TREATMENT UPDATE:

Kidney Cancer

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Treatment Update: Kidney Cancer

TABLE OF CONTENTS

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Each year, more than 80,000 people in the United States are diagnosed with kidney cancer. It is more common in men than in women and usually affects people between the ages of 50 and 70.

There are several types of kidney cancer, also known as renal cancer. Renal cell carcinoma accounts for about 85 to 90 percent of kidney cancers. This cancer develops within the kidney's microscopic filtering systems, the lining of tiny tubes leading to the bladder. About two-thirds of renal cell carcinomas are called "clear cell." The rest are called "non-clear cell," an umbrella term that includes less common types such as "papillary" and "chromophobe" renal cell carcinomas.

Urothelial carcinoma (sometimes called "transitional cell carcinoma") accounts for 10 to 15 percent of kidney cancers and begins in the area of the kidney where the initial collection of urine occurs.

In recent years, researchers have made a number of important discoveries about kidney cancer, including how changes in specific genes can promote tumor growth. These findings have led to the development of new treatment options.

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 and has not spread beyond the kidney.
- **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 grown into surrounding organs, such as the adrenal gland, or has spread extensively to other areas of the body, such as the lungs, bone or brain.

Treatment Options

Surgery

Surgery is the primary treatment for kidney cancer that has not spread to other parts of the body.

Depending on the stage and location of the cancer and other factors, surgery may remove the tumor or tumors along with some of the surrounding kidney tissue (known as a partial nephrectomy), or the entire kidney (known as a radical nephrectomy). The adrenal gland (the small gland that sits on top of each kidney) and fatty tissue around the kidney may also be removed.

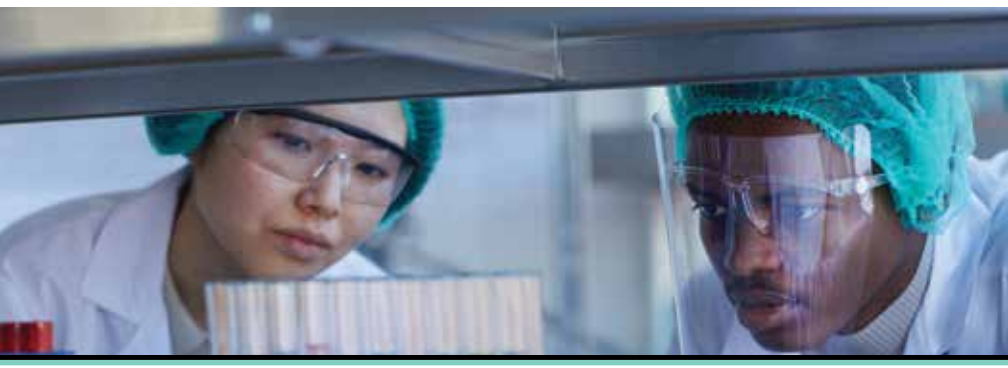
A laparoscopic approach is often used in surgery. With this approach, the surgeon makes several small incisions in the abdomen. A tiny light, camera and surgical instruments are inserted into the incision to view and remove the tumor. In many cases, laparoscopic surgery has been shown to be as effective as traditional surgery, with an easier recovery. Before deciding on an approach, discuss the risks and benefits of traditional versus laparoscopic surgery with your surgeon.

If the cancer has spread (metastasized) and formed tumors in other parts of the body, the original tumor in the kidney can sometimes still be treated with surgery, followed by other forms of treatment.

Targeted Therapy

Targeted therapies focus on specific molecules and cell mechanisms thought to be important for cancer cell survival and growth, taking advantage of what researchers have learned in recent years about how kidney tumors grow.

The targeted therapies temsirolimus (Torisel) and everolimus (Afinitor) are approved by the U.S. Food and Drug Administration (FDA) for the treatment of kidney cancer. Both of these drugs work by blocking the actions of mTOR, a protein which activates mechanisms in cells that promote cancer growth.



Some targeted therapies are designed to stop angiogenesis (blood vessel growth). Between 2005 and 2012, five anti-angiogenesis drugs were approved by the FDA for the treatment of metastatic kidney cancer:

- **Sunitinib (Sutent), pazopanib (Votrient), axitinib (Inlyta) and sorafenib (Nexavar)** work by blocking the action of proteins released by tumors which promote the formation of blood vessels, thereby "starving" the tumors. The protein pathways that are blocked include vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF).
- **Bevacizumab (Avastin)** acts by binding directly to and inactivating VEGF.

In November 2017, the FDA expanded the approval of sunitinib to include treatment for people who underwent a radical nephrectomy and are at high risk of kidney cancer recurrence.

Two targeted therapies were approved by the FDA in 2016 to treat people with advanced renal cell carcinoma who previously received anti-angiogenic therapy:

- **Cabozantinib (Cabometyx),** a drug that targets multiple tyrosine kinases (enzymes that are part of many cell functions, including growth and division). At too-high levels, these enzymes can be involved in the development of renal cell carcinoma, and blocking them may help keep cancer cells from growing.
- **Lenvatinib (Lenvima)** in combination with everolimus (Afinitor); this is the first regimen that targets both tyrosine kinases and the protein mTOR.

In March 2021, the FDA approved tivozanib (Fotivda), a kinase inhibitor, for people with relapsed (recurred) or refractory (not responding to treatment) advanced renal cell carcinoma following two or more prior therapies.

Immunotherapy

Our immune system works constantly to keep us healthy. It recognizes and fights against danger, such as infections, viruses and growing cancer cells. In general terms, immunotherapy uses our own immune system as a treatment against cancer.

In November 2015, the FDA approved the immunotherapy drug nivolumab (Opdivo) to treat people whose metastatic kidney cancer progressed while on an anti-angiogenic therapy (treatments designed to prevent the development of blood vessels). Nivolumab is a type of immune checkpoint inhibitor. It works by interfering with a molecular "brake" known as PD-1 that prevents the body's immune system from attacking cancer cells. Cancer cells take advantage of PD-1 by expressing another molecule called PD-L1, which directly interacts with PD-1 to protect cancer cells from the body's immune system.

In April 2018, the FDA approved the combination of nivolumab and another immunotherapy drug, ipilimumab (Yervoy), as an initial treatment for certain people with advanced kidney cancer. Ipilimumab is thought to help the immune system destroy cancer cells by blocking the action of CTLA-4, a protein that normally helps keep immune system cells (called T-cells) in check.

Chemotherapy

Chemotherapy is not a standard treatment for most kidney cancers, as kidney cancer cells are usually resistant to chemotherapy drugs. Some drugs, such as vinblastine, floxuridine, 5-fluorouracil (5-FU), capecitabine and gemcitabine have been shown to help a small percentage of people with renal cell carcinomas. In these cases, chemotherapy is often used only after targeted therapy and/or immunotherapy has already been tried. However, chemotherapy is often the first and best option for some very rare kidney cancers such as renal medullary carcinoma, collecting duct carcinoma, Wilms tumors and malignant rhabdoid tumors.

Combination Treatment Approaches

Since 2019, four combination treatment approaches for kidney cancer have been approved by the FDA:

- A combination of the targeted therapy axitinib and the immunotherapy pembrolizumab (Keytruda) was approved in April 2019.
- Axitinib (Inlyta) in combination with the immunotherapy avelumab (Bavencio), was approved for the initial treatment of advanced renal cell carcinoma in May 2019.
- The immunotherapy nivolumab, in combination with the targeted therapy cabozantinib, was approved as an initial treatment for advanced renal cell carcinoma in January 2021.
- In August 2021, the targeted therapy lenvatinib plus the immunotherapy pembrolizumab was approved as an initial treatment for advanced renal cell carcinoma.

The Importance of Clinical Trials

Clinical trials are the standard by which we measure the worth of new treatments and the quality of life of patients as they receive 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 that you should know:

- Often, people who take part in clinical trials gain access to and benefit from new treatments.
- Before you participate in a clinical trial, you will be fully informed as to the risks and benefits of the trial, including any possible side effects.
- Most clinical 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.

Treatment Side Effects

All cancer treatments can cause side effects. It's important that you report any side effects that you experience to your health care team so they can help you manage them. Report them right away—don't wait for your next appointment. Doing so will improve your quality of life and allow you to stick with your treatment plan. It's important to remember that not all people being treated for kidney cancer experience all side effects, and people may experience side effects not listed here.

Side Effects of Targeted Therapy and Immunotherapy

Targeted therapies don't have the same effect on the body as does chemotherapy, but they can still cause side effects. Common side effects of targeted therapy include diarrhea, skin rashes, liver problems (such as hepatitis and elevated liver enzymes), high blood pressure and problems with blood clotting and wound healing.

Immunotherapy travels through the bloodstream, helping to prompt an immune response. Although immunotherapy drugs are generally fairly well-tolerated, certain side effects may be experienced, including those listed in the "General Side Effects" section. Rare and serious side effects include the development of an inflammation in the lungs or in the colon, causing difficulty breathing or severe diarrhea. These symptoms must be treated immediately.

Another complication of immunotherapy can be extreme fatigue. If this occurs, contact a member of your health care team immediately, so that you can receive immediate medical attention.

General Side Effects

Some side effects may occur across treatment approaches. This section provides tips and guidance on how to manage these side effects should they occur.

Managing Digestive Tract Symptoms

Nausea and vomiting

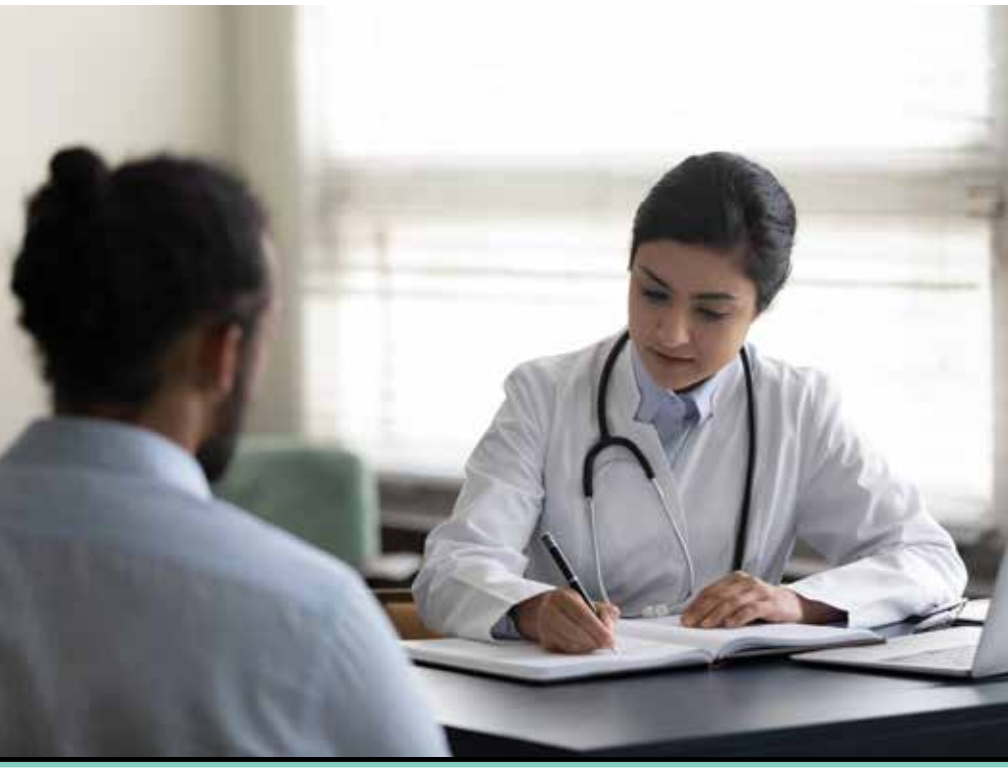
- Avoid food with strong odors, as well as overly sweet, greasy, fried or highly seasoned food.
- Eat meals that are chilled, which often makes food more easily tolerated.
- Nibble on dry crackers or toast. These bland foods are easy on the stomach.
- Having something in your stomach when you take medication may help ease nausea.

Diarrhea

- Drink plenty of water. Ask your doctor about using drinks such as Gatorade which provide electrolytes. Electrolytes are body salts that must stay in balance for cells to work properly.
- Over-the-counter medicines such as loperamide (Imodium A-D and others) and prescription drugs are available for diarrhea but should be used only if necessary. If the diarrhea is bad enough that you need medicine, contact a member of your health care team.
- Choose foods that contain soluble fiber, like beans, oat cereals and flaxseed, and high-pectin foods such as peaches, apples, oranges, bananas and apricots.
- Avoid foods high in refined sugar and those sweetened with sugar alcohols such as sorbitol and mannitol.

Loss of appetite

- Eating small meals throughout the day is an easy way to take in more protein and calories, which will help maintain your weight. Try to include protein in every meal.
- To keep from feeling full early, avoid liquids with meals or take only small sips (unless you need liquids to help swallow). Drink most of your liquids between meals.
- Keep high-calorie, high-protein snacks on hand such as hard-boiled eggs, peanut butter, cheese, ice cream, granola bars, liquid nutritional supplements, puddings, nuts, canned tuna or trail mix.
- If you are struggling to maintain your appetite, talk to your health care team about whether appetite-building medication could be right for you.



Managing Fatigue

Fatigue (extreme tiredness not helped by sleep) is one of the most common side effects of many cancer treatments. If you are taking a medication, your doctor may lower the dose of the drug, as long as it does not make the treatment less effective. If you are experiencing fatigue, talk to your doctor about whether taking a smaller dose is right for you.

There are a number of other tips for reducing fatigue:

- Take several short naps or breaks during the day.
- Take walks or do some light exercise, if possible.
- Try easier or shorter versions of the activities you enjoy.
- Ask your family or friends to help you with tasks you find difficult or tiring.

There are also prescription medications that may help, such as modafinil. Your health care team can provide guidance on whether medication is the right approach for your individual circumstances.

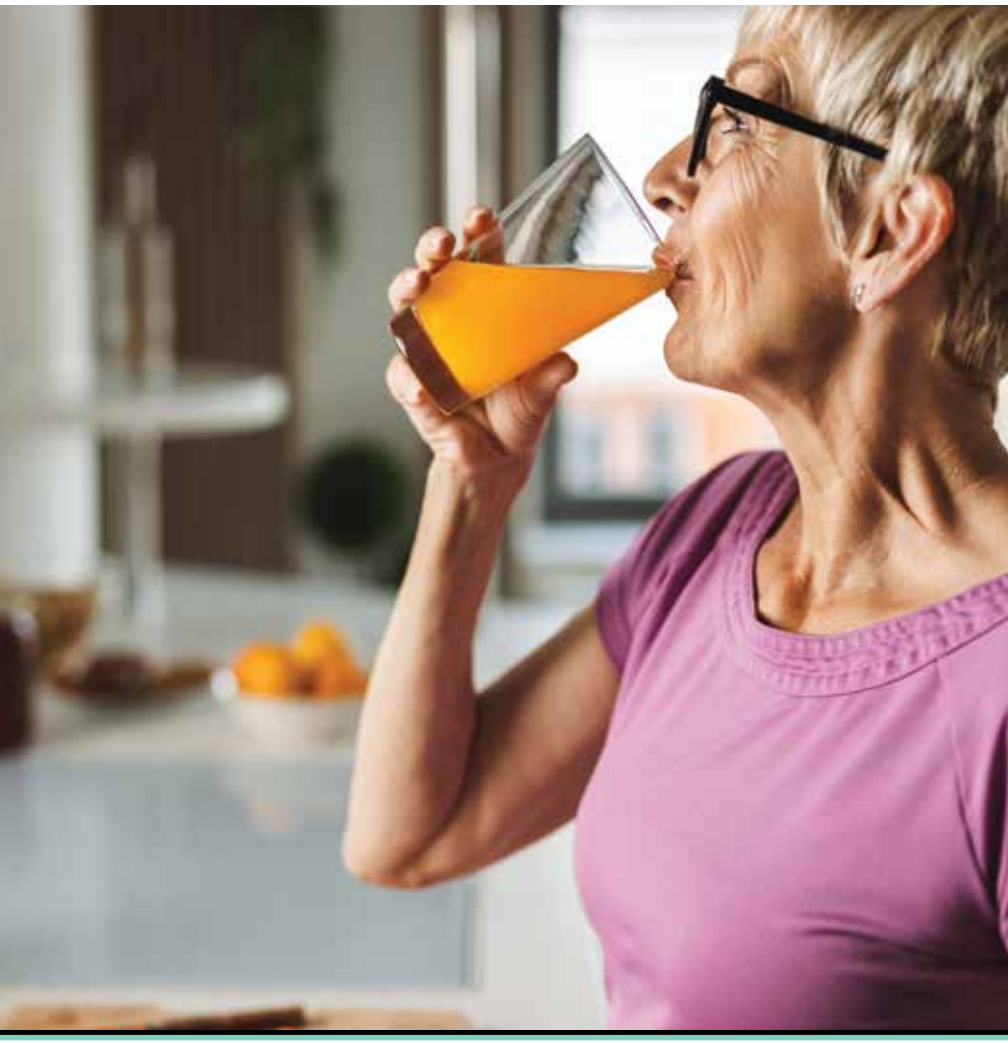
Managing Pain

There are a number of options for pain relief, including prescription and over-the-counter medications. It's important to talk to a member of your health care team before taking any over-the-counter medication to determine if it is safe and will not interfere with your treatments. Many pain medications can lead to constipation, which may make your pain worse. Your doctor can prescribe medications that help to avoid constipation.

Physical therapy, acupuncture and massage may also be of help in managing your pain. Consult with a member of your health care team before beginning any of these activities.

Managing Dehydration

The drugs that are used to treat cancer can make you feel dehydrated. Keeping a water bottle with you is one easy way to help you stay well-hydrated. Hydration can also be provided by liquids other than water, such as Gatorade, juice, soup and fruit smoothies. Be sure to stop taking in fluids early enough in the evening so that your sleep is not disrupted.



Communicating With Your Health Care Team

As you manage your kidney cancer, it's important to remember that you are a consumer of health care. The best way to make decisions about health care is to educate yourself about your diagnosis and get to know the members of your health care team, including doctors, nurses, nurse practitioners, physician assistants, dietitians, social workers and patient navigators.

Here are some tips for improving communication with your health care team:

Start a health care journal. Having a health care journal or notebook (either on paper or in a digital format) will allow you to keep all of your health information in one place. You may want to write down the names and contact information of the members of your health care team, as well as any questions for your doctor.

Prepare a list of questions. Before your next medical appointment, write down your questions and concerns. Because your doctor may have limited time, ask your most important questions first and be as specific as possible.

Bring someone with you to your appointments or have them be present during telehealth sessions. Even if you have a journal and a prepared list of questions or concerns, it's always helpful to have support during your appointments. The other person can serve as a second set of ears. They may also think of questions to ask your doctor or remember details about your symptoms or treatment that you may have forgotten.

Write down your doctor's answers. Taking notes will help you remember your doctor's responses, advice and instructions. You can also ask the person who accompanies you to take notes for you, either in your journal or on a tablet or smartphone.

Record your visit if your doctor allows it. Recording the conversation with your doctor gives you a chance to hear specific information again or share it with family members or friends.

Incorporate other health care professionals into your team. Your medical oncologist is an essential member of your health care team, but there are other health care professionals who can help you manage your diagnosis and treatment:

- Your primary care physician should be kept updated about your kidney cancer treatment and any test results.
- Urologists specialize in disorders of the kidneys and urinary tract, and are an important part of the multi-disciplinary team approach in the treatment of kidney cancer.
- Your local pharmacist is a great source of knowledge about the medications you are taking. Have all of your prescriptions filled at the same pharmacy to avoid the possibility of harmful drug interactions.
- Make sure your oncologist knows of any other medical conditions you have or any pain you are experiencing so that they can consult with your primary care physician or specialists as needed.

Remember, there is no such thing as over-communication.

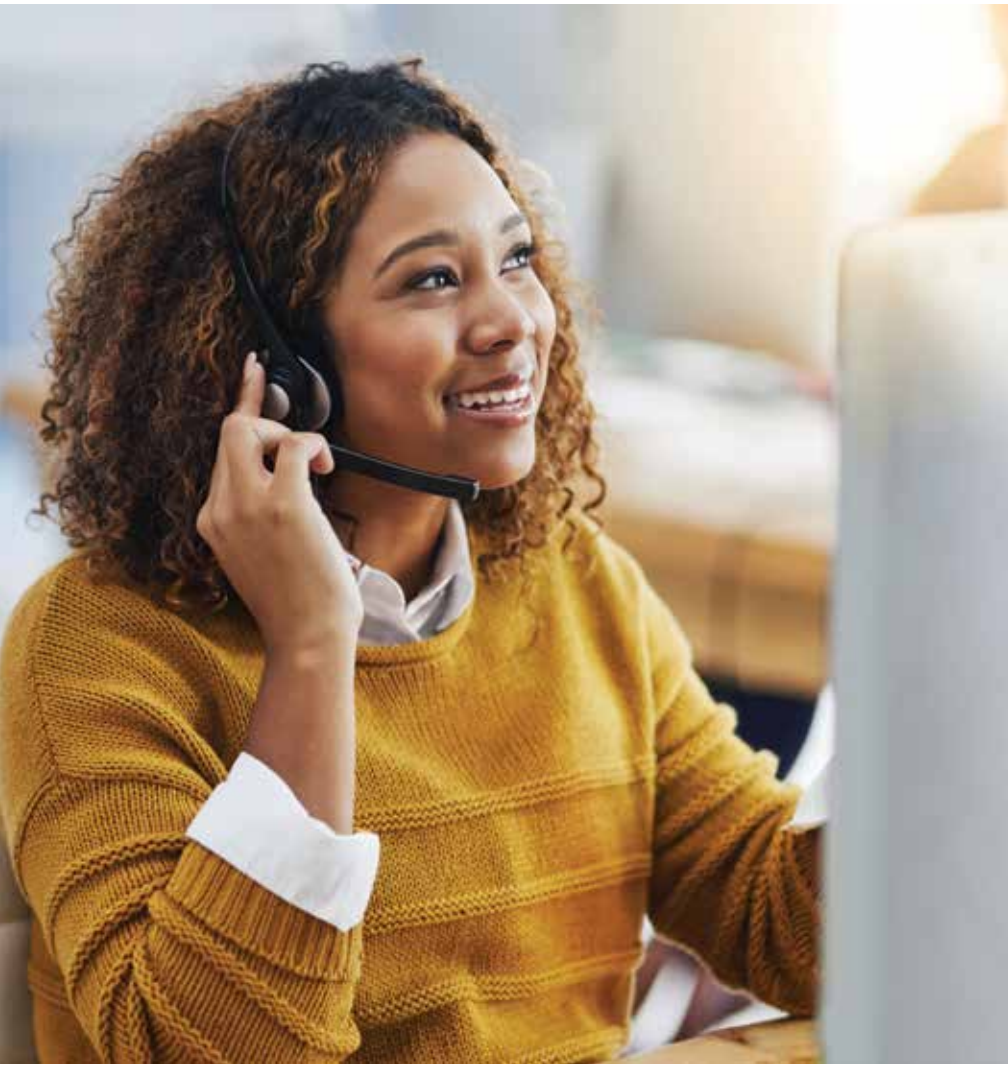
Cancer*Care*'s Free Support Services and Programs

It can be very difficult to receive a diagnosis of kidney cancer, and adjusting to the necessary changes in your life can be challenging.

Cancer*Care*® can help. We are a national nonprofit organization providing free, professional services to anyone affected by cancer. Our licensed oncology social workers can provide support and education, help in navigating the complicated health care system and offer information on support groups and other resources.

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

You will likely also build your own personal support network composed of family and friends. In doing so, it's best to take some time to think about the people in your life and how they are best suited to help. Match the task to their strengths—ask a family member who loves to shop to pick up something for you at the store, or ask a friend who's a good listener to come over for a chat.



Frequently Asked Questions

Q: I've heard the term "precision medicine." What does that mean?

A: Each tumor has its own biological makeup, based on the genes found in its cells. An important area of cancer research is understanding this biology. With this information, it's possible for doctors to know whether a particular tumor is likely to respond to a specific treatment, allowing them to suggest the right treatment for each person's tumor. This approach is known as precision (or personalized) medicine.

To better understand the biological makeup of a person's tumor, doctors look for tumor "markers" in cell genes. Markers can predict whether a given treatment will be effective against a tumor and whether there is a high risk of the tumor coming back. Tumor markers and genetic traits are an important step on the road toward precision medicine, and they are being actively studied in clinical trials for kidney cancer and other types of cancer.

Q: Can you tell me about the investigational drug batiraxcept?

A: The FDA has granted fast track designation to batiraxcept for the treatment of clear cell renal cell carcinoma that progressed following systemic therapy. Batiraxcept is a novel (new) decoy protein that binds to a protein called GAS6, inhibiting tumor growth. The FDA's fast track is a process that facilitates the development and expedites the review of drugs to treat serious conditions. The purpose is to get important new drugs to the patient earlier.

Q: Does kidney cancer run in families?

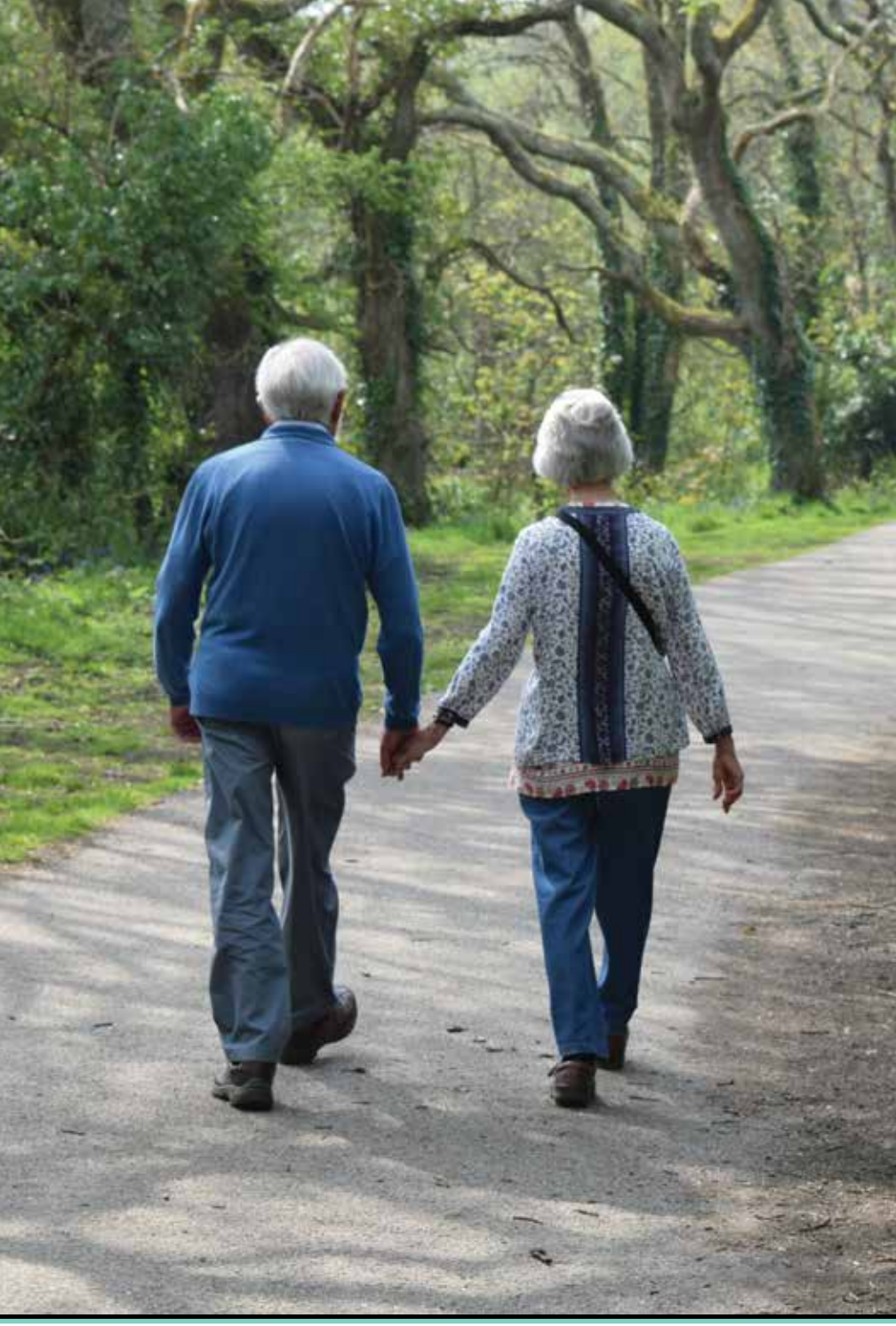
A: There is research indicating there might be a hereditary component in some cases of kidney cancer. If you have a family history of kidney cancer and have also been diagnosed, or if you were diagnosed with kidney cancer at the age of 50 or younger, you should talk to your doctor about the possibility of meeting with a genetic counselor. It's important to note that there are many risk factors for kidney cancer not related to heredity, including smoking, obesity and high blood pressure.

Q: What is a treatment summary and why is it important?

A: Keeping your own records up-to-date in the form of a treatment summary can be helpful, as it allows you and your family members to have instant access to the specifics of your kidney cancer diagnosis and treatment. A treatment summary should include:

- Your name and date of birth
- Date of diagnosis
- Prescribed therapy/therapies, including dates started and stopped and dosages when appropriate
- Dates and types of baseline and post-diagnosis testing and the results of these tests
- Other medications and supplements you are taking
- Names, affiliations and contact information of all members of your health care team

Ask the members of your health care team what they suggest be included. Take your personal record with you when you visit any doctor, not just your oncologist.



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National Coalition for Cancer Survivorship
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www.canceradvocacy.org

Medicine Assistance Tool
www.medicineassistancetool.org

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