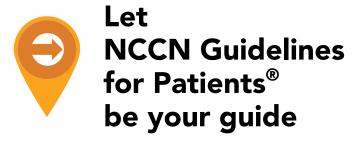


# Kidney Cancer





# It's easy to get lost in the cancer world



- ✓ Step-by-step guides to the cancer care options likely to have the best results
  - ✓ Based on treatment guidelines used by health care providers worldwide
    - ✓ Designed to help you discuss cancer treatment with your doctors

# Kidney Cancer



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- For providers of cancer care all over the world
- Expert recommendations for cancer screening, diagnosis,

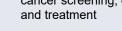
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These NCCN Guidelines for Patients are based on the NCCN Guidelines® for Kidney Cancer, Version 2.2022 – September 8, 2021.

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# **Kidney Cancer**



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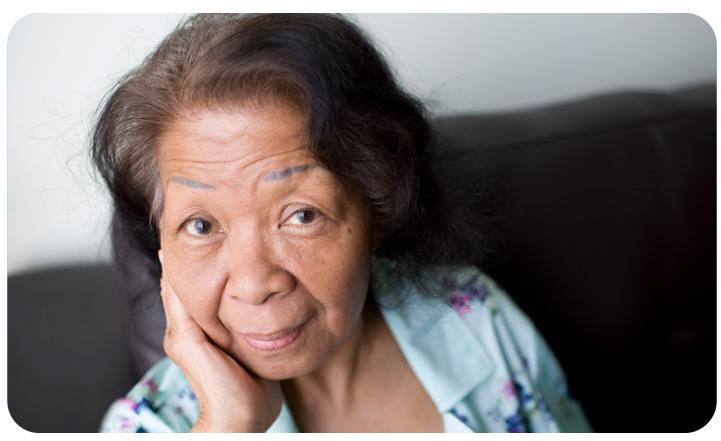
# **Kidney Cancer**

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# 1 Kidney cancer basics

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The kidneys are a pair of organs found behind the other organs in your abdomen. The kidneys make hormones and filter blood to remove waste and extra water from the body. This chapter will discuss the kidneys and provide an overview of kidney cancer.

# The kidneys

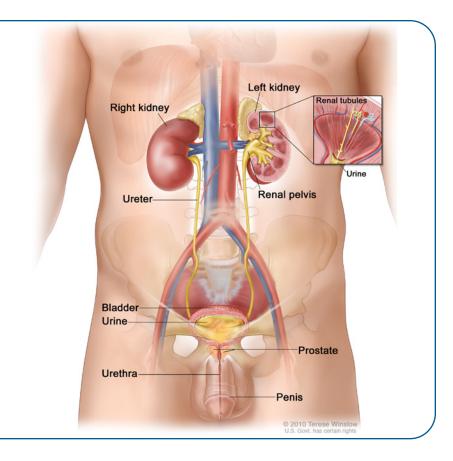
The kidneys are a pair of organs found behind the other organs in your abdomen. Each kidney is about the size of an adult's fist. The kidney is covered by a thin layer of tissue, like the skin of an apple. This layer of tissue is called the renal capsule. Renal refers to the kidney.

The kidneys are part of the urinary system. The urinary system is a group of organs that remove waste from the body in the form of urine (or pee). This system includes the kidneys, ureters, bladder, and urethra. The kidneys make hormones that help control blood pressure. They also make hormones that tell the body to make more red blood cells. By filtering the blood, the kidneys also control and balance the levels of fluids and chemicals in your body.

An adrenal gland sits on top of each kidney. The kidney and adrenal gland are surrounded by a layer of fat. Covering the fat is an outer layer of fibrous tissue called Gerota's fascia. Gerota's fascia is important. When kidney cancer grows into and beyond Gerota's fascia it is a sign of advanced kidney cancer.

# The kidneys and urinary system

The kidneys are the main organs of the urinary system. The ureters, bladder, and urethra hold and transport urine before it is released from the body.



# How the kidneys work

The kidneys perform many jobs to keep your body healthy. The main job of the kidneys is to filter blood to remove waste and extra water from the body. By filtering the blood, the kidneys also control and balance the levels of fluids and chemicals in your body.

The renal artery carries blood with waste into the kidney. Blood then flows through tiny filtering tubes in the kidney called renal tubules. Blood is cleaned as it flows through the renal tubules. The renal tubules take waste and other substances out of the blood. These substances are made into urine.

The clean, filtered blood flows out of the kidney through the renal vein. The renal vein merges with a larger vein called the vena cava. The

vena cava takes clean blood back up to the heart.

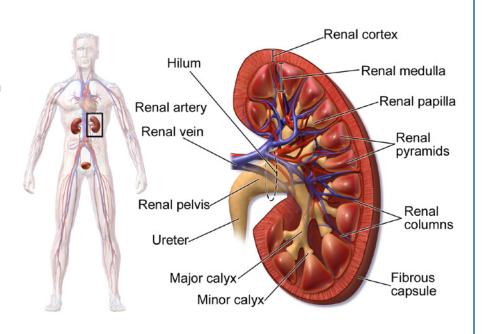
Urine flows out of the renal tubules and collects in a hollow space in the middle of the kidney called the renal pelvis. Urine leaves the renal pelvis through a long tube called the ureter. The ureter carries urine to the bladder. The bladder holds urine until it is released from the body, when you urinate (or pee). A shorter tube, called the urethra, takes urine from the bladder to outside the body.

Most people have two kidneys. However, each kidney works on its own and does not need the other to function. This means that the body can often work well with less than one complete kidney. Many people live full, healthy lives with only one kidney.

# The kidneys filter blood to remove waste

Blood enters the kidney through the renal artery. Renal tubules remove excess water and other waste from the blood to make urine. Urine drips out of the renal tubules into the renal pelvis, then leaves the kidney through the ureter. Clean, filtered blood leaves the kidney through the renal vein.

'https://commons.wikimedia.org/wiki/ File:Blausen\_0592\_KidneyAnatomy\_01.png



# Kidney cancer

Cancer is a disease that starts in the cells of your body. Most cancer is named after the cell from which it formed. Kidney cancer starts in the tissues of the kidneys.

Almost all kidney cancers are carcinomas. Carcinomas are cancers that start in cells that line the inner or outer surfaces of the body. In the kidneys, carcinomas most often start in the cells that line the renal tubules. This is called renal cell carcinoma (RCC). About 9 out of 10 kidney cancers are RCCs. RCC may appear as multiple tumors in one kidney or involve both kidneys.

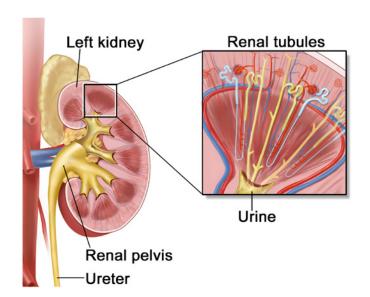
Because it is the most common type, RCC is often simply referred to as kidney cancer. RCC is the focus of this book.

There are other, less common cancers that can arise in the kidney. While they can sometimes be confused with RCC, it is important to note that they are treated differently.

- Transitional cell carcinoma (TCC) TCC starts in the cells that line the renal pelvis, where the ureters meet the kidneys. This is also called urothelial carcinomas or transitional cell cancer. See NCCN Guidelines for Patients: Bladder Cancer, available at NCCN.org/patientquidelines.
- Wilms tumor (nephroblastoma) In Wilms tumor (WT), cancer cells are found in the kidney. It usually occurs in young children.
- Renal sarcoma Renal sarcoma starts in the blood vessels or connective tissue of the kidney. See NCCN Guidelines for Patients: Soft Tissue Sarcoma, available at NCCN.org/patientguidelines.

#### Renal cell carcinoma

Most kidney cancers arise in cells that line the small tubes in the kidney called renal tubules.



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# RCC subtypes

Renal cell carcinoma (RCC) is the most common type of kidney cancer. RCC can be broken down into subtypes by looking at the cancer cells under a microscope. This is called histology. Tumor histology and other factors are an important part of choosing a treatment plan.

#### Clear cell RCC

Clear cell RCC (ccRCC) is the most common subtype. It occurs in about 7 out of 10 people with RCC. Under a microscope, clear cells look very pale or clear.

#### Non-clear cell RCC

Non-clear cell RCC is also called nccRCC. There are several subtypes.

- Papillary RCC is the most common subtype of nccRCC (about 1 out of 10 with RCC). Most papillary tumors look like long, thin finger-like growths under a microscope. It is also called PRCC.
- Chromophobe RCC cells are pale, but larger than clear cells, and look different.

# Rare types of nccRCC

Other rare types of nccRCC include the following:

- Collecting duct RCC (cdRCC) forms in the cells of the collecting ducts or tubules.
- Renal medullary carcinoma (RMC) can be found in young people of African descent who carry the sickle cell trait, sickle cell disease, or other diseases that can cause sickling of the red blood cells.
- Translocation RCC can be found at all ages but tends to be diagnosed in children or younger adults. These tumors have unique fusions of genes that promote the cancer.
- Unclassified RCC describes cancer cells that don't look like any of the subtypes or more than one subtype is present.

#### Sarcomatoid features

Almost any type of renal cell carcinoma can become sarcomatoid (sRCC) or have sarcomatoid features. This means that the cells of the cancer look like the cells of a sarcoma (cancer of the connective tissues, such as muscles, nerves, fat, blood vessels, and fibrous tissue). Sarcomatoid renal cancers are rare, but tend to grow more quickly than other types of kidney cancer and are more likely to spread to other parts of the body. This makes them more difficult to treat.

# How kidney cancer spreads

Tumors can grow in any part of the kidney and can grow into the renal vein and vena cava. Kidney cancer can also spread to other parts of the body in a process called metastasis. In metastasis, cancer cells travel through your blood or lymph to form new tumors. The new tumors are called metastatic tumors or metastases. Distant metastases typically occur in lung, bone, liver, adrenal glands, and brain.

- Local spread In locally advanced disease, cancer has spread to a nearby area close to the primary tumor. Kidney cancer can invade nearby tissues like surrounding fat, blood vessels, lymph nodes, adrenal glands, and Gerota's fascia.
- Distant metastasis In metastatic disease, cancer has spread to distant parts of the body far from the primary site. Kidney cancer tends to spread to distant sites such as the lungs, lymph nodes, and bones, but less frequently to the liver and brain.

Treatment will be based on size and location of the tumor(s).

# Key points

- The kidneys filter blood to remove extra water and other waste the body doesn't need.
- Blood flows into the kidney through the renal artery and out through the renal vein.
- Renal tubules are tiny tubes in the kidneys that remove waste from blood and make urine.
- Renal cell carcinoma (RCC) starts in cells that line the renal tubules. RCC is the most common type of kidney cancer. Clear cell RCC and non-clear cell RCC are subtypes.
- Almost any type of RCC can become sarcomatoid (sRCC) or have sarcomatoid features.
- Tumors can grow in any part of the kidney and can grow into the renal vein and vena cava.
- In a process called metastasis, cancer cells travel through your blood or lymph to form new tumors in other parts of the body.
- Treatment for RCC is based on the histology, size and location of the tumor(s), and if cancer has metastasized to other areas in the body.

# 2 Diagnosing kidney cancer

- 13 Test results
- 13 General health tests
- 15 Blood tests
- 16 Urine tests
- 16 Imaging tests
- 18 Biopsy
- 18 Biomarker testing
- 19 Genetic testing
- 20 Key points



Most kidney cancers are found by chance during imaging tests for other health problems. Further testing is used to confirm (diagnose) kidney cancer. This chapter presents an overview of some of the tests you might receive and what to expect.

# Test results

Results from blood tests, imaging studies, and biopsy or surgery will be used to determine your treatment plan. It is important you understand what these tests mean. Ask questions and keep copies of your test results. Online patient portals are a great way to access your test results.

Keep these things in mind:

- Bring someone with you to doctor visits, if possible.
- Write down questions and take notes during appointments. Don't be afraid to ask your care team questions. Get to know your care team and let them get to know you.
- Get copies of blood tests, imaging results, and reports about the specific type of cancer you have.
- Organize your papers. Create files for insurance forms, medical records, and test results. You can do the same on your computer.
- Keep a list of contact information for everyone on your care team. Add it to your phone. Hang the list on your refrigerator or keep it in a place where

someone can access it in an emergency. Keep your primary care physician informed of changes to this list.

# General health tests

# **Medical history**

A medical history is a record of all health issues and treatments you have had in your life. Be prepared to list any illness or injury and when it happened. Bring a list of old and new medicines and any over-the-counter medicines, herbals, or supplements you take. Tell your doctor about any symptoms you have. A medical history will help determine which treatment is best for you. It is also called a health history.

# **Family history**

Some cancers and other diseases can run in families. Your doctor will ask about the health history of family members who are blood relatives. This information is called a family

Bring a list of any medications, vitamins, over-the-counter drugs, herbals, or supplements you are taking.

history. You can ask family members about their health issues like heart disease, cancer, and diabetes, and at what age they were diagnosed.

Kidney cancer often occurs for unknown reasons. Some people have genetic health conditions that increase the risk for kidney cancer. Genetic usually means that it is passed down from parent to child through genes. Genes tell cells what to become and what to do.

#### Physical exam

During a physical exam, your health care provider may:

- Check your temperature, blood pressure, pulse, and breathing rate
- Weigh you
- Listen to your lungs and heart

- Look in your eyes, ears, nose, and throat
- Feel and apply pressure to parts of your body to see if organs are of normal size, are soft or hard, or cause pain when touched. Tell your doctor if you feel pain.
- Feel for enlarged lymph nodes in your neck, underarm, and groin. Tell your doctor if you have felt any lumps or have any pain.

Your kidneys sit deep inside your abdomen and normally can't be felt during a physical exam. However, if the kidney is enlarged due to a large tumor, your doctor may be able to feel it during an exam.

Doctors should perform a physical exam along with a complete health history. For possible tests, see Guide 1.

#### Guide 1

# Possible tests for suspicious mass

Medical history and physical exam

Complete blood count, differential, comprehensive metabolic panel, lactate dehydrogenase

Urinalysis

CT scan of abdomen with or without pelvis. Or MRI scan. Imaging with and without contrast is preferred.

Chest x-ray

As needed: bone scan, brain MRI, chest CT, core needle biopsy (not fine-needle aspiration)

If multiple kidney masses, 46 years of age or under, or family history, possible genetic evaluation (see hereditary renal cell carcinoma).

# **Blood tests**

Blood tests check for signs of disease and how well organs are working. They require a sample of your blood, which is removed through a needle placed into your vein.

# Complete blood count and differential

A complete blood count (CBC) measures the levels of red blood cells, white blood cells, and platelets in your blood. Your doctor will want to know if you have enough red blood cells to carry oxygen throughout your body, white blood cells to fight infection, and platelets to control bleeding.

A differential counts the number of each type of white blood cell. It also checks if the counts are in balance with each other.

# Comprehensive metabolic panel

A comprehensive metabolic panel (CMP) is a test that measures 14 different substances in your blood. A CMP provides important information about how well your kidneys and liver are working, among other things. A CMP might include a serum creatinine test, liver function tests (LFTs), and a urinalysis. These tests might also be called blood chemistry tests.

# Alkaline phosphatase

Alkaline phosphatase (ALP) is an enzyme found in the blood. High levels of ALP can be a sign cancer has spread to the bone or liver. A bone scan might be performed if you have high levels of ALP.

#### Calcium

Calcium is the most common mineral in the body. It is needed for healthy teeth, bones, and other body tissues. You might have higher calcium levels if your kidneys aren't working normally. Bone damage from cancer can cause your bones to release calcium into the bloodstream.

#### Creatinine

Creatinine is a waste produced in the muscles. Every person generates a fixed amount of creatinine every day based on how much muscle they have. It is filtered out of the blood by the kidneys. The level of creatinine in the blood tells how well the kidneys are working. Higher levels of creatinine mean the kidneys aren't working as well as they were when someone had lower levels of creatinine.

# Lactate dehydrogenase

Lactate dehydrogenase (LDH) or lactic acid dehydrogenase is an enzyme found in most cells. Dying cells release LDH into the blood. Fast-growing cells, such as tumor cells, also release LDH.

#### **Liver function tests**

Liver function tests (LFTs) look at the health of your liver by measuring chemicals that are made or processed by the liver. Levels that are too high or low signal that the liver is not working well or that cancer has spread to the liver.

# Urine tests

Urine tests look for signs of disease and assess your general health. Abnormal results may signal there's a problem with your kidneys or other organs. Abnormal results may be caused by kidney cancer or other health conditions. For a urine test, you will be asked to fill a small container with urine. The urine sample will be sent to a lab for testing.

# **Urinalysis**

A urinalysis detects and/or measures several substances in the urine using a microscope and chemical tests. Blood in urine (hematuria) may be caused by kidney cancer or other health problems. Those with kidney cancer may have a normal urinalysis or have evidence of blood in the urine.

# **Urine cytology**

In a urine cytology, urine is looked at under a microscope to check for cancer cells. This test may be used if your doctor suspects urothelial cancer in the urinary tract or bladder.

# Imaging tests

Imaging tests take pictures of the inside of your body. Images can be made with scanning machines or scoping tools. Imaging tests may show if the tumor involves any veins, arteries, and other organs. A radiologist, an expert in interpreting imaging tests, will write a report and send this report to your doctor. Your doctor will discuss the results with you.

#### Bone scan

A bone scan uses a radiotracer to take pictures of the inside of bones. A radiotracer is a substance that releases small amounts of radiation. Before the pictures are taken, the tracer will be injected into your vein. It can take a few hours for the tracer to enter your bones.

A special camera will take pictures of the tracer in your bones. Areas of bone damage use more radiotracer than healthy bone and show up as bright spots on the pictures. Bone damage can be caused by cancer, cancer treatment, or other health problems. This test may be used if you have bone pain, are at high risk for bone metastases, or if there are changes in certain test results. Bone scans might be used to monitor treatment.

#### CT scan

A computed tomography (CT or CAT) scan uses x-rays and computer technology to take pictures of the inside of the body. It takes many x-rays of the same body part from different angles. All the images are combined to make one detailed three-dimensional (3D) picture.

A CT scan of your chest, abdomen, and/or pelvis may be one of the tests used to look for cancer. In most cases, contrast will be used. Contrast material is used to improve the pictures of the inside of the body. Contrast materials are not dyes, but substances that help enhance and improve the images of several organs and structures in the body. It is used to make the pictures clearer. Contrast might be taken by mouth (oral) or given through a vein (IV). The contrast is not permanent and will leave the body in your urine immediately after the test.

Tell your doctors if you have had allergic reactions to contrast in the past. This is important. You might be given medicines, such as diphenhydramine (Benadryl®) and prednisone (steroids), to avoid the effects of those allergies. Contrast might not be used if you have a serious allergy or if your kidneys aren't working well.

#### **MRI**

A magnetic resonance imaging (MRI) scan uses radio waves and powerful magnets to take pictures of the inside of the body. It does not use x-rays. MRI scans can look for cancer that has grown into major blood vessels in the abdomen such as the inferior vena cava. Contrast might be used.

#### **Brain MRI**

An MRI may be used to look at possible tumor spread (metastasis) in the brain.

#### **Ultrasound**

An ultrasound (US) uses high-energy sound waves to form pictures of the inside of the body. A probe will be pressed onto your abdomen. This is similar to the sonogram used for pregnancy. Ultrasound is painless and does not use x-rays, so it can be repeated as needed. An ultrasound can show if there is a mass in your kidney and if the mass is solid or fluid-filled. It can also help evaluate if the mass has blood flow. Kidney cancer tumors are more likely to be solid and have blood flow.

# X-ray

An x-ray uses low-dose radiation to take one picture at a time of the inside of the body. A chest x-ray is used to see if cancer has spread to your lungs.

#### **CT** machine

A CT machine is large and has a tunnel in the middle. During the test, you will need to lie on a table that moves through the tunnel.



# **Biopsy**

A biopsy removes a sample of tissue or fluid. Samples removed during a biopsy or surgery will be sent to a pathologist, an expert in examining cells under a microscope to confirm the presence of cancer. The pathologist will determine the cancer subtype called tumor histology.

For most cancers, a biopsy must be done to confirm cancer before starting cancer treatment. For many with a high suspicion of kidney cancer that appears to be contained, the primary treatment is surgery to remove the tumor. After the tumor is removed, it is tested.

Types of possible biopsies include:

- Fine-needle aspiration (FNA) or fineneedle biopsy (FNB) uses a thin needle to remove a sample of tissue or fluid. An ultrasound (US) may guide the FNA biopsy.
- Core needle biopsy removes tissue samples with a hollow needle about the same size as a needle used for an IV (intravenous) line.

# **Biopsy of metastases**

A metastasis is the spread of cancer to an area of the body such as lung, bone, or brain. A biopsy of the metastasis may be needed to confirm the presence of cancer. If there is more than one metastasis, each site may be biopsied. The type of biopsy used depends on the location of the suspected metastases and other factors.

# Biomarker testing

A sample from a biopsy of your tumor may be tested to look for specific DNA (deoxyribonucleic acid) mutations, protein levels, or other molecular features. It is sometimes called molecular testing or tumor profile testing. Biomarker testing includes tests of genes or their products (proteins). It identifies the presence or absence of mutations and certain proteins that might affect treatment. Proteins are written like this: SDHB. Genes are written like this: SDHB.

# **Tumor mutation testing**

A sample of your tumor or blood may be used to see if the cancer cells have any specific DNA mutations. This is a different type of DNA testing than the genetic testing for mutations you may have inherited from your parents. In tumor mutation testing, only the tumor is tested and not the rest of your body. Some mutations can be targeted with specific therapies.

#### PD-1 and PD-L1

Programmed death-1 (PD-1) and programmed death-ligand 1 (PD-L1) are immune proteins found in some cancer cells. These proteins can cause your immune cells to ignore the cancer cells and suppress the anti-tumor immune response.

# Genetic testing

Genetic testing is done using blood or saliva (spitting into a cup). The goal is to look for gene mutations inherited from your parents called germline mutations. Some mutations can put you at risk for more than one type of cancer. You can pass these genes on to your children. Also, close blood relatives might carry these mutations.

Close blood relatives:

- First-degree relatives include parents, siblings, and children.
- Second-degree relatives include halfsiblings, aunts, uncles, nieces, nephews, grandparents, and grandchildren.

Tell your doctor if there is a family history of cancer. Depending on your family history or other features of your cancer, your health care provider might refer you for hereditary genetic testing to learn more about your cancer. A genetic counselor will speak to you about the results.

# **Hereditary syndromes**

Certain genetic syndromes may put someone at risk for developing kidney cancer. A syndrome is a group of signs or symptoms that occur together and suggest the presence of or risk for a disease. A hereditary syndrome is found in blood relatives.

A genetic risk assessment will identify if you are at risk for cancer and if you may benefit from genetic testing, additional screening, or preventive interventions. Depending on the genetic risk assessment, you might undergo genetic testing and genetic counseling to see if

you have a hereditary syndrome that puts you at risk for developing kidney cancer, along with possibly other cancers or medical issues.

Kidney cancer caused by a hereditary syndrome is called hereditary renal cell carcinoma (HRCC).

It is important that those who have hereditary causes of RCC see their doctors often, especially if they have already been diagnosed with RCC. Those with confirmed hereditary causes of RCC will be monitored differently than those with sporadic RCC. You will have regular testing to check for a new kidney tumor and may also need follow up with other specialists depending on the type of hereditary RCC.

More information on HRCC can be found in Chapter 7: Hereditary RCC.

# Key points

- Tests are used to find cancer, plan treatment, and check how well treatment is working.
- A medical history and physical exam will inform your doctor about your overall health.
- Blood and urine tests check for signs of disease and how well organs are working.
- Imaging tests take pictures of the inside of your body. Imaging tests are used to find and diagnose kidney cancer.
- A biopsy removes a sample of tissue or fluid for testing. Biopsies are not usually done before surgery for kidney cancer.
- A sample of your tumor may be tested to look for specific DNA (deoxyribonucleic acid) mutations, protein levels, or other molecular features. Some mutations and proteins can be targeted with specific therapies.
- Genetic testing might be done to look for gene mutations, inherited from your parents, called germline mutations.
- A genetic syndrome that puts someone at risk for developing kidney cancer and possibly other cancers is called hereditary renal cell carcinoma (HRCC).
- Results from blood tests, imaging studies, and biopsy will determine your treatment plan. Often, information is collected over time, even as treatment begins.
- Online portals are a great way to access your test results.



# Create a medical binder

A medical binder or notebook is a great way to organize all of your records in one place.

- Make copies of blood tests, imaging results, and reports about your specific type of cancer. It will be helpful when getting a second opinion.
- Choose a binder that meets your needs.
   Consider a zipper pocket to include a pen, small calendar, and insurance cards.
- Create folders for insurance forms, medical records, and tests results. You can do the same on your computer.
- Use online patient portals to view your test results and other records. Download or print the records to add to your binder.
- Organize your binder in a way that works for you. Add a section for questions and to take notes.
- Bring your medical binder to appointments. You never know when you might need it!

# 3 Kidney cancer stages

- 22 Staging
- 24 Kidney cancer stages
- 26 Key points



A cancer stage helps to predict the likely course your cancer will take called a prognosis. It describes the size and location of the tumor and if cancer has spread to lymph nodes, organs, or other parts of the body. This chapter explains kidney cancer stages.

# **Staging**

A cancer stage is a way to describe the extent of the cancer at the time you are first diagnosed. The American Joint Committee on Cancer (AJCC) created a staging system to determine how much cancer is in your body, where it is located, and what subtype you have. AJCC is just one type of staging system.

Staging is based on a combination of information to reach a final numbered stage. Often, not all information is available at the initial evaluation. More information can be gathered as treatment begins. Doctors may explain your cancer stage in different ways than those described next.

#### **TNM** scores

The tumor, node, metastasis (TNM) system is used to stage kidney cancer. In this system, the letters T, N, and M describe different areas of cancer growth. Based on imaging and pathology results, your doctor will assign a score or number to each letter. The higher the number, the larger the tumor or the more the cancer has spread to lymph nodes or other organs. These scores will be combined to assign the cancer a stage. A TNM example might look like this: T1N0M0 or T1, N0, M0.

The TNM letters represent the following:

- T (tumor) Depth and size of the main (primary) tumor in the kidney
- N (node) If cancer has spread to nearby (regional) lymph nodes
- M (metastasis) If cancer has spread (metastasized) to distant parts of the body

#### Grade

Grade describes how abnormal the tumor cells look under a microscope (called histology). Higher-grade cancers tend to grow and spread faster than lower-grade cancers. GX means the grade can't be determined, followed by G1, G2, G3, and G4. G4 is the highest grade for renal cell carcinoma.

# **Numbered stages**

Numbered stages are based on TNM scores. Stages range from stage 1 to stage 4, with 4 being the most advanced. Doctors write these stages as stage I, stage II, stage III, and stage IV. For example, stage 1 might be T1, N0, M0.

- Staging before surgery is called clinical stage
- Staging after surgery is called pathologic stage

Other terms might be used instead of numbered cancer stages. These include:

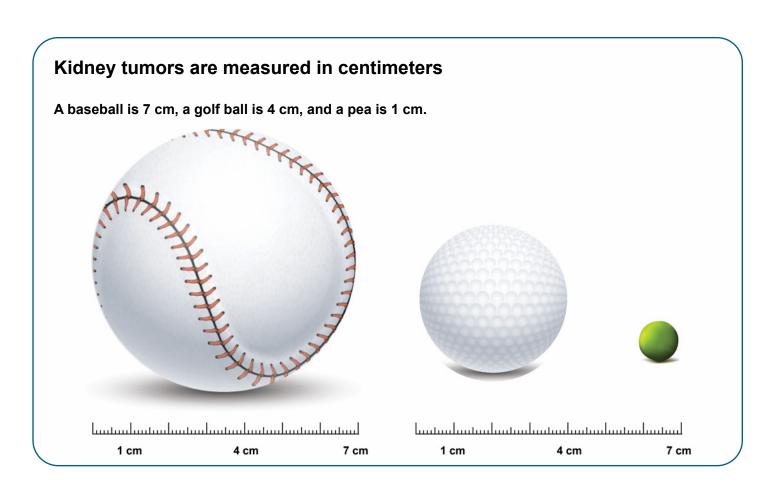
- Resectable Tumor can be removed completely with surgery.
- Unresectable Tumor cannot be removed with surgery. It might involve nearby blood vessels or organs making it unsafe to remove.

- 3
- Locoregional or locally advanced This refers to a tumor that has spread to or beyond the blood vessels, tissue, organs, or lymph nodes surrounding the kidney. It may be a stage 3 or 4 tumor, depending on how far outside the kidney the tumor has spread.
- Metastatic Cancer has spread to other parts of the body, including distant lymph nodes. The most common sites are the lungs, lymph nodes, bones, liver, and the brain. This might be referred to as advanced disease.

#### T = Tumor

A tumor can grow outside the kidney and into nearby structures. Kidney tumors are measured in centimeters (cm). A baseball is 7 cm, a golf ball is 4 cm, and a pea is 1 cm. Your kidney is about the size of your fist or about 11 cm by 5 cm.

- > **T1** Tumor is 7 cm or smaller and is limited to the kidney
- T2 Tumor is larger than 7 cm and is limited to the kidney
- T3 Tumor extends outside the kidney into major veins and tissues, but not into Gerota's fascia
- > **T4** Tumor invades beyond Gerota's fascia and might be in the adrenal gland



# N = Regional Lymph Nodes

There are hundreds of lymph nodes throughout your body. They work as filters to help fight infection and remove harmful things from your body. Regional lymph nodes are found near the kidney. Regional lymph nodes include renal hilar, caval, and aortic. Cancer found in a regional lymph node is called a lymph node metastasis. This is different than a distant metastasis, which is found far from the main tumor in the kidney.

The removal of lymph nodes is called lymph node or nodal dissection.

- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastasis is found
- N1 Metastasis in regional lymph node(s) is found

#### **M** = Distant Metastasis

Cancer that has spread to distant parts of the body is metastatic. Common metastatic sites include the bone, liver, lungs, brain, adrenal glands, and distant lymph nodes.

- M0 No distant metastasis is found.
- M1 Metastasis is found

# Kidney cancer stages

Kidney cancers of the same stage tend to have a similar outcome (prognosis) and are treated in a similar way. In general, earlier cancer stages have better outcomes. Some people will do better than expected. Others will do worse. Factors such as your general health are also very important. See Guide 2.

Guide 2 Kidney cancer stages	
Stage 1	• T1, N0, M0
Stage 2	• T2, N0, M0
Stage 3	<ul><li>T1 or T2, N1, M0</li><li>T3, NX or N0 or N1, M0</li></ul>
Stage 4	• T4, Any N , M0 • Any T, Any N, M1

# Stage I

T1, N0, M0

The tumor is found only in the kidney and is smaller than 7 cm (T1). Cancer has not spread to nearby lymph nodes (N0) or to other parts of the body (M0).

# Stage 2

T2, N0, M0

The tumor is larger than 7 cm and is found only in the kidney (T2). Cancer has not spread to nearby lymph nodes (N0) or to other parts of the body (M0).

#### Stage 3

T1 or T2, N1, M0

The tumor is found only in the kidney (T1 or T2), but cancer has spread (metastasized) to nearby lymph nodes (N1). This is locally advanced kidney cancer. Cancer has not metastasized to distant sites (M0). The tumor has not grown into the adrenal gland or beyond Gerota's fascia.

# Stage 3

T3, NX or N0 or N1, M0

The tumor has grown outside the kidney into nearby veins and tissues (T3). It has not grown into the adrenal gland or beyond Gerota's fascia. Cancer may or may not be in nearby lymph nodes. If cancer is found in nearby lymph nodes, it is called locally advanced kidney cancer. Cancer has not spread to distant sites (M0).

#### Stage 4

T4, Any N, M0

The tumor has grown beyond Gerota's fascia and maybe into the adrenal gland (T4). Cancer is found in nearby lymph nodes (N1). Cancer has not metastasized to distant sites in the body (M0). This is locally advanced kidney cancer.

# Stage 4

Any T, Any N, M1

The tumor is any size and may or may not extend beyond the kidney. Cancer may or may not have spread to nearby lymph nodes. Cancer has metastasized to distant parts of the body (M1). This is advanced or metastatic kidney cancer.

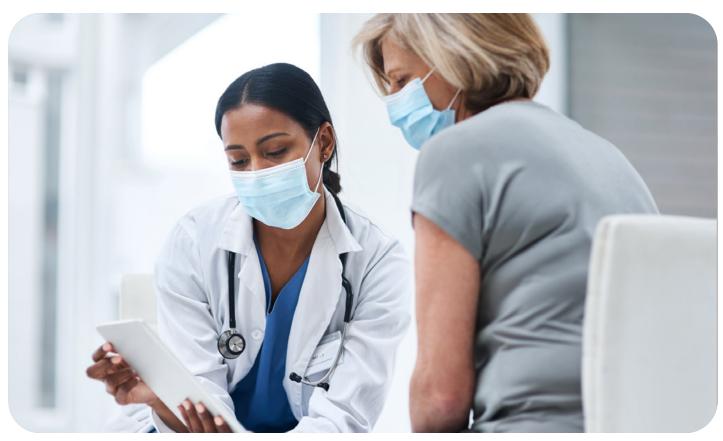
# Key points

- A cancer stage helps to predict the likely course your cancer will take, called a prognosis. It describes the size and location of the tumor and if cancer has spread to lymph nodes, organs, or other parts of the body.
- Staging is used to make treatment decisions.
- In stage 1 kidney cancer, the tumor is 7 cm or smaller and found only in the kidney.
- In stage 2 kidney cancer, the tumor is larger than 7 cm and found only in the kidney.
- In stage 3 kidney cancer, the tumor has grown outside the kidney into nearby veins and tissues, but has not grown into the adrenal gland or beyond Gerota's fascia. Cancer may or may not be in nearby lymph nodes. Cancer has not spread to distant sites.
- In stage 4 kidney cancer, the tumor can be any size. It may have spread outside the kidney.

# Treatment overview

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There is more than one treatment for kidney cancer. This chapter describes treatment options and what to expect. Together, you and your doctor will choose a treatment plan that is best for you.

# Treatment team

Those with kidney cancer should seek treatment at experienced cancer centers.

Treating kidney cancer takes a team approach. Treatment decisions should involve a multidisciplinary team (MDT). An MDT is a team of doctors, health care workers, and social care professionals from different professional backgrounds who have knowledge (expertise) and experience with your type of cancer. This team is united in the planning and implementing of your treatment. Ask who will coordinate your care.

Some members of your care team will be with you throughout cancer treatment, while others will only be there for parts of it. Get to know your care team and let them get to know you.

Depending on your diagnosis, your team might include the following specialists:

- A urologist is an expert in treating diseases of the urinary system.
- A urologic oncologist specializes in diagnosing and treating cancers of the urinary tract.
- A pathologist analyzes the cells, tissues, and organs removed during a biopsy or surgery and provides cancer diagnosis,

Get to know your care team and let them get to know you.

staging, and information about biomarker testing.

- A diagnostic radiologist interprets the results of x-rays and other imaging tests.
- An interventional radiologist performs needle biopsies and ablation procedures, and places ports for treatment.
- A surgical oncologist performs operations to remove cancer in organs outside the urinary tract.
- A cardiovascular surgeon performs operations relating to the heart and blood vessels. This surgeon may assist a surgical oncologist or surgical urologist.
- A medical oncologist treats cancer in adults using systemic therapy.
- A radiation oncologist prescribes and plans radiation therapy to treat cancer.
- An anesthesiologist gives anesthesia, a medicine so you do not feel pain during surgery or procedures.

- Palliative care nurses and advanced practice providers help provide an extra layer of support with your cancer-related symptoms.
- Residents and fellows are doctors who are continuing their training, some to become specialists in a certain field of medicine.
- Oncology nurses provide your handson care, like giving systemic therapy, managing your care, answering questions, and helping you cope with side effects. Sometimes, these experts are called nurse navigators.
- Nutritionists and dietitians can provide guidance on what foods are most suitable for your condition.
- Psychologists and psychiatrists are mental health experts who can help manage issues such as depression, anxiety, or other mental health conditions that can affect how you feel.
- Social workers help people solve and cope with problems in their everyday lives.

You know your body better than anyone. Help other team members understand:

- How you feel
- What you need
- What is working and what is not

Keep a list of names and contact information for each member of your team. This will make it easier for you and anyone involved in your care to know whom to contact with questions or concerns.

# **Ablation**

Ablation uses extreme cold or extreme heat, radio waves, microwaves, or chemicals to destroy cancer cells. It can destroy small tumors and metastases with little harm to nearby tissue. You might have multiple treatments to destroy the tumor or metastasis. Ablation might be used if you are not healthy enough for surgery.

There are many types of ablation used to destroy cancer cells. Those most commonly used to treat a kidney tumor or its metastasis include:

- Cryotherapy or cryosurgery kills cancer cells by freezing them with a very cold substance.
- Radiofrequency ablation (RFA) kills cancer cells by heating them with highenergy radio waves.
- Microwave ablation refers to the use of electromagnetic energy to kill cancer cells.

All types of ablation use a special needle, called a probe, which is inserted into the tumor. With cryotherapy, a medical gas is passed through the probe to cause below-freezing temperatures. This freezes the tumor to destroy it. With RFA, the probe emits radio waves to heat the tumor and destroy it. The probe can be inserted through the skin and guided into place with a CT scan, ultrasound, or other imaging tests. It can also be inserted and guided into place during laparoscopic surgery.

Imaging tests are used to monitor the tumor during treatment to make sure the whole tumor is destroyed (ablated). The probe will be removed when treatment is done.

# Active surveillance

Active surveillance happens before treatment. Surveillance or follow-up care happens after treatment. Active surveillance closely monitors tumor growth. During this time, you will have imaging tests on a regular basis. You will not have treatment. Treatment will start if the tumor grows or if you are having pain or discomfort. There may be other reasons to start treatment. Ask your doctor what might "trigger" the need for treatment and how often you will have imaging tests.

Active surveillance may be an option for a tumor smaller than 2 cm that has not metastasized or in those with other serious health issues who may not be healthy enough for surgery or other treatments. Age and other health conditions increase the risk of severe side effects and complications from treatment.

# Surgery

Surgery is an operation or procedure to remove cancer from the body. Often, surgery is the main or primary treatment to remove the cancer from the kidney. This is only one part of a treatment plan. Surgery can also provide supportive care by easing pain or discomfort. This is called palliative surgery.

When preparing for surgery, you should seek the opinion of an experienced surgeon. The surgeon should be an expert in performing your type of surgery. Hospitals that perform many surgeries often have better results. You can ask for a referral to a hospital or cancer center that has experience in treating your type of cancer.

The removal of the cancer through surgery can be accomplished in different ways depending on the specific circumstances, such as the size and location of the tumor, and if there is cancer in any surrounding organs and tissues. Surgery is based on the safest and best way to remove the cancer.

# Open surgery

Open surgery or laparotomy removes tissue through one large surgical cut below your ribs. This approach lets your doctor directly view and access the tumor in your kidney to remove it. Open surgery may take several hours or longer. After the surgery, you will need to stay in the hospital to recover.

# Minimally invasive surgery

Minimally invasive surgery (key-hole surgery) uses a few small incisions. Small tools are inserted through each incision to perform the surgery. One of the tools, called a laparoscope, is a long tube with a video camera at the end. The camera lets your doctor see your kidney and other tissues inside your abdomen. Other tools are used to remove the tumor. Laparoscopic surgery can also be done using robotic arms to control the surgical tools. This is called robot-assisted laparoscopic surgery.

# Partial nephrectomy

In a partial nephrectomy, the tumor and tissue immediately surrounding the tumor is removed, leaving behind a still-functioning kidney. The adrenal gland and lymph nodes are also left in your body. A partial nephrectomy might be referred to as nephron-sparing or kidney-sparing surgery since it saves (spares) as much of your kidney as possible. Your kidney can still function even if part of it has been removed. This is a benefit of partial

nephrectomy. If you have poor kidney function or are at risk for poor kidney function, this surgery might be an option. It might be an option if you have only one kidney, limited kidney function, or tumors in both kidneys.

Partial nephrectomy is often used for treating kidney cancer when the tumor is small and only in the kidney. A partial nephrectomy can be used to remove larger tumors, but location of the tumor in your kidney and your overall health are considered in any type of surgery. For most small tumors, a partial nephrectomy can remove all the cancer with good long-term results. But, the surgeon's skill and experience are key factors.

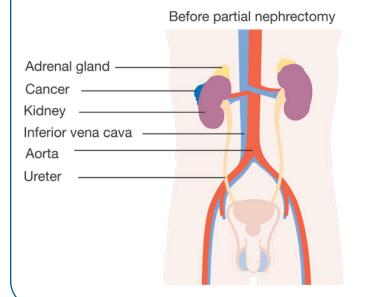
Partial nephrectomy is a complex surgery. It is more technically difficult than surgery that removes the whole kidney. A partial nephrectomy should only be done by an expert surgeon who does this type of surgery often. This surgery should only be done when the entire tumor can be safely removed, leaving the healthy part of the kidney intact.

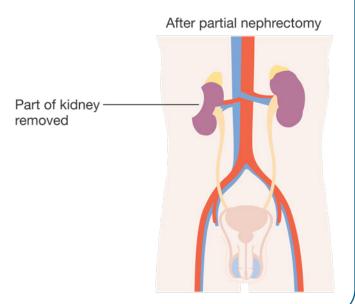
With any type of surgery, there are health risks and side effects. A side effect is an unhealthy or unpleasant condition caused by treatment. Some possible side effects of a partial nephrectomy include infections, bleeding, pain from the surgical cuts, and urine leaking from the kidney.

# Partial nephrectomy

In a partial nephrectomy, the tumor and tissue immediately surrounding the tumor are removed, leaving behind a still-functioning kidney.

 $https://commons.wikimedia.org/wiki/File: Diagram\_showing\_before\_and\_after\_a\_partial\_nephrectomy\_CRUK\_102.svg$ 





# Radical nephrectomy

A radical nephrectomy is surgery that removes the tumor with the whole kidney and the fatty tissue around the kidney. This surgery may also remove the adrenal gland (found on top of the kidney) and nearby lymph nodes. How much tissue is removed depends on the extent of the tumor.

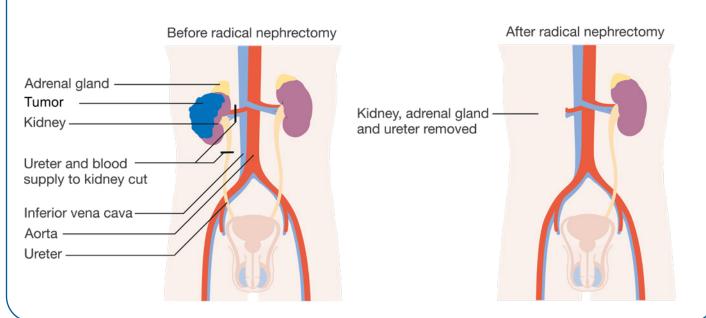
Surgery to remove an adrenal gland is called an adrenalectomy. The attached adrenal gland may be removed if it looks abnormal on imaging tests. It may also be removed if the tumor is near the top part of the kidney where the adrenal gland sits. Surgery to remove nearby lymph nodes is called a lymph node dissection. A lymph node dissection is not often done as part of a standard radical nephrectomy. Nearby lymph nodes may be removed if they look enlarged on imaging tests or during surgery.

If the tumor has grown into the renal vein and vena cava, then the veins may be cut open to remove all of the cancer. In rare cases, your heart may need to be stopped for a short time for surgery on the vena cava. While the heart is stopped, a heart-lung machine is used to circulate blood in the body. This is a very difficult and complex procedure. It should only be done by a team of experts who have a lot of experience.

# Radical nephrectomy

A radical nephrectomy is surgery to remove the tumor with the entire kidney and the fatty tissue around the kidney. This surgery may also remove the adrenal gland on top of the kidney and nearby lymph nodes.

https://commons.wikimedia.org/wiki/File:Diagram\_showing\_before\_and\_after\_a\_radical\_nephrectomy\_CRUK\_104.svg



Radical nephrectomy is used to treat kidney cancer when the tumor is large or has invaded nearby tissue. There are many factors that go into deciding which type of surgery might be best for your cancer. Each case is different. Each person is different.

With any type of surgery, there are risks. Some possible side effects of a radical nephrectomy include infection, bleeding, pain, and reduced kidney function. Since the whole kidney is removed, there is an increased risk for chronic kidney disease. Chronic kidney disease means your remaining kidney can't filter blood the way it should. In chronic kidney disease, kidney function may slowly get worse over a long period of time.

# Cytoreductive nephrectomy

A cytoreductive nephrectomy is surgery to remove the primary tumor when you have metastatic kidney cancer. Metastatic cancer has spread from where it first formed to other parts of your body. Cytoreductive surgery is often used to prolong life, reduce pain, or improve quality of life, but not as a cure. Some or all of your kidney might be removed along with the primary tumor in a cytoreductive nephrectomy. Removing the primary tumor may improve how well other treatments work against the remaining cancer and metastases.

A cytoreductive nephrectomy is usually followed by a targeted therapy and/or immunotherapy. It can also be considered in unique cases when a person has a good response to treatment and still has a large primary tumor. It may also be necessary to consider removal of the tumor if a person develops problems due to the kidney tumor such as blood in the urine or severe pain.

Not all cancer can be removed from your body with surgery when there are many metastases. Removing some of the cancer metastases, along with the primary tumor, and part or all of your kidney, might help to reduce the amount of cancer in your body, called cancer burden. The goal of cytoreductive surgery is to reduce cancer burden.

# Metastasectomy

New tumors that formed far from the primary tumor are called metastases. A metastasectomy is different from a mastectomy (surgery to remove the breast). A metastasectomy is surgery to remove one or more metastases. This surgery may be used when the primary tumor can be completely removed and there is only one metastasis. Not all metastases can be removed by surgery. Location is a key factor. Metastasectomy works best for metastases in the brain, bone, or lung.

A metastasectomy may be done at the same time as surgery to remove the primary tumor, or it may be done during a separate operation. The amount of time needed for the surgery and recovery depends on many factors. Some factors include the size and location of the metastases.

# Oligometastases

Oligometastases are a type of metastasis in which cancer cells from the original (primary) tumor travel through the body and form a small number of new tumors (metastatic tumors) in other parts of the body. Treatment for oligometastases or oligometastatic disease includes metastasectomy, radiation therapy, or ablation.

# Systemic therapy

Systemic therapy works throughout the body. Types include targeted therapy, immunotherapy, and chemotherapy. Systemic therapy might be used alone or with other therapies. Goals of systemic therapy should be discussed before starting treatment. Your wishes about treatment are important.

- When systemic therapy or chemoradiation is given <u>before</u> surgery, it is called neoadjuvant or preoperative therapy.
- When systemic therapy is given <u>before</u> <u>and after</u> surgery, it is called perioperative therapy.
- When systemic therapy or radiation therapy is given <u>after</u> surgery, it is called adjuvant or postoperative therapy.
- When systemic therapy is given for advanced or metastatic disease, it may be called palliative therapy.

# Warnings!

You might be asked to stop taking or avoid certain herbal supplements or foods when you are on a systemic therapy. Some supplements can affect the ability of a drug to do its job. This is called a drug interaction. It is critical to speak with your care team about any supplements you may be taking.

#### Some examples include:

- Turmeric
- Gingko biloba
- Green tea extract
- > St. John's Wort

# Did you know?

The terms "chemotherapy" and "systemic therapy" are often used interchangeably, but they are not the same. Chemotherapy, targeted therapy, and immunotherapy are all types of systemic therapy.

Certain medicines can also affect the ability of a drug to do its job. Antacids, heart medicine, and antidepressants are just some of the medicines that might interact with a systemic therapy. Therefore, it is important to tell your doctor about any medications, vitamins, over-the-counter (OTC) drugs, herbals, or supplements you are taking. Bring a list with you to every visit.

#### Chemotherapy

Chemotherapy kills fast-growing cells throughout the body, including cancer cells and some normal cells. Chemotherapy is very effective for other types of cancers but is rarely used in the treatment of kidney cancer. It might be an option for treatment of some rare forms of non-clear cell RCC.

#### Targeted therapy

Targeted therapy focuses on specific or unique features of cancer cells. In kidney cancer, targeted therapies are used to stop or inhibit the action of molecules that help cancer cells grow. Targeted therapy is used to treat stage 4 (with or without metastases) kidney cancer or cancer that has returned (relapsed). Targeted therapy may have fewer side effects than other types of cancer treatment.

Targeted therapy drugs treat kidney cancer in different ways. Some target and block the signals that cause new blood vessels to form. Others block the signals that tell the kidney cancer cells to grow and make more cancer cells. Often, these drugs have more than one target. Targeted therapy drugs are named based on what they target.

There are 2 types of targeted therapy:

- Monoclonal antibodies affect the outside or surface of the cancer cell. A monoclonal antibody (mAb) is a lab-grown protein. There are many kinds of mAbs.
- Kinase inhibitors affect the inside of the cancer cell. Kinases move chemicals, called phosphates, from one molecule

to another. By transferring phosphates, kinases send signals that tell cells to grow. Kinase inhibitors block these signals.

There are 2 main targets of targeted therapy used in treating kidney cancer:

- Angiogenesis inhibitors target blood vessel growth by blocking vascular endothelial growth factor (VEGF).
- Mammalian target of rapamycin (mTOR) kinase inhibitors target cancer cell growth.

#### Tyrosine kinase inhibitors

Tyrosine kinase inhibitors (TKIs) block the signals that cause kidney cancer to grow and spread. Tyrosine kinases are proteins in cells that are important for many cell functions. This includes sending signals in cells for cell growth, survival, and death. TKIs do not rid the body of cancer. They stop cell growth.

There are many different types of tyrosine kinases. Each TKI works in a slightly different way.

- Some tyrosine kinases, such as VEGF, send signals that tell new blood vessels to grow into the tumor. Axitinib (Inlyta®) blocks VEGF. It is a VEGF receptor inhibitor.
- Some TKIs target and block more than one type of tyrosine kinase. These are called multi-kinase inhibitors. Many of the multi-kinase inhibitors also block VEGF receptors. Sunitinib (Sutent®), pazopanib (Votrient®), cabozantinib (Cabometyx™), and lenvatinib (Lenvima®) are multi-kinase inhibitors.

#### Helpful hint

There's a trick to knowing what drugs are used for. Look at the last few letters of the drug generic name.

- ✓ If it ends in -mab, it is an mAb.
- ✓ If it ends in -tinib, it is a TKI.
- ✓ If it ends in -limus, it is an mTOR.

#### mTOR kinase inhibitors

Mammalian target of rapamycin (mTOR) is a protein in cells that is important for cell growth and survival. mTOR moves chemicals, called phosphates, from one molecule to another. By transferring phosphates, mTOR sends signals that tell cells to grow and divide. An mTOR inhibitor blocks this signal.

Everolimus (Afinitor®) and temsirolimus (Torisel®) are a type of targeted therapy called mTOR kinase inhibitors that block mTOR from transferring the phosphate. This stops the cell from producing proteins important to RCC and receiving signals to grow and divide. By blocking the action of mTOR, these drugs slow tumor growth.

#### **Angiogenesis inhibitors**

Angiogenesis is the growth of new blood vessels. An angiogenesis inhibitor blocks this growth. Kidney cancer cells are very good at getting new blood vessels to grow into the tumor to "feed" it. Kidney cancer cells release high amounts of a protein called VEGF.

Bevacizumab (Avastin®), bevacizumab-bvzr (Zirabev™), and bevacizumab-awwb (MVASI®) are a type of mAb called an angiogenesis inhibitor. Bevacizumab stops VEGF from sending signals that tell new blood vessels to form. This slows or stops blood vessel growth and "starves" the tumor. Although bevacizumab targets tumor blood vessels, it can also affect normal blood vessels. This can result in side effects. A side effect is a problem caused by treatment.

A biosimilar might be used in place of bevacizumab. A biosimilar is a drug that is very much like one that has been approved by the U.S. Food and Drug Administration (FDA). It must be used in the exact same way and at the same dose as the other drug. Ask your doctor why one therapy might be chosen over another. The reason might be related to tumor mutations, cost, toxicity, or availability. Your wishes are also important.

#### **Immunotherapy**

Immunotherapy is a therapy that increases the activity of your immune system. By doing so, it improves your body's ability to find and destroy cancer cells. Immunotherapy can be given alone or with other types of treatment. It is used to treat stage 4 (with or without metastases) kidney cancer or cancer that has returned (relapsed).

For more information on checkpoint inhibitors and immunotherapy side effects, see *NCCN Guidelines for Patients: Immunotherapy Side Effects*, available at <a href="NCCN.org/">NCCN.org/</a> <a href="patientguidelines">patientguidelines</a>.

There are 2 types of immunotherapy used in treating kidney cancer:

- Monoclonal antibody therapy targeting immune checkpoints—also known as immune checkpoint inhibitors (ICIs)
- Cytokine therapy (used only in certain cases)

## Monoclonal antibody therapy targeting immune checkpoints

Antibody therapy or immune checkpoint inhibitory antibodies are used to help the body fight cancer, infection, or other diseases. Antibodies are proteins made by the immune system that bind to specific markers on cells or tissues. Monoclonal antibodies (mAbs) are a type of antibody made in a lab.

There are 4 immunotherapy mAbs that are approved to treat kidney cancer. All block immune checkpoints and are referred to as immune checkpoint inhibitors (ICIs).

#### These include:

- Pembrolizumab (Keytruda®) blocks the action of PD-1 (programmed death-1).
- Nivolumab (Opdivo®) targets PD-1.
- Ipilimumab (Yervoy®) blocks CTLA-4 (cytotoxic T-lymphocyte–associated protein 4).
- Avelumab (Bavencio<sup>®</sup>) blocks the action of PD-L1 (programmed death-ligand 1).

An Immunotherapy may be used with other immunotherapies or targeted therapies.

#### **Cytokine therapy**

Cytokines are proteins made by our immune system. Some cytokines stimulate the immune system and others slow it down. Interleukin (IL) and interferon are types of cytokine therapy made in a lab that are used only in rare cases for cancer treatment.

#### Radiation therapy

Radiation therapy (RT) uses high-energy radiation from x-rays, photons, electrons, and other sources to kill cancer cells and shrink tumors. RT may be used as supportive care or palliative care to help ease pain or discomfort caused by cancer.

Stereotactic body radiation therapy (SBRT) uses a machine to aim radiation beams at tumors in the body. The goal is to kill or ablate the tumor or metastasis. SBRT can be done with either photons or protons. With this method you will receive high-dose radiation for 1 to 5 treatments. SBRT is very precise, which reduces the chance of damage to nearby tissues.

#### Clinical trials

A clinical trial is a type of medical research study. After being developed and tested in a lab, potential new ways of fighting cancer need to be studied in people. If found to be safe and effective in a clinical trial, a drug, device, or treatment approach may be approved by the U.S. Food and Drug Administration (FDA).

Everyone with cancer should carefully consider all treatment options available for their cancer type, including standard treatments and clinical trials. Talk to your doctor about whether a clinical trial may make sense for you.

#### **Phases**

Most cancer clinical trials focus on treatment. Treatment trials are done in phases.

- Phase I trials study the dose, safety, and side effects of an investigational drug or treatment approach. They also look for early signs that the drug or approach is helpful.
- Phase II trials study how well the drug or approach works against a specific type of cancer.
- Phase III trials test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.
- Phase IV trials study the long-term safety and benefit of an FDA-approved treatment.



Finding a clinical trial

In the United States

NCCN Cancer Centers
NCCN.org/cancercenters

The National Cancer Institute (NCI)
<a href="mailto:cancer.gov/about-cancer/treatment/clinical-tri-als/search">cancer.gov/about-cancer/treatment/clinical-tri-als/search</a>

#### Worldwide

The U.S. National Library of Medicine (NLM)

clinicaltrials.gov/

#### Who can enroll?

Every clinical trial has rules for joining, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. These requirements ensure that participants are alike in specific ways and that the trial is as safe as possible for the participants.

#### Informed consent

Clinical trials are managed by a group of experts called a research team. The research team will review the study with you in detail, including its purpose and the risks and benefits of joining. All of this information is also provided in an informed consent form. Read the form carefully and ask questions before signing it. Take time to discuss with family, friends, or others whom you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.

#### Start the conversation

Don't wait for your doctor to bring up clinical trials. Start the conversation and learn about all of your treatment options. If you find a study that you may be eligible for, ask your treatment team if you meet the requirements. If you have already started standard treatment you may not be eligible for certain clinical trials. Try not to be discouraged if you cannot join. New clinical trials are always becoming available.

#### Frequently asked questions

There are many myths and misconceptions surrounding clinical trials. The possible benefits and risks are not well understood by many with cancer.

#### Will I get a placebo?

Placebos (inactive versions of real medicines) are almost never used alone in cancer clinical trials. It is common to receive either a placebo with a standard treatment, or a new drug with a standard treatment. You will be informed, verbally and in writing, if a placebo is part of a clinical trial before you enroll.

#### Do I have to pay to be in a clinical trial?

It depends on the study, your health insurance, and the state in which you live. The study drug is provided by and paid for by the clinical trial. Lab tests that are in addition to what is standard of care will be paid for by the study. However, routine standard of care items such as clinic visits, routine labs, and CT scans that would still be done if you were on a standard, approved treatment and not enrolled in a clinical trial are still billed to your insurance company. You would be responsible for these copays. Your treatment team and the research team can help determine if you are responsible for any costs.

#### Supportive care

Supportive care is health care that relieves symptoms caused by cancer or its treatment and improves quality of life. It might include pain relief (palliative care), emotional or spiritual support, financial aid, or family counseling. Supportive care is given during all cancer stages. Tell your care team how you are feeling and about any side effects. Best supportive care is used with other treatments to improve quality of life. Best supportive care, supportive care, and palliative care are often used interchangeably.

#### Bone health

Kidney cancer may spread to your bones. This puts your bones at increased risk for injury and disease. Such problems include bone fractures, bone pain, and squeezing (compression) of the spinal cord. High levels of calcium in the blood, called hypercalcemia, may also occur.

Medicine may be given to help relieve bone pain and reduce the risk of other bone problems. Some medicines work by slowing or stopping bone breakdown, while others help increase bone thickness. It is recommended that you take calcium and vitamin D with these bone health medicines.

#### **Bone metastases**

Bone metastases might be treated with palliative radiation therapy. Medicine to support bone health and to prevent broken bones might also be given.

#### **Distress**

Distress is an unpleasant experience of a mental, physical, social, or spiritual nature. It can affect how you feel, think, and act. Distress might include feelings of sadness, fear, helplessness, worry, anger, and guilt.

Depression, anxiety, and sleeping problems are common in cancer. Talk to your doctor and with those whom you feel most comfortable about how you are feeling. There are services and people who can help you. Support and counseling services are available.

For more information, see NCCN Guidelines for Patients: Distress During Cancer Care, available at NCCN.org/patientguidelines.

#### **Fatigue**

Fatigue is extreme tiredness and inability to function due to lack of energy. Fatigue may be caused by cancer or it may be a side effect of treatment. There are treatments for fatigue. Let your care team know how you are feeling and if fatigue is getting in the way of doing the things you enjoy. Eating a balanced diet, exercise, yoga, and massage therapy can help. You might be referred to a nutritionist or dietitian to help with fatigue.

#### Nausea and vomiting

Nausea and vomiting are a common side effect of treatment. You will be given medicine to prevent and treat nausea and vomiting.

For more information, see *NCCN Guidelines for Patients: Nausea and Vomiting*, available at <u>NCCN.org/patientguidelines</u>.

#### Pain

Tell your care team about any pain or discomfort. You might meet with a palliative care specialist or with a pain specialist to manage pain. Some people may benefit from palliative radiation therapy or ablation therapy to help relieve the pain. During this treatment, a radiation beam is focused on the tumor.

#### **Treatment side effects**

All cancer treatments can cause unwanted health issues. Such health issues are called side effects. Side effects depend on many factors. These factors include the drug type and dose, length of treatment, and the person. Some side effects may be harmful to your health. Others may just be unpleasant.

Ask for a complete list of side effects of your treatments. Also, tell your treatment team about any new or worsening symptoms. There may be ways to help you feel better. There are also ways to prevent some side effects.

#### **Trouble eating**

Sometimes side effects from surgery, cancer, or other treatments might cause you to feel not hungry or sick to your stomach (nauseated). You might have a sore mouth. Healthy eating is important during treatment. It includes eating a balanced diet, eating the right amount of food, and drinking enough fluids. A registered dietitian who is an expert in nutrition and food can help. Speak to your care team if you have trouble eating or maintaining your weight.

#### Keep a pain diary

A pain diary is a written record that helps you keep track of when you have pain, how bad it is, what causes it, and what makes it better or worse. Use a pain diary to discuss your pain with your care team. You might be referred to a specialist for pain management.

Include in your pain diary:

- · The time and dose of all medicines
- · When pain starts and ends or lessens
- Where you feel pain
- Describe your pain. Is it throbbing, sharp, tingling, shooting, or burning? Is it constant, or does it come and go?
- Does the pain change at different times of day? When?
- Does the pain get worse before or after meals? Does certain food or drink make it better?
- Does the pain get better or worse with activity? What kind of activity?
- Does the pain keep you from falling asleep at night? Does pain wake you up in the night?
- Rate your pain from 0 (no pain) to 10 (worst pain you have ever felt).
- Does pain get in the way of you doing the things you enjoy?

#### Key points

- Surgery is a main or primary treatment for kidney cancer.
- Active surveillance closely monitors tumor growth using imaging tests.
- Ablation uses extreme cold or extreme heat, radio waves, microwaves, or chemicals to destroy cancer cells.
- Systemic therapy works throughout the body. It includes chemotherapy, targeted therapy, and immunotherapy.
- Targeted therapies can block the ways cancer cells grow, divide, and move in the body.
- Immunotherapy uses your body's natural defenses to find and destroy cancer cells.
- Radiation therapy (RT) uses high-energy radiation from x-rays, gamma rays, protons, and other sources to kill cancer cells and shrink tumors.
- A clinical trial is a type of research that studies a treatment to see how safe it is and how well it works.
- Supportive care is health care that relieves symptoms caused by cancer or its treatment and improves quality of life. Supportive care is given with your cancer treatment.
- All cancer treatments can cause unwanted health issues called side effects. It is important for you to tell your care team about all your side effects so they can be managed.
- Pain may be treated with medication or radiation, with or without systemic therapy. A pain diary might help you manage pain.

It is important to tell your care team about all side effects so they can be managed.

# **5** Stages 1, 2, and 3

- 44 Overview
- 45 Stage 1a
- 46 Stage 1b
- 46 Stages 2 and 3
- 48 Key points



5

Usually, kidney cancer is treated with surgery. Depending on the stage, active surveillance or ablation might be options. After treatment, you will have follow-up care. Together, you and your doctor will choose a treatment plan and follow-up care that is best for you.

#### Overview

Usually, kidney cancer is treated with surgery.

In a partial nephrectomy, the tumor and tissue immediately surrounding the tumor are removed, leaving behind a stillfunctioning kidney. In a radical nephrectomy, the tumor with the whole kidney and the fatty tissue around the kidney are removed. The adrenal gland and nearby lymph nodes may also be removed.

Depending on the stage, active surveillance or ablation might be an option. After treatment, you will have follow-up care. No single follow-up plan is appropriate for everyone. Follow-up frequency and duration should be individualized, and may extend beyond 5 years. Treatment options for stages 1, 2, and 3 can be found in Guide 3.

Guide 3 Primary treatment options based on cancer stage						
Stage T1a	<ul> <li>Partial nephrectomy (preferred)</li> <li>Ablation</li> <li>Active surveillance</li> <li>Radical nephrectomy (in some cases)</li> </ul>		Followed by surveillance			
Stage T1b	<ul><li>Partial nephrectomy</li><li>Radical nephrectomy</li><li>Active surveillance (in some cases)</li></ul>	<b>→</b>	Followed by surveillance			
Stage 2	<ul><li>Partial nephrectomy</li><li>Radical nephrectomy</li></ul>	<b>→</b>	Followed by     Clinical trial     Surveillance			
Stage 3	<ul><li>Radical nephrectomy</li><li>Partial nephrectomy, if indicated</li></ul>	<b>→</b>	Followed by • If clear cell, clinical trial (preferred) • Surveillance			

#### Stage 1a

In stage 1a cancer, the tumor is 4 cm or smaller and found only in the kidney. A partial nephrectomy is the preferred treatment option. Ablation and active surveillance are also options. A radical nephrectomy would be used only in some cases. Follow-up care is described next.

#### **During active surveillance**

Those with tumors smaller than 2 cm in size are ideal candidates for active surveillance due to the low likelihood that the tumor will spread during observation. This may also be a good option for smaller tumors that are primarily cystic (fluid filled).

#### Active surveillance includes:

- Physical exam and health history, with blood and urine tests every year
- Abdominal CT or MRI with contrast within 6 months of stating surveillance, then CT, MRI, or ultrasound (US) at least every year
- A baseline and periodic chest x-ray or CT to look for lung metastases
- Other tests as needed based on symptoms, side effects, and other health concerns

#### After ablation

Follow-up care after ablation includes:

- Physical exam and health history, with blood and urine tests every year
- Abdominal CT or MRI with and without IV contrast at 1 to 6 months following ablation, then CT or MRI (preferred), or US annually for 5 years or longer as needed. If the patient is unable to receive IV contrast, MRI is preferred
- If there is imaging or other concerns for recurrence, then more frequent imaging, kidney tumor biopsy, or further treatment may be needed
- Chest x-ray or CT annually for 5 years in certain cases

## After a partial or radical nephrectomy Follow-up care after surgery includes:

- Physical exam and health history, with blood and urine tests every year
- Baseline abdominal CT or MRI (preferred), or US within 3 to 12 months of surgery, then annually for 3 years or longer as needed
- Chest x-ray or CT annually for at least 5 years, then as needed
- > Imaging tests might be given more often

#### Stage 1b

In stage 1b cancer, the tumor is larger than 4 cm but not larger than 7 cm in size and found only in the kidney. Treatment options include a partial or radical nephrectomy. Active surveillance might be an option in certain cases.

## After a partial or radical nephrectomy Follow-up care after surgery includes:

- Physical exam and health history, with blood and urine tests every year
- Baseline abdominal CT or MRI (preferred), or US within 3 to 12 months of surgery, then annually for 3 years or longer as needed
- Chest x-ray or CT annually for at least 5 years, then as needed
- Imaging tests might be given more often than described above.

#### Stages 2 and 3

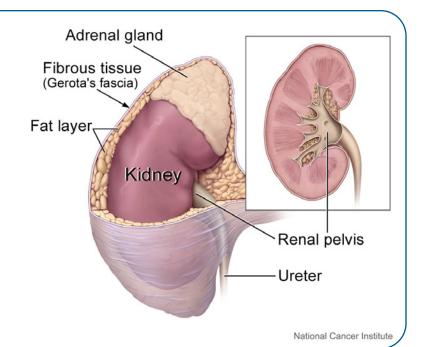
In stage 2 cancer, the tumor is larger than 7 cm and found only in the kidney. Treatment is a partial or radical nephrectomy.

In stage 3 kidney cancer, the tumor has grown outside the kidney into nearby veins and tissues, but has not grown into the adrenal gland or beyond Gerota's fascia. Cancer may or may not be spread to nearby lymph nodes. Cancer has not spread to distant sites. Stage 3 kidney cancer is treated with a radical nephrectomy. A partial nephrectomy might be an option in certain cases.

#### The kidney and adrenal gland

An adrenal gland sits on top of each kidney. The kidney and adrenal gland are surrounded by a layer of fatty tissue. Surrounding the fat is a layer of fibrous tissue called Gerota's fascia.

Derivative work of Kidney and Adrenal Gland by Alan Hoofring from NCI Visuals Online. Available at: https://visualsonline.cancer.gov/details.cfm?imageid=4355



#### Follow-up care

Follow-up care after surgery in stage 2 and 3 cancer includes:

- Physical exam with a health history every 3 to 6 months for 3 years, then annually up to 5 years, and as needed thereafter
- Comprehensive metabolic panel and other tests as needed every 3 to 6 months for 3 years, then annually up to 5 years, and as needed thereafter
- Baseline abdominal CT or MRI within 3 to 6 months, then CT or MRI (preferred), or US, every 3 to 6 months for at least 3 years and then annually up to 5 years
- Abdominal imaging beyond 5 years as needed
- Baseline chest CT within 3 to 6 months with continued imaging (CT preferred) every 3 to 6 months for at least 3 years and then annually up to 5 years
- > Imaging beyond 5 years as needed
- Additional imaging such as bone scan or brain imaging if having symptoms

#### After 5 years

Long-term follow-up care will include a physical exam and health history, along with imaging, blood, and urine tests. The goal of care is to monitor kidney function and watch for cancer return or metastatic disease. Those with hereditary RCC will likely need lifelong follow-up care.



# Let us know what you think!

Please take a moment to complete an online survey about the NCCN Guidelines for Patients.

NCCN.org/patients/response

#### Key points

- In stage 1a cancer, the tumor is 4 cm or smaller and found only in the kidney.
- In stage 1b cancer, the tumor is larger than 4 cm but not larger than 7 cm in size and found only in the kidney.
- In stage 2 kidney cancer, the tumor is larger than 7 cm and found only in the kidney. In stage 2A, the tumor is 7 cm to 10 cm in diameter. In stage 2B the tumor is larger than 10 cm.
- In stage 3 kidney cancer, the tumor has grown outside the kidney into nearby veins and tissues, but has not grown into the adrenal gland or beyond Gerota's fascia. Cancer may or may not be spread to nearby lymph nodes. Cancer has not spread to distant sites.
- Follow-up care will include a physical exam and health history, along with imaging, blood, and urine tests. The goal of care is to monitor kidney function and watch for cancer return or metastatic disease. Those with hereditary RCC will likely need lifelong follow-up care.

Need help paying for medicine or treatment?

Ask your care team what options are available.

# 6 Stage 4 and relapse

50 Stage 4
52 Relapse
54 Follow-up care
55 Disease progression
56 Key points



6

This chapter discusses treatment options for stage 4 and relapsed disease. Relapse is the return of cancer. In metastatic disease, cancer has spread to distant sites in the body. Not all stage 4 cancer is metastatic. Together, you and your doctor will choose a treatment plan that is best for you.

#### Stage 4

In stage 4 kidney cancer, the tumor has grown outside the kidney and Gerota's fascia and/or has spread to a distant site. Kidney cancer that has spread to a distant site is called metastatic RCC (mRCC). Not all stage 4 kidney cancer is metastatic. Non-metastatic stage 4 kidney cancer is called advanced RCC.

Treatment for stage 4 kidney cancer is based on your symptoms. If there are metastases, treatment will be based on the number and location of metastases.

#### Surgery is possible

If surgery is possible, then you might have cytoreductive nephrectomy or systemic therapy. In cytoreductive nephrectomy, all or part of the kidney with the tumor is removed. When there are many metastases, it is not always possible to remove them all. Removing the primary tumor may improve how well other treatments work against the remaining cancer and metastases. A cytoreductive nephrectomy is usually followed by a targeted therapy and/ or immunotherapy.

Systemic therapy is preferred in clear cell RCC with poor-risk features. Risk is based on your overall health, blood test results, and ability to perform daily tasks called performance status.

For clear cell systemic therapy options, see Guide 4.

#### Surgery is not possible

If surgery is not possible, then a sample of the tumor will be taken and tested to determine if the cancer is a clear cell or non-clear cell subtype. Subtype affects treatment options, which are described under <u>Relapse</u>.

#### **Next steps**

Treatment is the same as found under Relapse.

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#### First-line therapy options: Clear cell RCC

#### Favorable risk:

- · Axitinib with pembrolizumab
- · Cabozantinib with nivolumab
- Lenvatinib with pembrolizumab

#### **Preferred options**

#### Intermediate or poor risk:

- · Axitinib with pembrolizumab
- · Cabozantinib with nivolumab
- · Ipilimumab with nivolumab
- · Lenvatinib with pembrolizumab
- Cabozantinib

#### Other recommended

#### Favorable risk:

- · Axitinib with avelumab
- Cabozantinib
- · Ipilimumab with nivolumab
- Pazopanib
- Sunitinib

#### Intermediate or poor risk:

- · Axitinib with avelumab
- Pazopanib
- Sunitinib

#### **Used in some cases**

#### Favorable risk:

- · Active surveillance
- Axitinib
- High-dose IL-2 (must have excellent performance status and normal organ function)

#### Intermediate or poor risk:

Axitinib

#### Relapse

Recurrence or relapse is the return of cancer. Risk factors help estimate the risk of cancer recurrence and survival. These factors include overall performance status (activity level), blood counts, blood calcium and LDH levels, and the time from primary surgery to metastatic disease. If a person with metastatic RCC has no risk factors, they are considered favorable risk. If a person has 1 to 2 risk factors, they are considered intermediate risk. Those with 3 or more risk factors are considered poor risk.

Before starting treatment, a sample of your tumor will be tested to determine the subtype of renal cell carcinoma (RCC). When kidney cancer cells form new tumors in other parts of the body, it is referred to as oligometastatic disease. A biopsy might be taken of one or more of these metastases.

First-line therapies are tried first. Options are based on the systemic therapy you had before and your overall health. A biosimilar might be used in place of bevacizumab. A biosimilar is a drug that is very much like one that has been approved by the U.S. Food and Drug Administration (FDA). It must be used in the exact same way and at the same dose as the other drug. Ask your doctor why one therapy might be chosen over another. The reason might be related to tumor mutations, cost, toxicity, or availability. Your wishes are also important.

#### Clear cell

Treatment options include:

- Clinical trial
- First-line systemic therapy in Guide 4
- For oligometastatic disease, metastasectomy, radiation therapy, or ablation
- Best supportive care

First-line therapies are tried first. Options are based on the systemic therapy you had before and your overall health.

#### Non-clear cell

General treatment options for non-clear cell RCC include:

- Clinical trial (preferred)
- > Systemic therapy
- For oligometastatic disease, metastasectomy, radiation therapy, or ablation
- Best supportive care

Some information about specific subtypes of non-clear cell RCC:

- For collecting duct or medullary subtypes, it is possible that platinum-based chemotherapy might be used.
- For renal medullary carcinoma, platinumbased chemotherapy is preferred. Oral targeted therapies generally do not produce a response in those with renal medullary carcinoma.

For systemic therapy options for non-clear cell RCC, see Guide 5.

#### **Guide 5**

#### Systemic therapy options: Non-clear cell RCC

#### **Preferred options**

- Clinical trial
- Cabozantinib
- Sunitinib

### Other recommended

- · Lenvatinib with everolimus
- Nivolumab
- Pembrolizumab

#### Used in some cases

- Axitinib
- Bevacizumab
- Bevacizumab with erlotinib for selected patients with advanced papillary RCC including hereditary leiomyomatosis and renal cell carcinoma (HLRCC)-associated RCC
- · Bevacizumab with everolimus
- Erlotinib
- Everolimus
- Pazopanib
- Temsirolimus

#### Notes:

An FDA-approved biosimilar might be used for bevacizumab.

#### Follow-up care

Follow-up tests are used to monitor your health. No single follow-up plan is right for everyone. It will be based on your treatment, side effects, health issues, symptoms, and subtype of kidney cancer. Follow-up care will include blood and imaging tests. A baseline test is a starting point to which future tests are compared. After the baseline test, ongoing imaging tests are used to show if the cancer grows or shrinks over time. See Guide 6.

A biosimilar is a drug that is very much like one that has been approved by the FDA. It must be used in the exact same way and at the same dose as the other drug.

#### Guide 6

#### Follow-up care: Relapsed or stage 4 disease

Medical history and physical exam every 6 to 16 weeks for those receiving systemic therapy, or more frequently as needed and adjusted for type of systemic therapy being used

Blood and other lab tests as needed

Imaging of chest, abdomen, and pelvis:

- CT or MRI imaging as baseline prior to treatment or observation.
- Follow-up imaging every 6 to 16 weeks as needed. Time between imaging might be shorter or longer.

Possible imaging of head:

- MRI (preferred) or CT at baseline and as needed.
- · Annual surveillance scans as needed.

MRI of spine as needed

Bone scan as needed

#### Disease progression

When disease progresses, treatment options are clinical trial or systemic therapy and best supportive care. Supportive care is given to relieve the symptoms of cancer or side effects of cancer treatment. Best supportive care aims to improve quality of life and relieve any discomfort you may have. It may include surgery, systemic, or other treatments. Radiation therapy may be used to relieve pain from cancer that has spread to your bones or brain. Drugs that strengthen your bones may also help with pain and other problems caused by bone metastases.

#### Clear cell

Next-line or subsequent therapies are those tried after first-line therapies. You will have a different drug therapy than before. For next-line systemic therapy options in those with clear cell RCC, see Guide 7.

#### Non-clear cell

Systemic therapy for non-clear cell RCC can be found in Guide 5.

Guide 7 Next-line therapy options: Clear cell RCC					
Preferred options	<ul><li>Cabozantinib</li><li>Lenvatinib with everolimus</li><li>Nivolumab</li></ul>				
Other recommended	<ul> <li>Axitinib</li> <li>Axitinib with pembrolizumab</li> <li>Cabozantinib with nivolumab</li> <li>Ipilimumab with nivolumab</li> <li>Lenvatinib with pembrolizumab</li> <li>Pazopanib</li> <li>Sunitinib</li> <li>Tivozanib (if received 2 or more prior systemic therapies)</li> </ul>				
Used in some cases	<ul> <li>Everolimus</li> <li>Bevacizumab (or an FDA-approved biosimilar)</li> <li>High-dose IL-2 (must have excellent performance status and normal organ function)</li> <li>Temsirolimus</li> </ul>				

#### Key points

- In stage 4 kidney cancer, the tumor has grown outside the kidney and Gerota's fascia and/or has spread to a distant site.
- Kidney cancer that has spread to a distant site is called metastatic RCC (mRCC). Not all stage 4 kidney cancer is metastatic. Non-metastatic stage 4 kidney cancer is called advanced RCC.
- Treatment is based on your symptoms and clear cell or non-clear cell subtype. If there are metastases, treatment will be based on the number and location of metastases.
- Follow-up testing will monitor for relapse or disease progression.
- Supportive care is given to relieve the symptoms of cancer or side effects of cancer treatment.
- Best supportive care aims to improve quality of life and relieve any discomfort you may have. It may include radiation therapy, surgery, systemic therapy, or other treatments.



## We want your feedback!

Our goal is to provide helpful and easy-to-understand information on cancer.

Take our survey to let us know what we got right and what we could do better:

NCCN.org/patients/feedback

# **7**Hereditary RCC

- 58 Overview
- **60** Treatment
- 63 Key points



Certain genetic conditions can put you at risk for developing kidney cancer. This is called hereditary renal cell carcinoma (HRCC). Most people with confirmed HRCC are treated with kidney-sparing surgery. Other options might include ablation or systemic therapy, depending on the type of HRCC. Seek treatment with a doctor or hospital that is experienced in your type of HRCC.

 Hereditary paraganglioma/ pheochromocytoma (PGL/PCC) syndrome

For more information on HRCC, see Guide 8.

#### Overview

Kidney cancer often occurs for unknown reasons. Some people have genetic health conditions that increase the risk for developing kidney cancer. This is called hereditary renal cell carcinoma (HRCC).

HRCC is the result of mutations passed down from parent to child through genes. Those with one of the conditions listed below have a higher risk for kidney cancer. This accounts for only a small portion of kidney cancer cases.

- Von Hippel-Lindau (VHL) disease
- Hereditary papillary renal carcinoma (HPRC)
- Birt-Hogg-Dubé syndrome (BHDS)
- Tuberous sclerosis complex (TSC)
- Hereditary leiomyomatosis and renal cell carcinoma (HLRCC)
- BAP1 tumor predisposition syndrome (BAP1-TPDS)

#### Guide 8 Hereditary RCC types

Syndrome	Mutation	Common RCC subtype		
von Hippel-Lindau (VHL)	VHL gene	Clear cell		
Hereditary papillary renal carcinoma (HPRC)	<i>MET</i> gene	Type 1 papillary		
Birt-Hogg-Dubé syndrome (BHDS)	FLCN gene	Chromophobe, hybrid oncocytic tumors, papillary RCC		
Tuberous sclerosis complex (TSC)	TSC1 and TSC2 gene	Angiomyolipoma, clear cell		
Hereditary leiomyomatosis and renal cell carcinoma (HLRCC)	FH gene	HLRCC or <i>FH</i> -associated RCC/ type 2 papillary		
BAP1 tumor predisposition syndrome (BAP1-TPDS)	BAP1 gene	Clear cell, chromophobe		
Hereditary paraganglioma/ pheochromocytoma (PGL/PCC) syndrome	SDHA, SDHB, SDHC, and SDHD genes	Clear cell (not usually <i>SDHB</i> ), chromophobe, papillary type 2, renal oncocytoma, oncocytic neoplasm		

#### **Treatment**

Most with confirmed HRCC are treated with kidney-sparing surgery (partial nephrectomy). Other options might include ablation or systemic therapy, depending on the type of HRCC. Seek treatment with a doctor or hospital that is experienced in your type of HRCC.

#### **BAP1-TPDS**

*BAP1* tumor predisposition syndrome (*BAP1*-TPDS) is caused by mutations in the *BAP1* gene and is associated with increased risks for uveal and skin melanoma, mesothelioma, and RCC. There are no specific treatment guidelines for this syndrome.

#### Birt-Hogg-Dubé syndrome

Birt-Hogg-Dubé syndrome (BHDS) is associated with multiple non-cancerous (benign) skin tumors, lung cysts, and an increased risk of kidney lesions (cysts, benign tumors, and kidney cancer). When possible, a partial nephrectomy is the treatment of choice for kidney tumors. A person may have multiple tumors during their lifetime and, therefore, might have more than one surgery. This will be taken into consideration. Ablation may be an option if surgery is not possible or the best choice for your situation.

#### Hereditary leiomyomatosis and RCC

Hereditary leiomyomatosis and renal cell carcinoma (HLRCC) increases the risk for developing multiple smooth muscle tumors (leiomyomas) in the skin and uterus (fibroids), as well as an aggressive form of papillary kidney cancer. Since HLRCC tumors can be aggressive, surveillance is not recommended. A total radical nephrectomy should be

considered. There are no specific FDAapproved therapies for HLRCC. Treatment with erlotinib plus bevacizumab (or its biosimilar) has shown benefit in those with metastatic RCC from HLRCC.

#### Hereditary papillary renal carcinoma

Hereditary papillary renal carcinoma (HPRC) increases the risk of a type of kidney cancer known as papillary type 1 kidney cancer. Mutations in the *MET* gene cause abnormal cells to grow and spread in the body. Those with HPRC have an increased risk of multiple kidney tumors in one or both kidneys (also called bilateral kidney tumors). Currently, surgery is the primary method when a localized tumor reaches greater than 3 cm in size. When possible, a partial nephrectomy is the treatment of choice. A person may have multiple tumors during their lifetime and, therefore, might have more than one surgery. This will be taken into consideration when planning treatment. Ablation is also an option.

#### Hereditary paragangliomapheochromocytoma syndrome

Hereditary paraganglioma-pheochromocytoma (PGL/PCC) syndromes are characterized by paragangliomas and pheochromocytomas.

- Paragangliomas are tumors that arise from neuroendocrine tissues found along the spine from the base of the skull to the pelvis.
- Pheochromocytomas are a type of paraganglioma that is confined to the adrenal gland, a small hormoneproducing organ located on top of each kidney.

Paragangliomas and pheochromocytomas can occur in individuals with other inherited disorders, such as von Hippel-Lindau syndrome.

Malignant tumors without aggressive features and early stage should undergo surgical resection. A partial nephrectomy can be considered. For larger tumors and those with aggressive features (such as high grade or sarcomatoid), radical nephrectomy should be considered.

#### **Tuberous sclerosis complex**

Tuberous sclerosis complex (TSC) is characterized by the growth of numerous noncancerous (benign) tumors in many parts of the body. These tumors can occur in the skin, brain, kidneys, and other organs. Almost

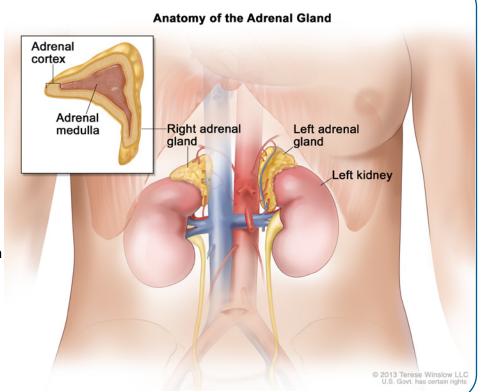
everyone with TSC has skin abnormalities. Kidney tumors are common in those with TSC. Partial nephrectomy is the treatment of choice for malignant (cancerous) kidney tumors, when possible. Ablation is also an option.

Renal angiomyolipoma is a benign lesion associated with TSC and is managed separately.

Everolimus is an FDA-approved therapy for asymptomatic, growing angiomyolipoma measuring larger than 3 cm in diameter.

# Hereditary paraganglioma-pheochromocytoma syndromes

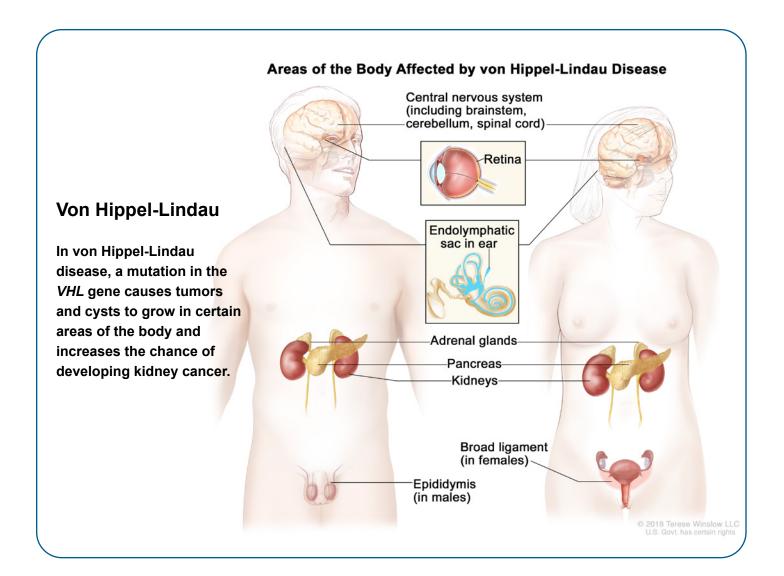
Pheochromocytomas are a type of paraganglioma that is confined to the adrenal gland, a small hormone-producing organ located on top of each kidney.



#### Von Hippel-Lindau

In von Hippel-Lindau (VHL) disease, a mutation in the *VHL* gene causes tumors and cysts to grow in certain areas of the body and increases the chance of developing kidney cancer and other cancers. The goal of treatment is to intervene at a time when there will be the most benefit and to limit the chance of developing metastatic disease. You should be referred to a hospital or cancer center with surgical expertise in complex partial nephrectomies and management of VHL.

Surgery has been the primary method when a localized tumor reaches greater than 3 cm in size. A person may have multiple tumors during their lifetime and, therefore, might have more than one surgery. This will be taken into consideration when planning treatment. Ablation may be an option if surgery is not possible. Belzutifan (Welireg<sup>™</sup>) was recently FDA approved for the treatment of VHL disease-related renal cell carcinomas, hemangioblastomas, and pancreatic neuroendocrine tumors and can be considered as an alternative to surgery. Pazopanib might be an option in some cases.



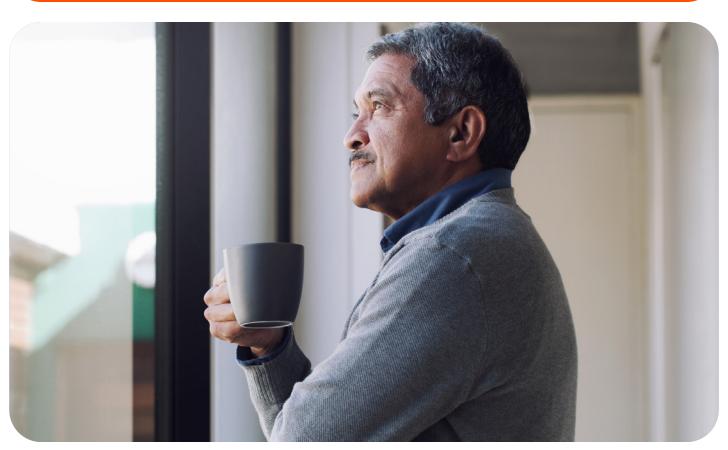
#### Key points

- Kidney cancer related to an inherited syndrome is called hereditary renal cell carcinoma (HRCC). There are several conditions that cause HRCC.
- Those who have HRCC should see their doctors often, especially if they have already been diagnosed with RCC. Regular imaging tests will look for new kidney tumors.
- Most with confirmed HRCC are treated with kidney-sparing surgery (partial nephrectomy). Other options might include ablation or systemic therapy, depending on the type of HRCC. Seek treatment with a doctor or hospital that is experienced in your type of HRCC.
- > BAP1 tumor predisposition syndrome (BAP1-TPDS) is caused by mutations in the BAP1 gene and is associated with increased risks for uveal and skin melanoma, mesothelioma, and RCC.
- Birt-Hogg-Dubé syndrome (BHDS) is associated with multiple non-cancerous (benign) skin tumors, lung cysts, and an increased risk of kidney lesions (cysts, benign tumors, and kidney cancer).
- Hereditary leiomyomatosis and renal cell carcinoma (HLRCC) increases the risk for developing multiple leiomyomas (smooth muscle tumors) in the skin and uterus (fibroids), as well as an aggressive form of papillary kidney cancer.
- Hereditary papillary renal carcinoma (HPRC) increases the risk of a type of kidney cancer known as papillary type 1 kidney cancer.

- Hereditary paragangliomapheochromocytoma (PGL/PCC) syndromes are characterized by paragangliomas and pheochromocytomas.
- Paragangliomas are tumors that arise from neuroendocrine tissues found along the spine from the base of the skull to the pelvis. Pheochromocytomas are a type of paraganglioma that is confined to the adrenal gland, a small hormoneproducing organ located on top of each kidney.
- Tuberous sclerosis complex (TSC) is characterized by the growth of numerous noncancerous (benign) tumors in many parts of the body.
- Von Hippel-Lindau (VHL) disease or VHL syndrome is caused by a mutation in the VHL gene.

# 8 Making treatment decisions

- 65 It's your choice
- 65 Questions to ask your doctors
- 74 Resources



It's important to be comfortable with the cancer treatment you choose. This choice starts with having an open and honest conversation with your doctor.

#### It's your choice

In shared decision-making, you and your doctors share information, discuss the options, and agree on a treatment plan. It starts with an open and honest conversation between you and your doctor.

Treatment decisions are very personal. What is important to you may not be important to someone else.

Some things that may play a role in your decision-making:

- What you want and how that might differ from what others want
- Your religious and spiritual beliefs
- Your feelings about certain treatments like surgery or chemotherapy
- Your feelings about pain or side effects such as nausea and vomiting
- Cost of treatment, travel to treatment centers, and time away from school or work
- Quality of life and length of life
- How active you are and the activities that are important to you

Think about what you want from treatment. Discuss openly the risks and benefits of specific treatments and procedures. Weigh options and share concerns with your doctor.

If you take the time to build a relationship with your doctor, it will help you feel supported when considering options and making treatment decisions.

#### **Second opinion**

It is normal to want to start treatment as soon as possible. While cancer can't be ignored, there is time to have another doctor review your test results and suggest a treatment plan. This is called getting a second opinion, and it's a normal part of cancer care. Even doctors get second opinions!

Things you can do to prepare:

- Check with your insurance company about its rules on second opinions. There may be out-of-pocket costs to see doctors who are not part of your insurance plan.
- Make plans to have copies of all your records sent to the doctor you will see for your second opinion.

#### **Support groups**

Many people diagnosed with cancer find support groups to be helpful. Support groups often include people at different stages of treatment. Some people may be newly diagnosed, while others may be finished with treatment. If your hospital or community doesn't have support groups for people with cancer, check out the websites listed in this book.

#### Questions to ask your doctors

Possible questions to ask your doctors are listed on the following pages. Feel free to use these questions or come up with your own. Be clear about your goals for treatment and find out what to expect from treatment.

### Questions to ask about testing and staging

1.	What tests will I have? How often will they be repeated? Will my insurance pay for these tests?
2.	When will I have a biopsy? Will I have more than one? What are the risks?
3.	How will my biopsy be performed? What else might be done at this time?
4.	How soon will I know the results and who will explain them to me?
5.	Who will talk with me about the next steps? When?
6.	What biomarker tests will I have? When? Will I have genetic testing?
7.	What will you do to make me comfortable during testing?
8.	Is my cancer resectable or unresectable? What does this mean?
9.	Is my cancer early stage, locally advanced, or metastatic?
10	.What type and subtype of kidney cancer do I have? Is this type common? Does the tumor have any rare features?
11	. Is the cancer in any other areas like my liver, lung, or bone?
12	.What does my stage mean in terms of length of survival and quality of life?

#### Questions to ask your doctors about their experience

1. What is your experience treating kidney cancer? 2. What is the experience of those on your team? 3. Do you only treat kidney cancer? What else do you treat? 4. How many patients like me (of the same age, gender, race) have you treated? 5. Will you be consulting with experts to discuss my care? Whom will you consult? 6. How many procedures like the one you're suggesting have you done? 7. Is this treatment a major part of your practice? 8. How many of your patients have had complications? What were the complications? 9. How many kidney cancer surgeries have you done? 10. Who will manage my day-to-day care?

#### Questions to ask about options

- 1. What will happen if I do nothing?
- 2. How do my age, overall health, and other factors affect the options?
- 3. Am I a candidate for a clinical trial? Can I join a clinical trial at any time?
- 4. Which option is proven to work best for my cancer, age, and other risk factors?
- 5. Does any option offer long-term cancer control? Are the chances any better for one option than another? Less time-consuming? Less expensive?
- 6. Can my cancer be cured? If so, what are the chances it will return?
- 7. Which treatment will give me the best quality of life? Which treatment will extend life? By how long?
- 8. What are my options if the treatment stops working?
- 9. Can I stop treatment at any time? What will happen if I stop treatment?
- 10. Is there a social worker or someone who can help me decide?
- 11. Is there a hospital or treatment center you can recommend for kidney cancer treatment? Can I go to one hospital for surgery and a different center for systemic or radiation therapy?

#### Questions to ask about treatment

- 1. How will my age, general health, cancer stage, and other health conditions limit my treatment choices?
- 2. What are my treatment choices? What are the benefits and risks? Which treatment do you recommend and why?
- 3. What can I do to prepare for treatment? Should I stop taking my medications? Should I store my blood in case I need a transfusion?
- 4. How much will the treatment cost? How much will my insurance pay for treatment?
- 5. What are the chances my cancer will return? How will it be treated if it returns?
- 6. Does the order of treatment matter?
- 7. How long do I have to decide about treatment?
- 8. Does this hospital or center offer the best treatment for me?
- 9. When will I start treatment? How long will treatment take?
- 10. I would like a second opinion. Is there someone you can recommend?
- 11. How will treatment affect my ability to do things I enjoy?
- 12. Which supportive services and support groups do you recommend?

#### Questions to ask about side effects

- 1. What are the side effects of systemic therapy? Surgery? Radiation therapy?
- 2. What are the side effects of kidney cancer?
- 3. How long will these side effects last? Do any side effects lessen or worsen in severity over time?
- 4. What side effects should I watch for? What side effects are expected and which are life threatening?
- 5. When should I call the doctor? Can I text? What should I do on weekends and other non-office hours?
- 6. What emergency department or ER should I go to? Will my treatment team be able to communicate with the ER team?
- 7. What medicines can I take to prevent or relieve side effects?
- 8. What can I do to help with pain and other side effects?
- 9. Will you stop treatment or change treatment if there are side effects? What do you look for?
- 10. What can I do to lessen or prevent side effects? What will you do?

11.\	Nhat	medicines	may	worsen	side	effects	of	treatm	nent?
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## Questions to ask about surgery

- 1. Which type of surgery do you recommend? How often do you perform this type of surgery?
- 2. Is laparoscopic or robotic surgery an option? Am I at risk for chronic kidney disease?
- 3. How much of my tumor will be removed? How much of my kidney will be removed?
- 4. What other organs or tissues might be removed during surgery? What will this mean in terms of my survival and recovery?
- 5. How will some of my other medical issues potentially affect my surgery or my risk of complications? Can I do anything before surgery to decrease these risks?
- 6. Will I have or need more than one surgery?
- 7. Will the incision be on my front, side, or back?
- 8. Does my cancer involve any veins or arteries? How might this affect surgery?
- 9. How long will it take me to recover from surgery?
- 10. How much pain will I be in? What will be done to manage my pain?
- 11. What is the chance that this surgery will shorten my life?
- 12. What other side effects can I expect from surgery? What complications can occur from this surgery?
- 13. What treatment will I have before, during, or after surgery? What will this treatment do?

## Questions to ask about radiation therapy

1. What type of radiation therapy (RT) will I have? 2. What will you target? 3. What is the goal of this RT? 4. How many treatment sessions will I require? Can you do a shorter course of RT? 5. Do you offer this type of RT here? If not, can you refer me to someone who does? 6. What side effects can I expect from RT? 7. Should I eat or drink before RT? 8. Will I be given medicine to help me relax during RT? 9. What should I wear?

## Questions to ask about clinical trials

1. What clinical trials are available for my type and stage of kidney cancer? 2. Has the treatment been used before? Has it been used for other types of cancer? 3. What are the risks and benefits of this treatment? 4. What side effects should I expect? How will the side effects be controlled? 5. How long will I be in the clinical trial? 6. Will I be able to get other treatment if this doesn't work? 7. How will I know if the treatment is working? 8. Will the clinical trial cost me anything? If so, how much? 9. What type of long-term follow-up care will I have?

#### Resources

#### **American Cancer Society**

cancer.org/cancer/kidneycancer/index

<u>cancer.org/content/dam/cancer-org/cancer-ontrol/en/worksheets/pain-diary.pdf</u>

#### Cancer Care

cancercare.org

#### **Cancer Support Community**

cancersupportcommunity.org

#### Chemocare

chemocare.com

#### **KCCure**

kccure.org

## **Kidney Cancer Association**

kidneycancer.org

#### **Kidney Cancer Coalition**

kidneycan.org

## **International Kidney Cancer Coalition**

ikcc.org

#### **Lab Tests Online**

labtestsonline.org

#### **MedlinePlus**

medlineplus.gov/genetics/condition

medlineplus.gov/kidneycancer.html

## **My Survival Story**

mysurvivalstory.org

#### **National Cancer Institute**

cancer.gov/types/kidney

# National Coalition for Cancer Survivorship

canceradvocacy.org/toolbox

# National Hospice and Palliative Care Organization

caringinfo.org

## **National Kidney Foundation**

kidney.org

#### OncoLink

oncolink.org

## **Radiological Society of North America**

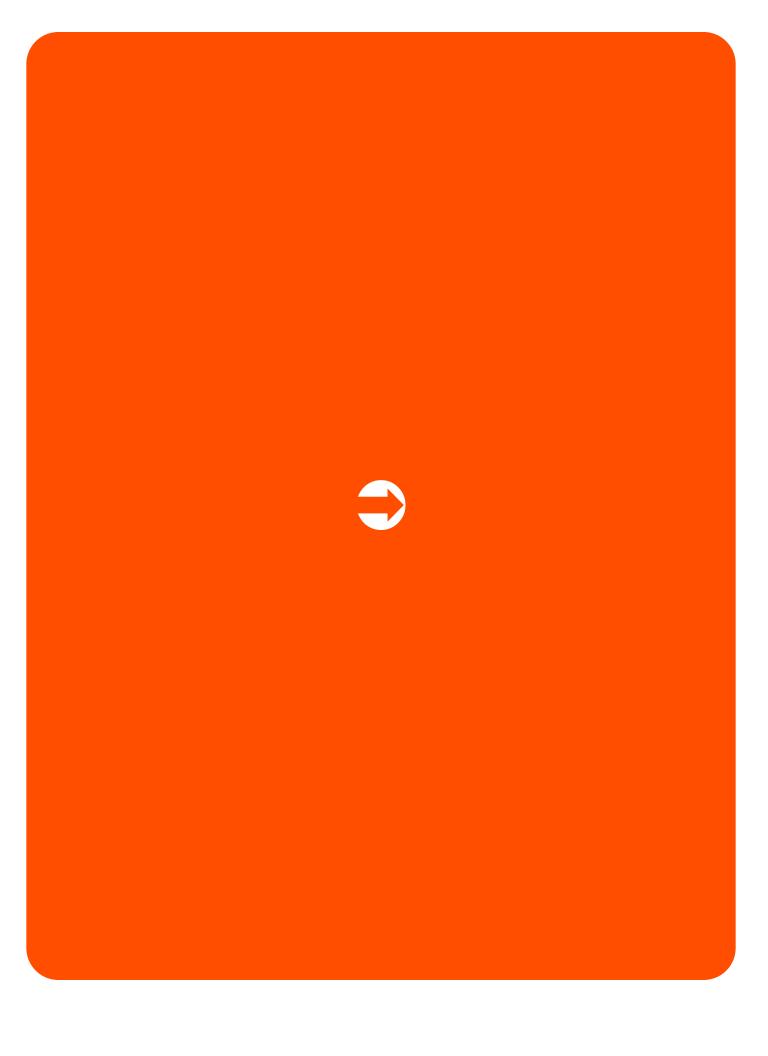
radiologyinfo.org

#### **Smart Patients**

smartpatients.com

#### **Urology Care Foundation**

<u>urologyhealth.org/urologic-conditions/kidney-</u>cancer



## Words to know

#### active surveillance

Frequent and ongoing testing to watch for cancer growth without giving active treatment.

#### adrenal gland

A small organ on top of each kidney that makes hormones.

#### adrenalectomy

Surgery that removes the adrenal gland. The adrenal gland might be removed in a radical nephrectomy.

#### alkaline phosphatase (ALP)

A protein found in most tissues in the body.

#### angiogenesis

The growth of new blood vessels.

#### angiogenesis inhibitor

A drug that blocks the growth of new blood vessels that feed cancer cells.

#### baseline

A starting point to which future test results are compared.

#### best supportive care

Treatment to improve quality of life and relieve discomfort.

#### biopsy

Removal of small amounts of tissue from the body to be tested for disease.

#### biosimilar

A drug that is very much alike or the same as another drug that has been approved by the U.S. Food and Drug Administration (FDA).

#### bone scan

An imaging test that uses radioactive material to check for cancer or damage in bones.

#### calcium

A mineral needed for healthy teeth, bones, and other body tissues.

#### cancer burden

The amount or extent of cancer in the body.

#### cancer stage

A rating of the growth and spread of cancer in the body.

#### cancer staging

The process of rating and describing the extent of cancer in the body.

#### carcinoma

Cancer that starts in cells that form the lining of organs and structures in the body.

#### chromophobe RCC (cRCC)

Subtype of RCC (renal cell carcinoma) based on how the cancer cells look when viewed with a microscope.

#### clear cell RCC (ccRCC)

The most common subtype of RCC (renal cell carcinoma) based on how the cancer cells look when viewed with a microscope. Also shown as ccRCC.

#### clinical trial

Research on a test or treatment to assess its safety or how well it works.

#### collecting duct RCC (cdRCC)

Subtype of RCC (renal cell carcinoma) based on how the cancer cells look when viewed with a microscope.

#### contrast

A chemical put into your body to make clearer pictures during imaging tests.

#### creatinine

A waste product of muscles that is filtered out of blood into urine by the kidneys.

#### cytokines

Proteins made naturally in the body or in a lab that boost or activate the immune system.

#### cytokine therapy

Treatment with drugs that are cytokines proteins made in a lab that boost or activate the immune system to fight cancer.

#### cytoreductive nephrectomy (CN)

Surgery to remove the primary tumor and the kidney when cancer that has spread to distant sites can't all be removed.

# cytotoxic T-lymphocyte-associated protein 4 (CTLA-4)

An immune system protein.

#### distant recurrence

Cancer that has come back after treatment and is found in a part of the body far from the first (primary) tumor.

#### first-line treatment

The first drug or set of drugs given to treat cancer.

#### general anesthesia

A controlled loss of wakefulness from drugs.

#### Gerota's fascia

The outer layer of fibrous tissue that surrounds the kidney.

#### interleukin-2 (IL-2)

A type of immunotherapy.

#### imaging test

Tests that make pictures of the inside of the body.

#### immune system

The body's natural defense against infection and disease.

#### immunotherapy

Treatment that activates or boosts the body's natural defense against disease (immune system) to fight cancer.

#### kinase inhibitors

A type of targeted therapy.

#### laparoscopic surgery

Surgery that uses small tools and a laparoscope—a thin tube with a light and camera at the end—inserted through a few small cuts in the belly area.

#### local recurrence

Cancer that has come back after treatment in or near the same place as the first (primary) tumor.

#### lymph nodes

Small groups of special disease-fighting cells located throughout the body.

#### lymph vessels

Tubes that carry lymph—a clear fluid containing white blood cells that fight disease and infection—throughout the body and connect lymph nodes to one another.

#### medical oncologist

A doctor who's an expert in treating cancer with drugs.

#### metastasectomy

Surgery to remove tumors that formed far from the first site of cancer. Used to reduce cancer burden and to ease symptoms.

#### metastasis

The spread of cancer cells from the first tumor to another body part.

#### monoclonal antibody (mAb)

A type of immune system protein made in a lab that can attach to substances in the body such as cancer cells. Can be a type of immunotherapy and a type of targeted therapy.

#### mammalian target of rapamycin (mTOR)

A protein in cells that sends chemical signals for cell growth and survival.

#### mTOR inhibitor

A drug that blocks the action of mTOR—a protein in cells that sends chemical signals for cell growth and survival. A type of targeted therapy.

#### nephrectomy

Surgery that removes a kidney.

#### non-clear cell RCC (nccRCC)

Subtypes of RCC (renal cell carcinoma) other than clear cell, based on how the cancer cells look when viewed with a microscope.

#### palliative care

Treatment for symptoms of a disease. Also sometimes called supportive care.

#### palliative nephrectomy

Surgery to remove the kidney to help relieve symptoms caused by cancer.

#### palliative surgery

Surgery that is used to relieve symptoms caused by the cancer.

#### papillary RCC (PRCC)

Most common type of RCC.

#### partial nephrectomy

Surgery to remove a tumor with part of the kidney.

#### pathologist

A doctor who's an expert in testing cells and tissue to find disease.

#### programmed death-ligand 1 (PD-L1)

An immune system protein found on some cancer cells.

#### programmed death receptor-1 (PD-1)

An immune system protein found on some cancer cells.

#### primary treatment

The main treatment used to rid the body of cancer.

#### primary tumor

The first mass of cancer cells in the body.

#### prognosis

The likely or expected course and outcome of a disease.

#### radiation oncologist

A doctor who's an expert in treating cancer with radiation.

#### radiation therapy (RT)

Use of high-energy rays to destroy cancer cells.

#### radical nephrectomy

Surgery that removes a tumor with the whole kidney, the fatty tissue around the kidney, and possibly the attached adrenal gland and nearby lymph nodes.

#### radiologist

A doctor who's an expert in reading imaging tests—tests that make pictures of the inside of the body.

#### radiotracer

A substance that releases small amounts of energy (radiation) that is put into the body to make pictures clearer.

#### receptor

A protein inside or on the surface of cells to which substances can attach to cause a certain effect in the cell.

#### recurrence

The return of cancer after treatment. Also called a relapse.

#### relapse

The return of cancer after treatment. Also called a recurrence.

#### renal artery

The blood vessel that carries blood into the kidney.

#### renal cell carcinoma (RCC)

The most common type of kidney cancer. It starts in the cells that line the renal tubules—tiny tubes that filter blood and make urine.

#### renal pelvis

The space in the middle of the kidneys where urine collects before leaving the kidneys though long, thin tubes called ureters.

#### renal sarcoma

Cancer that starts in the blood vessels or connective tissue of the kidneys.

#### renal tubules

Tiny tubes in the kidneys that filter blood and make urine from the waste and extra water filtered out of blood.

#### renal vein

The blood vessel that carries clean blood out of the kidney.

#### resection

Surgery to remove a tumor.

#### staging

The process of rating and describing the extent of cancer in the body.

#### stereotactic body radiation therapy (SBRT)

Radiation therapy given in higher doses to smaller areas over 1 to 5 sessions of treatment.

#### subtype

Smaller groups that a type of cancer is divided into based on how the cancer cells look under a microscope.

#### supportive care

Treatment given to relieve the symptoms of a disease. Also called palliative care.

#### surveillance

Monitors for the return of cancer.

#### targeted therapy

Treatment with drugs that target a specific or unique feature of cancer cells.

#### thermal ablation

Treatment that destroys tumors using extreme heat or extreme cold.

#### treatment plan

A written course of action through cancer treatment and beyond.

#### tumor

An abnormal mass formed by the overgrowth of cells.

#### tyrosine kinase

A type of protein in cells that is important for many cell functions, such as sending signals for cell growth and survival.

#### tyrosine kinase inhibitor (TKI)

A targeted therapy that blocks the action of tyrosine kinases—proteins in cells that send signals for cells to grow, divide, and survive.

#### ultrasound (US)

A test that uses sound waves to take pictures of the inside of the body.

#### U.S. Food and Drug Administration (FDA)

A federal government agency that regulates drugs and food in the United States.

#### ureter

A long, thin tube that carries urine from the kidney to the bladder.

#### urethra

The tube that carries urine from the bladder to outside the body.

#### urinalysis

A test that assesses the content of urine using a microscope and chemical tests.

#### Words to know

#### urinary system

The group of organs that removes waste from the body in the form of urine. It is made up of the kidneys, ureters, bladder, and urethra.

#### urologist

A doctor who is an expert in treating diseases of the urinary system in males and females and sex organs in males.

vascular endothelial growth factor (VEGF) A protein that binds to cells that form blood vessels, said vej-eff.

#### vena cava

The main, large vein that carries blood back to the heart.

von Hippel-Lindau (VHL) disease VHL gene helps control cell growth, cell division, and other important cell functions.



## Take our <u>survey</u>

And help make the NCCN Guidelines for Patients better for everyone!

NCCN.org/patients/comments

## **NCCN Contributors**

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Kidney Cancer, Version 2.2022. It was adapted, reviewed, and published with help from the following people:

Dorothy A. Shead, MS Senior Director Patient Information Operations Tanya M. Fischer, MEd, MSLIS Medical Writer Susan Kidney Senior Graphic Design Specialist

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Kidney Cancer, Version 2.2022 were developed by the following NCCN Panel Members:

\*Robert J. Motzer, MD/Chair Memorial Sloan Kettering Cancer Center

\*Eric Jonasch, MD/Vice-chair The University of Texas MD Anderson Cancer Center

Neeraj Agarwal, MD Huntsman Cancer Institute at the University of Utah

Ajjai Alva, MBBS University of Michigan Rogel Cancer Center

Michael Baine, MD
Fred & Pamela Buffet Cancer Center

Kathryn Beckermann, MD, PhD Vanderbilt-Ingram Cancer Center

Maria I. Carlo, MD Memorial Sloan Kettering Cancer Center

Toni K. Choueiri, MD Dana-Farber/Brigham and Women's Cancer Center

Brian A. Costello, MD, MS Mayo Clinic Cancer Center

Ithaar H. Derweesh, MD UC San Diego Moores Cancer Center

Arpita Desai, MD UCSF Helen Diller Family Comprehensive Cancer Center

Yasser Ged, MBBS
The Sidney Kimmel Comprehensive Cancer
Center at Johns Hopkins

Saby George, MD Roswell Park Comprehensive Cancer Center

John L. Gore, MD, MS Fred Hutchinson Cancer Research Center/ Seattle Cancer Care Alliance Naomi Hass, MD Abramson Cancer Center at the University of Pennsylvania

Steven L. Hancock, MD Stanford Cancer Institute

Payal Kapur, MD UT Southwestern Simmons Comprehensive Cancer Center

Christos Kyriakopoulos, MD University of Wisconsin Carbone Cancer Center

\*Elaine T. Lam, MD University of Colorado Cancer Center

Primo N. Lara, MD UC Davis Comprehensive Cancer Center

Clayton Lau, MD City of Hope National Medical Center

Bryan Lewis
Kidney Cancer Coalition

David C. Madoff, MD Yale Cancer Center/Smilow Cancer Hospital

\*Brandon Manley, MD Moffitt Cancer Center

M. Dror Michaelson, MD, PhD Massachusetts General Hospital Cancer Center

\*Amir Mortazavi, MD
The Ohio State University Comprehensive
Cancer Center - James Cancer Hospital
and Solove Research Institute

Lakshminarayanan Nandagopahl, MD O'Neal Comprehensive Cancer Center at UAB Phillip M. Pierorazio, MD The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

Elizabeth R. Plimack, MD, MS Fox Chase Cancer Center

Lee Ponsky, MD Case Comprehensive Cancer Center/ University Hospitals Seidman Cancer Center and Cleveland Clinic Taussig Cancer Institute

Sundhar Ramalingam, MD Duke Cancer Institute

Brian Shuch, MD UCLA Jonsson Comprehensive Cancer Center

Zachary L. Smith, MD Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine

\*Jeffrey Sosman, MD Robert H. Lurie Comprehensive Cancer Center of Northwestern University

#### NCCN Staff

Mary Dwyer, MS
Director, Guidelines Operations

Elizabeth Hollinger, BSN, RN Guidelines Layout Specialist

Angela Motter, PhD Oncology Scientist/Medical Writer

<sup>\*</sup> Reviewed this patient guide. For disclosures, visit <a href="NCCN.org/disclosures.">NCCN.org/disclosures.</a>

## **NCCN Cancer Centers**

Abramson Cancer Center at the University of Pennsylvania Philadelphia, Pennsylvania 800.789.7366 • pennmedicine.org/cancer

Fred & Pamela Buffett Cancer Center Omaha, Nebraska 402.559.5600 • unmc.edu/cancercenter

Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer
Center and Cleveland Clinic Taussig
Cancer Institute
Cleveland, Ohio
800.641.2422 • UH Seidman Cancer Center
uhhospitals.org/services/cancer-services
866.223.8100 • CC Taussig Cancer Institute
my.clevelandclinic.org/departments/cancer
216.844.8797 • Case CCC
case.edu/cancer

City of Hope National Medical Center Los Angeles, California 800.826.4673 • cityofhope.org

Dana-Farber/Brigham and
Women's Cancer Center |
Massachusetts General Hospital
Cancer Center
Boston, Massachusetts
617.732.5500
youhaveus.org
617.726.5130
massgeneral.org/cancer-center

Duke Cancer Institute

Durham, North Carolina

888.275.3853 • dukecancerinstitute.org

Fox Chase Cancer Center *Philadelphia, Pennsylvania* 888.369.2427 • foxchase.org

Huntsman Cancer Institute at the University of Utah Salt Lake City, Utah 800.824.2073 huntsmancancer.org

Fred Hutchinson Cancer Research Center/Seattle Cancer Care Alliance Seattle, Washington 206.606.7222 • seattlecca.org 206.667.5000 • fredhutch.org The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins Baltimore, Maryland 410.955.8964

www.hopkinskimmelcancercenter.org

Robert H. Lurie Comprehensive Cancer Center of Northwestern University Chicago, Illinois 866.587.4322 • cancer.northwestern.edu

Mayo Clinic Cancer Center Phoenix/Scottsdale, Arizona Jacksonville, Florida Rochester, Minnesota 480.301.8000 • Arizona 904.953.0853 • Florida 507.538.3270 • Minnesota

Memorial Sloan Kettering Cancer Center New York, New York 800.525.2225 • mskcc.org

mayoclinic.org/cancercenter

Moffitt Cancer Center Tampa, Florida 888.663.3488 • moffitt.org

The Ohio State University Comprehensive Cancer Center -James Cancer Hospital and Solove Research Institute Columbus, Ohio 800.293.5066 • cancer.osu.edu

O'Neal Comprehensive Cancer Center at UAB Birmingham, Alabama 800.822.0933 • uab.edu/onealcancercenter

Roswell Park Comprehensive Cancer Center Buffalo, New York 877.275.7724 • roswellpark.org

Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine St. Louis, Missouri 800.600.3606 • siteman.wustl.edu

St. Jude Children's Research Hospital/ The University of Tennessee Health Science Center Memphis, Tennessee 866.278.5833 • stjude.org 901.448.5500 • uthsc.edu Stanford Cancer Institute Stanford, California 877.668.7535 • cancer.stanford.edu

UC Davis Comprehensive Cancer Center Sacramento, California 916.734.5959 • 800.770.9261 health.ucdavis.edu/cancer

UC San Diego Moores Cancer Center La Jolla, California 858.822.6100 • cancer.ucsd.edu

UCLA Jonsson Comprehensive Cancer Center Los Angeles, California 310.825.5268 • cancer.ucla.edu

UCSF Helen Diller Family Comprehensive Cancer Center San Francisco, California 800.689.8273 • cancer.ucsf.edu

University of Colorado Cancer Center Aurora, Colorado 720.848.0300 • coloradocancercenter.org

University of Michigan Rogel Cancer Center Ann Arbor, Michigan 800.865.1125 • rogelcancercenter.org

The University of Texas MD Anderson Cancer Center Houston, Texas 844.269.5922 • mdanderson.org

University of Wisconsin Carbone Cancer Center Madison, Wisconsin 608.265.1700 • uwhealth.org/cancer

UT Southwestern Simmons Comprehensive Cancer Center Dallas, Texas 214.648.3111 • utsouthwestern.edu/simmons

Vanderbilt-Ingram Cancer Center Nashville, Tennessee 877.936.8422 • vicc.org

Yale Cancer Center/ Smilow Cancer Hospital New Haven, Connecticut 855.4.SMILOW • yalecancercenter.org

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# Kidney Cancer

2022

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