division of tumor cells.

People with advanced kidney cancer who had not received any

treatment or had not responded to an earlier treatment took part in a clinical trial. For 12 weeks, they took pazopanib once a day. Early findings showed that tumors shrank in about 25 percent of patients; in about 45 percent of the patients, the tumors neither shrank nor grew.

PEGYLATED GLUTAMINASE AND NORLEUCINE FOR ADVANCED TUMORS

A better understanding of how tumor cells grow has helped researchers develop new drugs and combinations of drugs that target the inner workings of different types of cancer. Such an approach is meant to make the treatments go directly to cancer cells before they can multiply into large tumors.

One such advance is the partnering of two similar substances for treating advanced tumors that do not respond to first treatments. Pegylated glutaminase and norleucine are compounds that can decrease the levels of glutamine in the body. Tumor cells thrive on glutamine, so this treatment tries to starve tumor cells to prevent them from growing. Early findings with this combination have been promising. Researchers continue to study it in people with kidney cancer as well as with other cancers that resist treatments.



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.