CANCERcare Connect®

Progress in the Treatment of Kidney Cancer

Presented by

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Find out about:

- Current treatment options
- Advances in research
- The role of clinical trials
- Ways to cope with cancer

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Help and Hope

Cancer*Care* is a national nonprofit organization that provides free support services to anyone affected by cancer: people with cancer, caregivers, children, loved ones, and the bereaved. Cancer*Care* programs—including counseling and support groups, education, financial assistance, and practical help—are provided by professional oncology social workers and are completely free of charge. Founded in 1944, Cancer*Care* provided individual help to more than 100,000 people last year and had more than 1 million unique visitors to our websites. For more information, call 1-800-813-HOPE (4673) or visit *www.cancercare.org*.

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If you are a health care professional interested in ordering free copies of this booklet for your patients, please use the online order form on our website, *www.cancercare.org*.

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Researchers have made exciting progress in the treatment of kidney cancer.

Each year, more than 54,000 people in the United States are diagnosed with kidney cancer. This type of cancer accounts for about two to three percent of adult cancers. No one knows what causes this cancer, but it usually occurs for no obvious reason and is rarely inherited. Kidney cancer is more common in men than in women and usually affects people between the ages of 50 and 70.

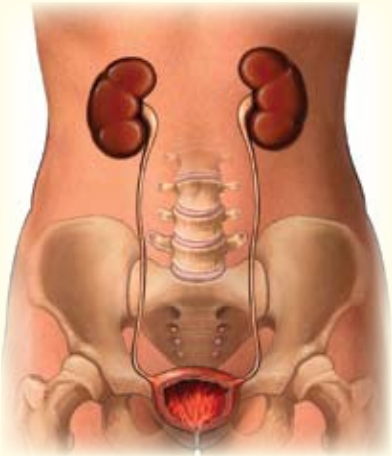
Kidney cancer tends to be "silent," causing no symptoms until it has spread beyond the kidneys. In fact, about 25 percent to 30 percent of kidney cancers have already spread to other parts of the body by the time they are diagnosed. The most common symptoms are blood in the urine, pain or pressure in the side or back, and a lump in the side or back (see box on page 5).

There are several different types of kidney cancer. Each is named based on how its cancer cells look under a microscope. The most common, called clear cell kidney cancer, makes up about 80 percent of all cases. The second most common type, called papillary, is found in about 10 percent to 12 percent of people diagnosed. Other types, which occur rarely, include chromophobe, collecting duct cell, and undifferentiated kidney cancer.

During the past 10 years, researchers have made a number of important discoveries about how kidney tumors develop. For example, researchers have found changes in the genes that promote the growth of kidney cancer. These findings have led to the development of new types of medications for treating kidney cancer.

How the Kidneys Work

The two kidneys, which are each about the size of a fist, are located on both sides of the spine, in the back of the body. The kidneys serve as the body's filtration system. Each day they remove excess salts and other substances from the roughly 200 quarts of blood that flows through them.



In the process, the kidneys produce about two quarts of urine a day, which carries waste out of the body. The kidneys also produce hormones that perform many functions, such as controlling blood pressure.

Each kidney works independently. People can live with only one kidney. If both kidneys fail to work, a dialysis machine can be used to filter the blood.

Stages of Kidney Cancer

The stage of kidney cancer is based on the size of the tumor and whether it has spread to other parts of the body. Knowing the stage of the cancer helps determine the course of treatment. Kidney cancer is divided into four stages:

Stage I The tumor is small (less than 7 centimeters) and has not spread beyond the kidney.

Stage II The tumor is larger than 7 centimeters.

Stage III The tumor has either:

- begun to grow out of the kidney, into the surrounding fat tissue, or

- spread to a nearby lymph node, or
- spread to the major blood vessels of the kidney.

Stage IV The tumor has spread into more than one lymph node, or it has spread extensively to other areas of the body, such as the lungs, bone, or brain.

Treatment Options

SURGERY

Surgery is the main treatment for kidney cancer that has not yet spread. One technique that surgeons are using more often is laparoscopy. For this technique, the surgeon makes several small incisions in the abdomen to insert a tiny light, a camera, and instruments used to view and remove the tumor. This type of surgery has been shown to be just as effective as traditional surgery and easier to recover from.

If cancer has spread beyond the kidneys, it is usually treated with surgery. A number of large studies of metastatic kidney cancer have shown that people whose tumors are removed live longer than those whose tumors are not removed.

IMMUNOTHERAPY

In another type of treatment, called immunotherapy, medications are used to increase the body's natural ability to fight cancer. Two such drugs—interleukin-2 (Proleukin) and interferon alfa (Intron A, Roferon-A)—can cause some kidney tumors to shrink by more than half. However, immunotherapy works in only 10 percent to 15 percent of patients.

Still, in about 5 percent to 10 percent of people with kidney cancer, interleukin-2 can lead to a long-term remission of metastatic cancer. In some cases the tumors even disappear, and people have lived more than 20 years after their kidney cancer diagnosis. Researchers are trying to find

Signs and Symptoms of Kidney Cancer

People with kidney cancer may experience:

- Blood in the urine
- Pain or pressure in the side or back
- A lump in the side or back
- Ankle and leg swelling
- High blood pressure
- Anemia (low levels of red blood cells)
- Weakness and fatigue
- Loss of appetite
- Weight loss
- Frequent fevers

ways to identify those patients most likely to benefit from immunotherapy. Immunotherapy is often combined with newer medications called targeted treatments.

TARGETED TREATMENTS

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. Research has shown that in general, adding these targeted treatments to immunotherapy—or using them instead of immunotherapy—nearly doubles the length of the time that the cancer is stopped from growing.

Today, three targeted treatments are approved for people with metastatic kidney cancer: sorafenib (Nexavar), sunitinib (Sutent), and temsirolimus (Torisel).

Sorafenib (Nexavar) Sorafenib was approved by the U.S. Food and Drug Administration (FDA) in 2005 to treat metastatic kidney cancer. It can be taken in pill form.

Sorafenib has been shown to shrink kidney tumors in many people who have already tried other treatments that didn't work. In a study of more than 900 people with kidney cancer, sorafenib shrank kidney tumors in about 80 percent of patients. In addition, it was very effective in slowing tumor growth. Common side effects of the medication, such as loose stools, are generally easy to treat.

Sorafenib as well as sunitinib, discussed below, takes advantage of one of the things we know about how kidney tumors grow.

Much like normal tissues, tumors need to have a blood supply. Blood vessels grow in several ways. One way is through the presence of proteins called **v**ascular **e**ndothelial **g**rowth **f**actor (VEGF) and **p**latelet **d**erived **g**rowth **f**actor (PDGF). These proteins stimulate blood vessels to grow into tumors. When tumor cells spread through the body, they release VEGF and PDGF to create new blood vessels. These blood vessels supply oxygen, minerals, and other nutrients to feed the tumor. Sorafenib works by stopping VEGF and PDGF from stimulating the growth of new blood vessels in tumors. Because normal tissues have an established blood supply, they are not affected by the medication.

Sunitinib (Sutent) In 2006, the FDA approved sunitinib for treatment of metastatic kidney cancer. Like sorafenib, sunitinib is a pill that can be taken by mouth. It is taken once a day for four weeks, followed by a two-week break, then another four-week cycle.

In clinical trials comparing sunitinib with the immunotherapy interferon, sunitinib was shown to stop the growth of metastatic kidney tumors for twice as long as interferon. Because it is so effective, sunitinib is often used as a first treatment for metastatic kidney cancer.

Researchers also have shown that sunitinib can shrink kidney tumors in many people who have already tried other treatments that did not work. For example, in one study, sunitinib was given to people who had been treated with immunotherapy first. Within about two months of taking sunitinib, more than 40 percent of these people's tumors had shrunk significantly. Tumors also shrank in another 25 percent of these patients, though not as much. This response lasted for at least a year.

The side effects of sunitinib include fatigue, mouth pain, hand and foot pain, diarrhea, and high blood pressure.

Temsirolimus (Torisel) In May 2007, the FDA approved temsirolimus for the treatment of metastatic kidney cancer. Temsirolimus works by blocking the actions of mTOR, a substance that acts like a master switch, turning on different mechanisms in cells that promote cancer growth. In clinical trials, people treated with temsirolimus were shown to live longer than those treated with interferon.

The side effects of temsirolimus are similar to those of the other targeted treatments used for metastatic kidney cancer. They include rash, mouth sores, fatigue, nausea, and sometimes low blood cell counts.

On the Horizon

Clinical trials are currently under way to study a number of important issues:

- Researchers are trying to determine which medications work best for people with kidney cancer who have not yet been treated. For example, researchers are looking for

The Importance of Clinical Trials

There's no question that clinical trials have led to advances in cancer treatment, creating a brighter future for people with cancer. Clinical trials are the standard by which we measure the worth of new treatments and quality of life as patients go through those treatments. For this reason, doctors and scientists urge patients to take part.

Your doctor can guide you in making a decision about whether a clinical trial is right for you. Here are a few things you should know:

- Often, patients who take part in clinical trials gain access to and benefit from new treatments.
- Before you participate in a trial, you will be fully informed as to the risks and benefits of the trial.
- No patient receives a placebo (a look alike treatment with no active ingredient) if there is a standard treatment available for the disease. Most trials are designed to test a new treatment against a standard treatment to find out whether the new treatment has any added benefit.
- You can stop taking part in a clinical trial at any time for any reason.

ways to identify people who are most likely to benefit from treatment with interleukin-2. Other clinical trials are trying to identify genetic changes in tumors that might help predict which patients will respond to a new medication, not yet approved by the FDA, called everolimus, which blocks the actions of mTOR.

- Several large clinical trials are testing combinations of medications to treat kidney cancer. One of the largest is called the BeST trial, comparing various combinations

of **Be**vacizumab (Avastin), **S**orafenib, and **T**emsirolimus. The hope is that researchers will be able to identify a combination that is more effective than one drug alone. Bevacizumab is an FDA-approved targeted treatment for metastatic colon (or rectal), lung, and breast cancers. It is being studied alone and with other medications for people with metastatic kidney cancer.

- Researchers are trying to find the best time to start kidney cancer treatment. While beginning treatment right after diagnosis is best for some people, waiting might be more appropriate for others.

- A number of clinical trials are trying to understand what happens when a patient's treatment stops working against his or her kidney cancer. To that end, researchers are studying the new medications axitinib, which blocks VEGF, and everolimus in people whose cancer has stopped responding to treatment with sorafenib and sunitinib. Like everolimus, axitinib has not yet been approved by the FDA.
- Researchers are testing the use of targeted treatments in people who have just had surgery for kidney cancer. The hope is that treatment with sunitinib and sorafenib after surgery might prevent a recurrence of kidney cancer.

Your Support Team

When you are diagnosed with kidney cancer, you're faced with a series of choices that will have a major effect on your life, and maybe you're not sure where to turn. But help is available. Your health care team, family members, and friends will likely be an

invaluable source of support at this time. You can also turn to these resources:

Oncology social workers provide emotional support for people with cancer and their loved ones. These professionals can help you cope with the challenges of a kidney cancer diagnosis and guide you to resources. Cancer*Care*® offers free counseling from oncology social workers on staff who understand the challenges faced by people with kidney cancer. We can work with you one-on-one to develop strategies for coping.

Support groups Many support groups are available for people with kidney cancer. Support groups provide a caring environment in which you can share your concerns with others in similar circumstances. Support group members come together to help one another, providing insights and suggestions on ways to cope. At Cancer*Care*, people living with cancer, caregivers, and loved ones can take part in support groups in person, online, or on the telephone.

Financial assistance is offered by a number of organizations, including Cancer*Care*, for cancer-related costs such as transportation to treatment, child care, or help needed around the home. Cancer*Care* also provides referrals to other organizations that offer assistance.

To learn more about how Cancer***Care*** helps, call us at 1-800-813-HOPE (4673) or visit www.cancercare.org.

Frequently Asked Questions

Q Is bevacizumab ever combined with sunitinib or sorafenib as a treatment for kidney cancer?

A Yes. Although bevacizumab is not yet approved by the FDA for kidney cancer, it is being tested in combination with sunitinib and sorafenib in clinical trials. Combining the medications has to be done very carefully, however, because some of the side effects of these medications are similar and their severity may be increased when they are taken together. For example, all of these drugs can raise blood pressure, so blood pressure would have to be checked frequently in someone who takes both drugs at the same time. Until the results of clinical trials are available, patients should not be taking more than one of these targeted treatments at a time.

Q Is sorafenib effective in tumors that contain papillary cancer cells, or is it only helpful against tumors with clear cells?

A Sorafenib has been tested mainly in people with clear cell kidney tumors, the most common type. But some preliminary research suggests that the medication also may be effective in treating papillary tumors, the second most common type of kidney cancer. The FDA has approved sorafenib for treatment of all types of metastatic kidney cancer, so the drug is an option for people with papillary tumors. However, more research is warranted and clinical trials are often the best option for those with non-clear cell kidney cancer.

Q I was taking sorafenib, and my doctor decided to lower my dose because I was having trouble coping with the side effects of the drug. Is a lower dose of sorafenib as effective as the original, full dose?

A At this time, we don't know. Lower doses may be just as effective as higher doses, but this has never really been tested in a clinical trial. That's why doctors try to start patients on the recommended dose and maintain that level.

Q Can people be treated with radiation while they are taking one of the new targeted treatments?

A Right now, we don't have any research to show whether it would be safe to undergo radiation while taking one of these new medications. However, studies designed to test the safety and effectiveness of combining radiation with targeted treatment are now under way. Your doctor might be able to give you information about whether such a clinical trial could be right for you.

Q My husband has a small kidney tumor—about two to three centimeters. We know he needs surgery, but what happens after that?

A Generally, surgery is the only treatment required for tumors that small. Your doctor will discuss the type of procedure he or she recommends, but chances are the tumor will be removed with laparoscopy, in which a small opening is made in the abdomen. The surgeon will want to see your husband after the operation to make sure he is recovering well. After that, your medical oncologist will follow up with periodic blood tests to check kidney function, as well as chest x-rays and scans of the abdomen and chest to make sure the kidney tumor has not come back. You can expect your husband to have a checkup every three months for the first year, every four months for the second to fifth year, and yearly after that.

Because there are currently no medicines that are proven to prevent kidney cancer from coming back after surgery, it's important to continue these screening tests.

Q I'm going to be treated with interleukin-2 for metastatic kidney cancer. My doctor says I'll have to be hospitalized during treatment. Why is that?

A Interleukin-2 is the most powerful medication currently used to treat metastatic kidney cancer. High doses of interleukin-2 cause severe side effects in about 50 percent to 60 percent of people. These effects include low blood pressure, excess fluid in the lungs, kidney damage, heart attacks, bleeding, chills, and fever. For that reason, people treated with interleukin-2 need to be watched carefully in the hospital, for as long as 10 days. Only hospitals and cancer centers experienced in treating people with high-dose interleukin-2 should recommend (or advise against) its use.

Some doctors and hospitals use lower doses of interleukin-2, which have fewer and milder side effects. But lower doses do not seem to be as effective in treating kidney cancer as high doses of the drug.

Q My doctor believes—and I agree—that sunitinib is right for me. But my health insurance doesn't cover the cost. How can I get some financial assistance?

A For many people, expensive cancer medicines pose a financial challenge. Fortunately, there are more than 475 programs that help those who qualify to get medications for free or at a low cost. For more information, contact the Partnership for Prescription Assistance, listed among the resources on page 16. Cancer*Care*® also provides financial help to eligible families for cancer-related costs such as transportation to treatment, child care, or help needed around the home. Contact us at 1-800-813-HOPE (4673) to learn more.

Glossary

anemia A condition that can cause fatigue, shortness of breath, and other symptoms due to low levels of red blood cells.

dialysis A process in which a person's blood is run through a machine that filters impurities. Dialysis is used in people whose kidneys are unable to filter blood.

immunotherapy The use of medications that increase the body's natural ability to fight cancer.

laparoscopy A surgical procedure in which several small incisions in the abdomen are made to insert a tiny light, a camera, and instruments that view and remove the tumor.

lymph node A small "filtering station" that removes waste and fluids and helps fight infections. When invaded by cancer cells, lymph nodes are a jumping-off point from which tumors can spread throughout the body.

metastatic Cancer that has spread from its original site (in this case, the kidney) to nearby lymph nodes or more distant parts of the body.

mTOR A substance that acts like a master switch, turning on a number of different reactions in cells that promote cancer growth.

PDGF This substance, "**p**latelet **d**erived **g**rowth **f**actor," plays an important role in promoting the growth of blood vessels that feed tumors.

remission When a cancer responds to treatment or is under control. In a complete remission, none of the signs and symptoms of the cancer can be detected through any available tests. In a partial remission, the cancer shrinks but does not completely disappear. Remissions can last from several weeks to many years. If the cancer returns, another remission can occur with further treatment.

response A medication's effect on a tumor—either shrinking it or stopping its growth.

VEGF This substance, "**v**ascular **e**ndothelial **g**rowth **f**actor," stimulates blood vessels to grow in tumors. When tumor cells spread throughout the body, they release VEGF and create new blood vessels that supply the tumor cells with oxygen, minerals, and other nutrients.

Resources

CancerCare®
1-800-813-4673
www.cancercare.org

American Cancer Society
1-800-227-2345
www.cancer.org

Cancer.Net
(Patient website of the American Society of Clinical Oncology)
www.cancer.net

Kidney Cancer Association
1-800-516-8051
www.kidneycancer.org

National Cancer Institute
Cancer Information Service
1-800-422-6237
www.cancer.gov

National Coalition for Cancer Survivorship
1-888-650-9127
www.canceradvocacy.org

Partnership for Prescription Assistance
1-888-477-2669
www.pparx.org

The Wellness Community
1-888-793-9355
www.thewellnesscommunity.org

To find out about clinical trials:

Coalition of Cancer Cooperative Groups
www.CancerTrialsHelp.org

National Cancer Institute
www.cancer.gov/clinicaltrials

The information presented in this patient booklet is provided for your general information only. It is not intended as medical advice and should not be relied upon as a substitute for consultations with qualified health professionals who are aware of your specific situation. We encourage you to take information and questions back to your individual health care provider as a way of creating a dialogue and partnership about your cancer and your treatment.

All people depicted in the photographs in this booklet are models and are used for illustrative purposes only.

This booklet was edited and produced by Elsevier Oncology.

With Cancer*Care*, the difference comes from:

- Professional oncology social workers
- Free counseling for you and your loved ones
- Education and practical help
- Up-to-date information

Our trusted team of professionally trained oncology social workers provides free counseling, education and practical help for you and your loved ones.

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