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TREATMENT UPDATE
Kidney Cancer

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Researchers have made exciting steps forward in the number of treatment options for advanced kidney cancer.

Each year, nearly 65,000 people in the United States are diagnosed with kidney cancer. This type of cancer accounts for about 3 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.

There are several different types of kidney cancer. Each is named based on how its cancer cells look under a microscope. The most common type, called clear cell kidney cancer, makes up about 70 percent of all cases. The second most common type, called papillary kidney cancer, is found in about 15 percent of cases. Other types, which occur rarely, include chromophobe, collecting duct cell, and unclassified 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.



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 (metastasized) and formed tumors in other parts of the body, the original tumor in the kidney is often still 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.



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

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 tumor metastases (tumors in other parts of the body) 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. (A remission is when signs and symptoms of cancer have disappeared.) In some cases, the tumors even disappear and people have lived more than 20 years

after their cancer diagnosis. Researchers are trying to find ways to identify those patients most likely to benefit from immunotherapy.

Targeted Treatments

Targeted treatments are more likely than chemotherapy to spare healthy tissues and usually cause fewer side effects. Targeted treatments focus on specific molecules and cell mechanisms thought to be important for cancer cell survival and growth. Some of these drugs block tumor cells' ability to grow. Other drugs disrupt the flow of blood to cancer cells, which the cells need in order to live. Research has shown that, in general, targeted drugs increase the length of time that the cancer is stopped from growing.

Seven targeted treatments have been approved by the U.S. Food and Drug Administration (FDA) for people with metastatic kidney cancer: sorafenib (Nexavar), sunitinib (Sutent), temsirolimus (Torisel), everolimus (Afinitor), bevacizumab (Avastin), pazopanib (Votrient), and axitinib (Inlyta).

Sorafenib (Nexavar) Sorafenib was approved by the FDA in December 2005. It is taken in pill form, usually twice a day. Sorafenib has been shown to shrink kidney tumors in many people for whom other treatments 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 effective in slowing tumor growth. Common side effects of the medication include calluses on the hands and feet, diarrhea, high blood pressure, loss of taste, fatigue, and decreased thyroid function.

Sorafenib, as well as the drug sunitinib, takes advantage of



what researchers have learned 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 vascular endothelial growth factor (VEGF) and platelet-derived growth factor (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. Sunitinib works by stopping VEGF and PDGF from stimulating the growth of new blood vessels in tumors. Because healthy tissues have an established blood supply, they are less affected by the medication.

Sunitinib (Sutent) In January 2006, the FDA approved sunitinib for the treatment of metastatic kidney cancer. Like

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, about 2¾ inches) 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.

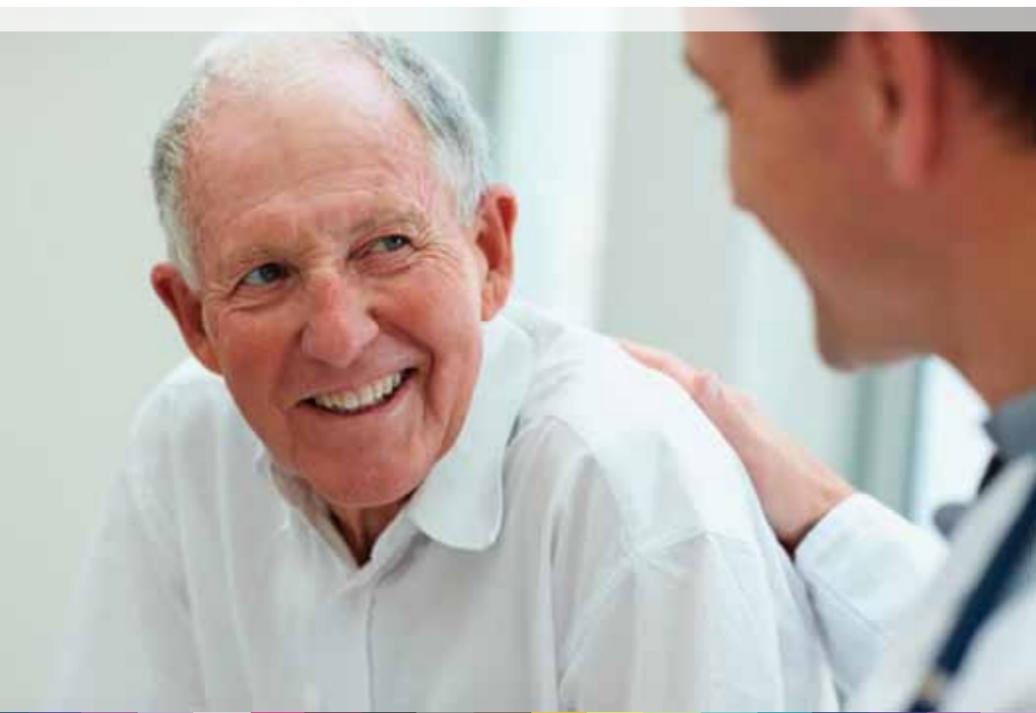
sorafenib, sunitinib is a pill that can be taken by mouth. It is taken once a day for four weeks, followed by a two-week break. The cycle is repeated for as long as the doctor prescribes.

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 cancer metastases 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, calluses on the hands and feet, diarrhea, high blood pressure, and decreased thyroid function.

Temsirolimus (Torisel) In May 2007, the FDA approved temsirolimus for the treatment of metastatic kidney cancer. Temsirolimus works by blocking the actions of mTOR, which



is a protein that acts like a master switch, “turning on” different mechanisms in cells that promote cancer growth. In clinical trials, people treated with temsirolimus, and those with higher risk metastatic kidney cancer, were shown to live longer than those treated with interferon.

This medication is given intravenously (in a blood vein). The side effects of temsirolimus include rash, mouth sores, fatigue, breathing problems, increased risk for infection, diarrhea, high blood sugar, high cholesterol, and sometimes low blood cell counts.

Everolimus (Afinitor) Like temsirolimus, everolimus is an mTOR inhibitor. A clinical trial showed that after taking everolimus for advanced kidney cancer, it was nearly five months before patients’ tumors began to grow again. Side effects include rash, mouth sores, fatigue, breathing problems, increased risk for infection, diarrhea, high blood sugar, high cholesterol, and sometimes low blood cell counts.

Bevacizumab (Avastin) In July 2009, the FDA approved the use of bevacizumab in metastatic kidney cancer when used with interferon. Bevacizumab (which is also prescribed for colon, lung, and brain cancers) works by preventing the growth of new blood vessels that feed tumors. Interferon stimulates the body’s immune system to fight cancer, but the exact way in which interferon works is not fully understood. It’s thought to have several effects on the body. It may:

- Strengthen the body’s immune system
- Reduce the ability of the cancer cells to protect themselves from the immune system
- Slow down or stop the cancer cells from dividing and growing

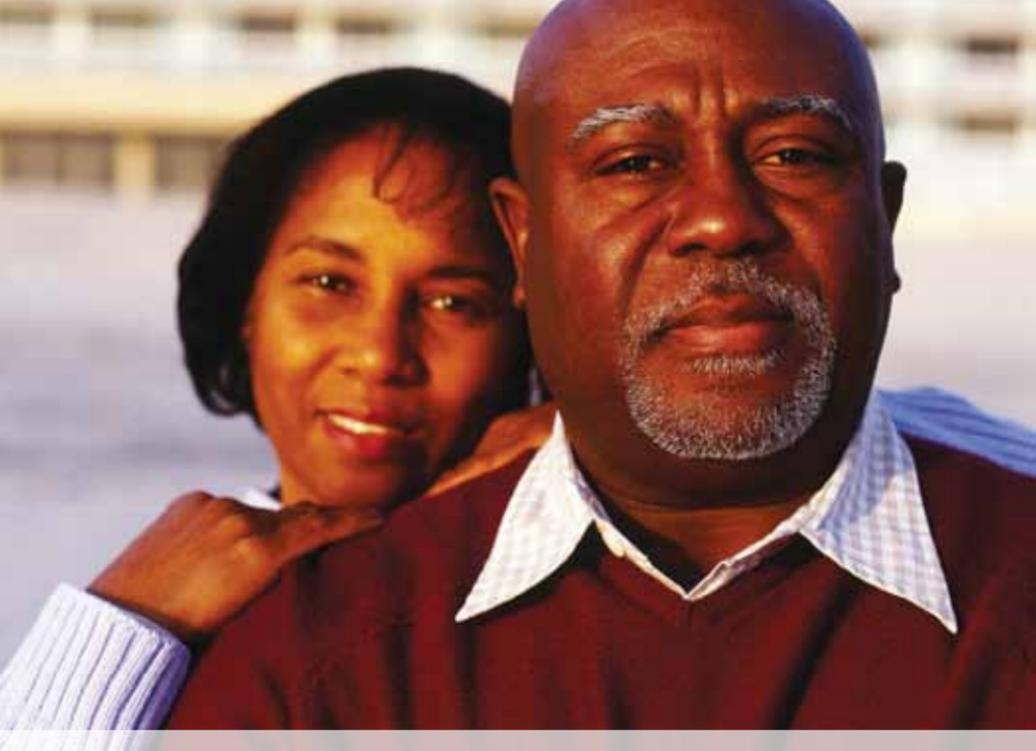
The Importance of Clinical Trials

Clinical trials are the standard by which we measure the worth of new treatments and their effect on the quality of life as patients go through those treatments. For this reason, doctors and researchers urge people with cancer to take part in clinical trials.

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, people who take part in clinical trials gain access to (and may be the first to benefit from) new treatments.
- Before you participate in a clinical trial, you will be fully informed about the possible risks and benefits.
- Some studies show that patients get higher quality care simply by taking part in a clinical trial, because most trials require that doctors and nurses watch patients extremely carefully, and this extra attention may be beneficial all by itself.
- You can choose to stop taking part in a clinical trial at any time for any reason—you are always in control of your voluntary participation.

Studies showed that the combination of bevacizumab and interferon increased the amount of time it takes for the cancer to start growing again by about five months compared with taking interferon alone. In people taking these two



medications together, the tumor size decreased by 30 percent compared with 12 percent in patients taking interferon alone. However, studies also showed that people taking these two drugs were more likely to have side effects, including a slight increased risk of bleeding, high blood pressure, fatigue, and loss of the body's vital proteins through the urine.

Bevacizumab is given intravenously. Interferon is given as an injection, usually in the thigh or abdomen.

Pazopanib (Votrient) was approved by the FDA in October 2009 for metastatic kidney cancer. This medication, which comes in pill form and is taken once a day, interferes with the growth of new blood vessels needed by solid tumors to grow and survive. Like sunitinib, sorafenib, and bevacizumab, pazopanib stops angiogenesis—the process of making new blood vessels. Because a tumor needs the nutrients delivered

by blood vessels to grow and spread, the goal of anti-angiogenesis treatments is to “starve” the tumor.

In a clinical trial with 435 patients taking part, the length of time before the tumor began growing again averaged 9.2 months for people who received pazopanib, compared with 4.2 months for those who did not receive the drug.

Side effects included diarrhea, high blood pressure, nausea, vomiting, fatigue, and decreased thyroid function. Because pazopanib can also cause liver irritation, regular blood tests for liver function should be performed. If not caught early, liver problems can become serious.

Axitinib (Inlyta) In January 2012, the FDA approved the use of axitinib for metastatic kidney cancer in people for whom other medications stopped working. Axitinib is an anti-angiogenesis pill that patients take twice a day. The safety and effectiveness of axitinib were studied in a clinical trial of more than 700 people whose kidney cancer had grown during or after a previous treatment. This clinical trial was designed to measure the length of time it took for kidney cancer metastases to begin growing again during and after treatment with axitinib, compared with sorafenib.

In those taking axitinib, it took nearly seven months for the cancer to begin growing again. That’s compared with nearly five months for those taking sorafenib.

Among the most common side effects of axitinib are diarrhea, high blood pressure, fatigue, calluses forming on the hands and feet, hoarse voice, and decreased thyroid function.

Researchers caution that people with high blood pressure should have it well controlled before taking axitinib.

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 you may not be 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.

Oncology social workers also 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. CancerCare 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.

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



Frequently Asked Questions

Q. What questions should I ask my doctor before I start my kidney cancer treatment?

A. Before you start treatment, work with your doctor to define the goals of treatment. Do you want treatment at any cost, or do you want to improve your quality of life as much as possible? That's an important discussion to have with your doctor. Other questions you may want to ask include:

- How can I best stay on the treatment plan?
- How does the drug work, and what side effects can I expect?
- What will be my schedule of visits?
- What other medications will I need to take?

Q. What can I do about fatigue due to kidney cancer treatments?

A. Fatigue, a common side effect of kidney cancer treatments, can be difficult to manage. Talk to your health care team to explore what can be done. Medications such as stimulants may be able to help, although they have their own side effects. Exercising regularly may help you cope with fatigue. Taking naps throughout the day can also make a difference in your energy level. It is very important to communicate with your health care team about how you feel in order to manage fatigue. The overall goal in managing fatigue is for your health care team to find a balance with treatment dosing to keep you on the treatment for the longest amount of time.

Q. I have tried all of the existing FDA-approved drugs for kidney cancer. Are there any newer drugs that I can try?

A. Talk to your doctor about enrolling in a clinical trial. You may be limited by the number of treatments you have previously received. Your doctor will be able to tell you more about clinical trial requirements and about specific kidney cancer trials that are available.

Q. I'm concerned about dehydration. What can I do to avoid it?

A. The drugs that are used to treat cancer can make you feel less likely to want to drink or eat. They can also make you feel dehydrated. For patients who have only one kidney, it is more difficult to keep a constant state of hydration. One easy tip to help you stay well hydrated is to keep liquid with you most of the time. You may want to carry a water bottle wherever you go. Be sure to stop drinking fluids early enough before you fall asleep so that you are not up all night going to the bathroom.

Resources

CancerCare

800-813-HOPE (4673)

www.cancer.org

American Cancer Society

800-227-2345

www.cancer.org

Cancer.Net

Patient information from the American Society of Clinical Oncology

www.cancer.net

Cancer Support Community

888-793-9355

www.cancersupportcommunity.org

Kidney Cancer Association

800-850-9132

www.kidneycancer.org

National Cancer Institute

800-422-6237

www.cancer.gov

National Coalition for Cancer Survivorship

877-622-7937

www.canceradvocacy.org

Partnership for Prescription Assistance

888-477-2669

www.pparx.org

TO FIND OUT ABOUT CLINICAL TRIALS

Coalition of Cancer Cooperative Groups

www.CancerTrialsHelp.org

National Cancer Institute

www.cancer.gov/clinicaltrials

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