

Kidney Cancer Treatment

If you've been diagnosed with kidney cancer, your cancer care team will discuss your treatment options with you. It's important to weigh the benefits of each treatment option against its possible risks and side effects. For some people with early-stage cancers, it's important to discuss if treatment is needed at all, since active surveillance can sometimes be a good option.

Local treatments

Local therapies treat the tumor but don't affect the rest of the body. They are more likely to be useful for earlier stage (less advanced) cancers, although they might also be used in some other situations.

- Surgery for Kidney Cancer
- Ablation and Other Local Therapy for Kidney Cancer
- Active Surveillance for Kidney Cancer
- Radiation Therapy for Kidney Cancer

Systemic treatments

Kidney cancer can also be treated by giving medicines by mouth or directly into the bloodstream. These are called **systemic therapies** because they can reach cancer cells almost anywhere in the body. These treatments can be helpful for more advanced kidney cancers, although they might also be used to help treat some earlier stage cancers. Different types of drugs might be used.

- Targeted Drug Therapy for Kidney Cancer
- Immunotherapy for Kidney Cancer
- Chemotherapy for Kidney Cancer

Common treatment approaches

Depending on the <u>stage of the cancer</u> and other factors, different types of treatment may be combined at the same time or used one after another. Some treatments can also be used as palliative treatment. <u>Palliative treatment</u> is meant to relieve symptoms, such as pain, but it is not expected to cure the cancer.

• Treatment of Kidney Cancer by Stage

Who treats kidney cancer?

Doctors on your cancer treatment team might include:

- A **urologist:** a doctor and surgeon who specializes in treating diseases of the urinary system (and male reproductive system)
- A radiation oncologist: a doctor who treats cancer with radiation therapy
- A **medical oncologist:** a doctor who treats cancer with medicines such as chemotherapy, targeted therapy, or immunotherapy
- a nephrologist: a doctor who treats diseases of the kidney

You might have many other specialists on your treatment team as well, including physician assistants (PAs), nurse practitioners (NPs), nurses, psychologists, nutritionists, social workers, and other health professionals.

Health Professionals Who Are Part of a Cancer Care Team

Making treatment decisions

It's important for you and your doctor to discuss all treatment options, including their goals and possible side effects, to help you make the decision that best fits your needs. You may feel that you need to make a decision quickly, but it's important to give yourself time to absorb the information you have learned. Ask your cancer care team questions.

If time permits, it is often a good idea to seek a second opinion. A second opinion can give you more information and help you feel more confident about the treatment plan you choose.

Questions to Ask About Kidney Cancer

<u>Seeking a Second Opinion</u>

Thinking about taking part in a clinical trial

Clinical trials are carefully controlled research studies that are done to get a closer look at promising new treatments or procedures. Clinical trials are one way to get state-of-the art cancer treatment. In some cases they may be the only way to get access to newer treatments. They are also the best way for doctors to learn better methods to treat cancer.

If you would like to learn more about clinical trials that might be right for you, start by asking your doctor if your clinic or hospital conducts clinical trials.

• Clinical Trials

Considering complementary and alternative methods

You may hear about alternative or complementary methods to relieve symptoms or treat your cancer that your doctors haven't mentioned. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

Complementary methods are treatments that are used **along with** your regular medical care. **Alternative** treatments are used **instead of** standard medical treatment. Although some of these methods might be helpful in relieving symptoms or helping you feel better, many have not been proven to work. Some might even be harmful.

Be sure to talk to your cancer care team about any method you are thinking about using. They can help you learn what is known (or not known) about the method, which can help you make an informed decision.

<u>Complementary and Integrative Medicine</u>

Help getting through cancer treatment

People with cancer need support and information, no matter what stage of illness they may be in. Knowing all of your options and finding the resources you need will help you make informed decisions about your care.

Whether you are thinking about treatment, getting treatment, or not being treated at all,

you can still get supportive care to help with pain or other symptoms. Communicating with your cancer care team is important so you understand your diagnosis, what treatment is recommended, and ways to maintain or improve your quality of life.

Different types of programs and support services may be helpful, and they can be an important part of your care. These might include nursing or social work services, financial aid, nutritional advice, rehab, or spiritual help.

The American Cancer Society also has programs and services - including rides to treatment, lodging, and more - to help you get through treatment. Call our Cancer Knowledge Hub at 1-800-227-2345 and speak with one of our caring, trained cancer helpline specialists. Or, if you prefer, you can use our chat feature on cancer.org to connect with one of our specialists.

- Palliative Care
- Programs & Services

Choosing to stop treatment or choosing no treatment at all

For some people, when treatments have been tried and are no longer controlling the cancer, it could be time to weigh the benefits and risks of continuing to try new treatments. Whether or not you continue treatment, there are still things you can do to help maintain or improve your quality of life.

Some people, especially if the cancer is advanced, might not want to be treated at all. There are many reasons you might decide not to get cancer treatment, but it's important to talk to your doctors as you make that decision. Remember that even if you choose not to treat the cancer, you can still get supportive care to help with pain or other symptoms.

If Cancer Treatments Stop Working

The treatment information given here is not official policy of the American Cancer Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor. Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask your cancer care team any questions you may have about your treatment options.

Surgery for Kidney Cancer

Surgery is often part of the main treatment for kidney cancer. Sometimes it might be the only treatment that's needed, especially for cancers that are still only in the kidney.

- Types of surgery for kidney cancer
- Radical nephrectomy
- Partial nephrectomy (nephron-sparing surgery)
- Lymphadenectomy (lymph node removal)
- Removal of metastases
- Risks and side effects of surgery
- More information about Surgery

Types of surgery for kidney cancer

Depending on the stage and location of the cancer and other factors, different types of surgery might be done.

- For tumors in the kidney, surgery might be done to remove the entire kidney (known as a **radical nephrectomy**) or the just the part of the kidney with the tumor (known as a **partial nephrectomy**).
- Sometimes, nearby lymph nodes might also be removed (known as a **lymphadenectomy**).
- If the cancer has spread (metastasized), sometimes surgery might be an option to remove the tumor(s) in another part of the body.

Some people whose cancer has spread to other organs may be helped by surgery to take out the kidney tumor. This might also help with symptoms such as pain or bleeding.

Radical nephrectomy

In this operation, the surgeon removes the kidney, the fatty tissue and Gerota's fascia around the kidney, and some nearby lymph nodes. Sometimes the adrenal gland on top of the kidney is removed as well, especially if there's a high risk of the cancer spreading there (such as if there's a larger tumor in the upper part of the kidney).

Open radical nephrectomy

This operation is done through a single, long incision in the skin to reach the kidney.

The surgeon can make the incision in several places. The most common places are the middle of the abdomen (belly), under the ribs on the same side as the cancer, or in the back, just behind the kidney. Each approach has its benefits in treating cancers of different sizes and in different parts of the kidney.

If the tumor has grown from the kidney through the renal vein (the vein leading away from the kidney) and into the inferior vena cava (the large vein that carries blood from the lower part of the body back up to the heart), the heart may need to be stopped for a short time in order to remove the tumor. The patient is put on cardiopulmonary bypass (a heart-lung machine) that circulates their blood while bypassing their heart. If you need this, a heart surgeon will work with your urologist during your operation.

Laparoscopic nephrectomy and robotic-assisted laparoscopic nephrectomy

These operations are done through several small incisions instead of one large one. If a radical nephrectomy is needed, many doctors and patients now prefer to use these methods when they can be done.

Laparoscopic nephrectomy: For this approach, the surgeon inserts special long, thin instruments through the small incisions to remove the kidney. One of the instruments is a laparoscope, which is a long tube with a small video camera on the end. This lets the surgeon see inside the abdomen. Usually, one of the incisions has to be made longer toward the end of the operation to remove the kidney (although it's not as long as the incision for an open radical nephrectomy).

Robotic-assisted laparoscopic nephrectomy: In this approach, the surgeon sits at a panel near the operating table and controls robotic arms with long, thin surgical instruments on the ends. The robotic system lets the surgeon move the instruments more easily and with more precision than during standard laparoscopic surgery.

Both types of laparoscopic surgery are complex and take time for surgeons to learn. If you are considering either type of laparoscopic surgery, be sure to find a surgeon with a lot of experience.

In experienced hands, either type of laparoscopic nephrectomy is about as effective as an open radical nephrectomy. The main benefits of these approaches are that they usually result in a shorter hospital stay, a faster recovery time, and less pain after surgery. However, the laparoscopic approach may not be a good option for larger tumors or for tumors that have grown into the renal vein or spread to lymph nodes around the kidney.

Partial nephrectomy (nephron-sparing surgery)

In a partial nephrectomy, the surgeon removes only the part of the kidney that contains the cancer, leaving the rest of the kidney in place. The benefit of this approach is that the person keeps more kidney function. Studies have shown the long-term results from partial nephrectomy are about the same as when the whole kidney is removed.

For people with early-stage kidney cancer, a partial nephrectomy might be a good option if:

- The kidney tumor is smaller usually less than about 10 centimeters (about 4 inches) across, and it isn't in the central part of the kidney.
- A person already has (or is likely to have) reduced kidney function, for example if they only have one working kidney, if they have tumors in both kidneys, if they're at risk for some type of chronic kidney disease, or if they have an <u>inherited condition</u>¹ that increases their risk of more kidney tumors later on.

A partial nephrectomy might **not** be an option if:

- The tumor is very large.
- The tumor is in the central part of the kidney.
- There is more than one tumor in the same kidney.
- The tumor has reached the renal vein or inferior vena cava, or the cancer has spread to the lymph nodes or distant organs.

Partial nephrectomy typically is a more complex operation than a radical nephrectomy, so it should only be done by a doctor with experience.

As with a radical nephrectomy, this operation can be done in different ways.

Open partial nephrectomy

For an open partial nephrectomy, the surgeon operates through one long incision in the skin. The surgeon can make the incision in several places, depending on factors like the location of the tumor.

Laparoscopic partial nephrectomy and robotic-assisted laparoscopic partial nephrectomy

These operations are done through several small incisions instead of one large one.

Laparoscopic partial nephrectomy: For this approach, the surgeon inserts special long, thin instruments through the small incisions to remove the kidney. One of the instruments is a laparoscope, which is a long tube with a small video camera on the end that lets the surgeon see inside the abdomen.

Robotic-assisted laparoscopic partial nephrectomy: In this approach, the surgeon sits at a panel near the operating table and controls robotic arms with long, thin surgical instruments on the ends. The surgeon can move the instruments more easily and with more precision than during standard laparoscopic surgery.

Done by an experienced surgeon, either type of laparoscopic partial nephrectomy is about as effective as an open partial nephrectomy. The main benefits of these approaches are that they usually result in a shorter hospital stay, a faster recovery time, and less pain after surgery.

However, both types of laparoscopic partial nephrectomy are complicated operations, and the laparoscopic approach may not be a good option for more complex kidney tumors.

It also takes time for surgeons to learn how to do these operations. If you are considering either type of laparoscopic surgery, be sure to find a surgeon with experience.

Lymphadenectomy (lymph node removal)

In this procedure, the surgeon removes nearby lymph nodes to see if they contain cancer. Some lymph nodes near the kidney are often removed as part of a radical nephrectomy.

A more extensive lymphadenectomy in which more lymph nodes are removed (known as a **lymph node dissection**) may be done if the tumor has features suggesting it is at high risk of spreading to the nodes, such as if it has a higher <u>grade</u>². Lymph nodes are also removed if they look enlarged on imaging tests or feel abnormal during the operation.

Some doctors might also remove these lymph nodes to check them for cancer spread even when they aren't enlarged, to help better <u>stage</u>³ the cancer. This might affect whether a person should get further (adjuvant) treatment after surgery.

Removal of metastases

In some people with kidney cancer, the cancer has already spread (metastasized) to other parts of the body by the time it's found. The most common sites of spread are the lungs, lymph nodes, bones, and liver. For some people, surgery to remove these tumors may still be helpful.

Attempting a surgical cure

If the cancer has spread to very few spots outside the kidney that can all be removed safely, surgery to remove these tumors may lead to long-term survival in some people.

The metastasis may be removed at the same time as a radical nephrectomy or later if the cancer <u>recurs</u>⁴ (comes back).

Surgery to relieve symptoms (palliative surgery)

If other treatments are no longer helpful, surgery might be done to help relieve pain or other symptoms caused by tumors, although this type of surgery isn't intended to cure the cancer.

Risks and side effects of surgery

The short-term risks of any type of surgery include reactions to anesthesia, bleeding (which might require blood transfusions), blood clots, and infections. Most people will have at least some pain after the operation, which can usually be helped with pain medicines, if needed.

Other possible risks of surgery include:

- Damage to organs and blood vessels (such as the spleen, pancreas, aorta, vena cava, or large or small bowel) during surgery
- Pneumothorax (unwanted air in the chest space around the lungs)
- Incisional hernia (bulging of internal organs near the surgical incision due to problems with wound healing)
- Leakage of urine into the abdomen (after partial nephrectomy)
- Kidney failure (if the remaining kidney fails to function well)

Ask your doctor what to expect after surgery. You might want to ask about your

recovery time, if there are any limits on what you can do, common side effects to watch out for, and when you should contact someone on your cancer care team if you're having problems.

More information about Surgery

For more general information about surgery as a treatment for cancer, see <u>Cancer</u> Surgery⁵.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u>⁶.

Hyperlinks

- 1. <u>www.cancer.org/cancer/types/kidney-cancer/causes-risks-prevention/risk-factors.html</u>
- 2. <u>www.cancer.org/cancer/types/kidney-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 3. <u>www.cancer.org/cancer/types/kidney-cancer/detection-diagnosis-</u> staging/staging.html
- 4. www.cancer.org/cancer/survivorship/long-term-health-concerns/recurrence.html
- 5. <u>www.cancer.org/cancer/managing-cancer/treatment-types/surgery.html</u>
- 6. <u>www.cancer.org/cancer/managing-cancer/side-effects.html</u>

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Ablation and Other Local Therapy for Kidney Cancer

Whenever possible, surgery is the main treatment for kidney cancer that can be removed. But for some people, such as those who aren't healthy enough for surgery, other treatments can sometimes be used to destroy (ablate) the kidney tumor.

These methods are usually only considered for small kidney tumors (typically no larger than 4 cm or about 1½ inches across).

These treatments might be helpful for some people, although there is much less data on how well they work over time than there is for surgery.

- Cryotherapy (cryoablation)
- Radiofrequency ablation (RFA)
- Other local treatments

Cryotherapy (cryoablation)

Cryotherapy uses extreme cold to destroy a tumor.

For this treatment, a hollow probe (needle) is inserted into the tumor, either through the skin (percutaneously) or during laparoscopy (in which a long, thin tube with a tiny video camera on the end is inserted into the abdomen through a small incision). Very cold gases are then passed through the probe, creating an ice ball at its tip that destroys the tumor.

To be sure the tumor is destroyed without too much damage to nearby tissues, the doctor carefully watches images of the tumor during the procedure (with <u>ultrasound</u>¹, <u>CT</u>², or <u>MRI</u>³scans) or measures the temperature of the nearby tissues.

The type of anesthesia used for cryotherapy depends on how the procedure is being done.

Possible side effects include bleeding and damage to the kidneys or other nearby organs.

Radiofrequency ablation (RFA)

Radiofrequency ablation (RFA) uses high-energy radio waves to heat and destroy the tumor. A thin, needle-like probe is placed through the skin and moved forward until the end is in the tumor. Placement of the probe is guided by ultrasound or CT scan. Once it is in place, an electric current is passed through the tip of the probe. This heats the tumor and destroys the cancer cells.

RFA is usually done as an outpatient procedure, using local anesthesia (numbing medicine) where the probe is inserted. You may be given medicine to help you relax as well.

Major complications are uncommon, but they can include bleeding and damage to the kidneys or other nearby organs.

Other local treatments

Other, newer types of local treatments might also be used to destroy tumors in the

kidney (or possibly in other parts of the body). These approaches haven't been around as long as cryotherapy or RFA, so there's less long-term data on them at this point. Still, they might be options for some people.

Microwave ablation

For this treatment, imaging tests are used to guide a needle-like probe (antenna) into the tumor. Electromagnetic microwaves are then created at the tip of the probe to heat to destroy the tumor.

Stereotactic ablative body radiotherapy (SABR)

Also known as **stereotactic body radiation therapy (SBRT)**, this is a type of advanced radiation therapy. Imaging tests are used to guide thin beams of radiation at the tumor from many different angles. SABR can usually be given over the course of a few treatments.

To learn more, see Radiation Therapy for Kidney Cancer.

Irreversible electroporation

For this treatment, imaging tests are used to guide long needles (electrodes) into place around the tumor. The needles are then used to create a strong electrical field within the tumor. This causes holes (pores) to form in the walls of the cancer cells, leading to their death.

This approach doesn't use heat or cold to destroy the cells, and it might prove to be useful in areas where it's important to protect vital structures like nearby blood vessels. But many doctors feel that more research is needed to show it is safe and effective.

Hyperlinks

- 1. <u>www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/ultrasound-for-</u> cancer.html
- 2. <u>www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/ct-scan-for-</u> <u>cancer.html</u>
- 3. www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/mri-for-cancer.html

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Active Surveillance for Kidney Cancer

Not all kidney tumors need to be treated right away. Some small kidney tumors turn out to be benign (not cancer). And even many small kidney cancers tend to grow slowly, without spreading.

One option for some people with small kidney tumors may be to watch the tumor carefully to see if it grows, without treating it right away. This is usually done with regular <u>imaging tests</u>¹ (ultrasound, CT or MRI scans) of the abdomen (belly). Blood tests and imaging tests of the chest might be done at times as well. If the tumor starts growing quickly or shows other worrisome signs, it can then be removed with surgery or treated another way.

Sometimes, the tumor might be biopsied to help determine if it is cancer or not. This could help determine if surveillance is a reasonable option, or if the tumor needs to be

treated.

Active surveillance might be a good choice for people who are older or who have other serious health problems, as it can allow them to avoid the risks of treatments such as surgery or ablation.

If a <u>biopsy</u>²hasn't been done, watching the tumor closely for a while can also give the doctor a better idea of whether it is likely to be cancer, based on how fast it is growing.

Hyperlinks

- 1. www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests.html
- 2. www.cancer.org/cancer/diagnosis-staging/tests/biopsy-and-cytology-tests.html

References

Campbell S, Uzzo RG, Allaf ME, et al. Renal Mass and Localized Renal Cancer: AUA Guideline. *J Urol*. 2017; 198:520-529.

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Radiation Therapy for Kidney Cancer

Radiation therapy uses high-energy rays or particles to kill cancer cells.

- When is radiation therapy used for kidney cancer?
- How is radiation therapy given?
- · Possible side effects of radiation therapy
- More information about radiation therapy

When is radiation therapy used for kidney cancer?

Radiation therapy isn't usually the first treatment for kidney cancer. But it might be an option if:

- The cancer is still only in the kidney, but a person isn't healthy enough for (or doesn't want to have) surgery or has only one kidney. Sometimes other ablative treatments might be tried before radiation.
- The cancer has spread, but there are no more than a few tumors in other parts of the body. Radiation might be an option to try to destroy these tumors, although other treatments, such as surgery or other ablative techniques, might be options as well.
- The cancer returns after treatment, especially if it has spread more widely. In this situation, radiation might be an option to help relieve (palliate) symptoms caused by tumors in some parts of the body, such as the brain or bones. This type of treatment is known as **palliative radiation therapy**.

How is radiation therapy given?

When radiation therapy is used to treat kidney cancer, a special machine is used to create and focus beams of radiation at the tumor. This type of treatment is known as <u>external beam radiation therapy (EBRT)</u>¹.

Each treatment is much like getting an x-ray, although the radiation dose is stronger. The treatment itself is painless and typically lasts only a few minutes, although the setup time — getting you into place for treatment — takes longer.

When treating a tumor in the kidney or a small area of cancer spread (such as a single

tumor in a lung), radiation is usually given as **stereotactic body radiation therapy (SBRT)**, also known as **stereotactic ablative body radiotherapy (SABR)**.

For this advanced type of EBRT, imaging tests are used to guide the delivery of thin beams of radiation to a precise area, such as a kidney tumor, from many different angles. Large doses of radiation can be given in each dose, so the entire course of treatment can often be given in just a few days.

SBRT is often known by the names of the machines that deliver the radiation, such as Gamma Knife, X-Knife, CyberKnife, or Clinac.

Possible side effects of radiation therapy

<u>Side effects</u>² of radiation therapy might include:

- Skin changes (similar to sunburn) and hair loss where the radiation passes through the skin
- Nausea or diarrhea (when radiation is aimed at the abdomen)
- Feeling tired

Other side effects are also possible, depending on where the radiation is aimed.

Most side effects go away shortly after treatment is finished, but some might last longer.

Radiation may also make side effects from some other treatments worse.

If you're getting radiation, ask a member of your cancer care team what side effects to expect.

More information about radiation therapy

To learn more about how radiation is used to treat cancer, see <u>Radiation Therapy</u>³.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u>⁴.

Hyperlinks

- 1. <u>www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/x-rays-and-other-radiographic-tests.html</u>
- 2. <u>www.cancer.org/cancer/managing-cancer/treatment-types/radiation/effects-on-</u> <u>different-parts-of-body.html</u>
- 3. www.cancer.org/cancer/managing-cancer/treatment-types/radiation.html
- 4. <u>www.cancer.org/cancer/managing-cancer/side-effects.html</u>

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⁵Atkins MB. Overview of the treatment of renal cell carcinoma. UpToDate. 2023. Accessed at https://www.uptodate.com/contents/overview-of-the-treatment-of-renal-cell-carcinoma on December 13, 2023.

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Targeted Drug Therapy for Kidney Cancer

As researchers have learned more about the gene and protein changes inside cells that cause them to become cancer cells, they have developed drugs that target some of these changes. These targeted drugs are different from

standard chemotherapy (chemo) drugs. They tend to work better against kidney cancer than standard chemo drugs, and they often have different side effects.

- When are targeted drugs used for kidney cancer?
- Targeted drugs used to treat kidney cancer
- More information about targeted therapy

When are targeted drugs used for kidney cancer?

Treating advanced kidney cancer

Targeted drugs are used mainly to treat advanced kidney cancer. One of these drugs is typically part of the first treatment for advanced cancers, often along with an immunotherapy drug.

Many different targeted drugs can be used to treat kidney cancer. If one doesn't work, another can be tried. It's not yet clear if one sequence of drugs is better than another. Studies are being done to help answer this.

Adjuvant therapy after surgery

The targeted drug sunitinib (Sutent) might also be an option as an **adjuvant treatment** after surgery to remove the kidney, to help lower the risk that the cancer will come back.

Targeted drugs used to treat kidney cancer

Most of the targeted drugs used to treat kidney cancer work by blocking proteins called **tyrosine kinases** inside cancer cells that normally help them grow, or that help them create new blood vessels that feed the tumor. Drugs that target these types of proteins are known as **tyrosine kinase inhibitors**, or **TKIs**.

Drugs that target tumor blood vessel growth (angiogenesis)

Sunitinib (Sutent)

Sunitinib acts by blocking both angiogenesis and several tyrosine kinases in cancer cells that are important for their growth and survival.

This drug is a pill taken daily, typically for 4 weeks on and 2 weeks off. Some doctors might recommend taking it 2 weeks on and 1 week off to reduce side effects.

Sunitinib can be used in people with advanced kidney cancer. It might also be an option

after surgery in people with a high risk of their cancer returning, to help lower the risk that the cancer will come back, although an immunotherapy drug such as pembrolizumab (Keytruda) is more likely to be used in this situation instead.

The most common side effects of sunitinib are:

- Nausea
- Diarrhea
- Changes in skin or hair color
- Mouth sores
- Weakness
- · Low white and red blood cell counts

Other possible effects include feeling tired, high blood pressure, heart problems, bleeding, hand-foot syndrome, and low thyroid hormone levels.

Pazopanib (Votrient)

Pazopanib blocks several tyrosine kinases involved in cancer cell growth, as well as the formation of new blood vessels in the tumor. This drug is a pill, typically taken once a day.

Common side effects of pazopanib include:

- High blood pressure
- Nausea
- Diarrhea
- Headaches
- Low blood cell counts
- Hair color change

It can cause abnormal liver function test results, but it rarely leads to severe liver damage that could be life threatening. Problems with bleeding, clotting, and wound healing can occur, as well.

In rare cases it can also cause a problem with the heart rhythm or even heart failure. If you are taking this drug, your doctor will monitor your heart with EKGs as well as check your blood tests for liver or other problems.

Cabozantinib (Cabometyx)

Cabozantinib blocks several tyrosine kinases that help cancer cells grow and survive, as well as some that help form new blood vessels in the tumor.

This drug can be used to treat advanced kidney cancer, either by itself or along with the immunotherapy drug nivolumab (Opdivo). It is taken as a pill, typically once a day.

Common side effects of cabozantinib include:

- Diarrhea
- Fatigue (feeling tired)
- Nausea and vomiting
- Poor appetite and weight loss
- High blood pressure
- Hand-foot syndrome
- Constipation

Less common but more serious side effects can include serious bleeding, blood clots, very high blood pressure, severe diarrhea, and holes forming in the intestines.

Lenvatinib (Lenvima)

Lenvatinib is a tyrosine kinase inhibitor that helps block new blood vessels from forming in the tumor, as well as targeting some of the proteins in cancer cells that normally help them grow.

This drug can be used along with the immunotherapy drug pembrolizumab in people with advanced kidney cancer. It can also be used with the targeted drug everolimus (see below). Lenvatinib is a capsule typically taken once a day.

Common side effects of lenvatinib include:

- Diarrhea
- Fatigue
- Joint or muscle pain
- · Loss of appetite
- Nausea and vomiting
- Mouth sores
- Weight loss

- High blood pressure
- Swelling in the arms or legs

Less common but more serious side effects can include serious bleeding, blood clots, very high blood pressure, severe diarrhea, holes forming in the intestines, and kidney, liver, or heart failure.

Bevacizumab (Avastin)

Bevacizumab works by slowing the growth of new blood vessels. It can be used to treat advanced kidney cancer, either alone or along with another drug. It is most often used after other drug treatments have been tried.

It is given by infusion into a vein (IV), typically once every 2 weeks.

More common side effects of bevacizumab include:

- High blood pressure
- Feeling tired
- Headaches

Less common but possibly serious side effects include bleeding, blood clots, holes forming in the intestines, heart problems, and slow wound healing.

Axitinib (Inlyta)

Axitinib blocks several tyrosine kinases that help form new blood vessels in the tumor.

This drug can be used alone or with certain immunotherapy drugs, like pembrolizumab or avelumab, as a treatment for people with advanced kidney cancer. Axitinib is a pill, typically taken twice a day.

Common side effects of axitinib include:

- High blood pressure
- Fatigue (feeling tired)
- Nausea and vomiting
- Diarrhea
- Poor appetite

- Weight loss
- Voice changes
- Hand-foot syndrome
- Constipation
- Changes in liver and thyroid function (which can be seen on lab tests)

A small number of people develop blood pressure high enough to be life-threatening. This drug can also cause problems with bleeding, clotting, and wound healing.

Tivozanib (Fotivda)

Tivozanib blocks several tyrosine kinases involved in cancer cell growth and the formation of new blood vessels in the tumor.

This drug can be used in people with advanced kidney cancer.

Tivozanib is a pill, typically taken daily for 3 weeks followed by 1 week off. This cycle is then repeated for as long as the drug is still helpful.

Common side effects of tivozanib include:

- High blood pressure
- Diarrhea
- Nausea
- Poor appetite
- Cough
- Mouth sores
- Feeling tired
- Voice changes

Less common but more serious side effects can include heart problems, life threatening high blood pressure, blood clots, bleeding, poor wound healing, abnormal thyroid tests, and damage to the kidney.

Belzutifan (Welireg)

Belzutifan is a *HIF inhibitor*. It blocks a protein called hypoxia-inducible factor 2 alpha (HIF-2a), which is involved in both cancer cell growth and new blood vessel formation in tumors.

Belzutifan can be used:

In people with <u>von Hippel-Lindau (VHL) disease¹</u> who have kidney cancer and don't need surgery right away.

• In people with advanced kidney cancer that has already been treated with a different targeted drug and with an immune checkpoint inhibitor (a type of immunotherapy drug).

This drug is taken as pills, typically once a day.

Common side effects of belzutifan include:

- Low red blood cell counts (anemia)
- Feeling tired and/or dizzy
- Nausea
- Headache
- Increased blood sugar levels
- Changes in lab tests showing the drug might be affecting the kidneys

Less common but more serious side effects can include very low red blood cell counts (severe anemia, which might require blood transfusions), and low oxygen levels in the body, for which you might need oxygen therapy or even be admitted to the hospital.

Drugs that target the mTOR protein

Temsirolimus (Torisel)

Temsirolimus works by blocking a protein known as **mTOR**, which normally helps cells grow and divide.

This drug can be used to treat advanced kidney cancers. It is usually used after other drug treatments have been tried. Temsirolimus is given by intravenous (IV) infusion, typically once a week.

The most common side effects of temsirolimus include:

- Skin rash
- Weakness

- Mouth sores
- Nausea
- Loss of appetite
- Fluid buildup in the face or legs
- Increases in blood sugar and cholesterol levels

Rarely, it can cause more serious side effects.

Everolimus (Afinitor)

Everolimus also blocks the mTOR protein.

This drug can be used to treat advanced kidney cancers. It can be used by itself or along with the targeted drug lenvatinib (see above), typically after at least one other drug treatment has been tried.

Everolimus is taken as a pill, typically once a day.

Common side effects of everolimus include

- Mouth sores
- An increased risk of infections
- Nausea
- Loss of appetite
- Diarrhea
- Skin rash
- Feeling tired or weak
- Fluid buildup (usually in the legs)
- Increases in blood sugar and cholesterol levels

A less common but serious side effect is lung damage, which can cause shortness of breath or other problems.

More information about targeted therapy

To learn more about how targeted drugs are used to treat cancer, see <u>Targeted Cancer</u> <u>Therapy</u>².

To learn about some of the side effects listed here and how to manage them,

see Managing Cancer-related Side Effects³.

Hyperlinks

- 1. <u>www.cancer.org/cancer/types/kidney-cancer/causes-risks-prevention/risk-factors.html</u>
- 2. www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy.html
- 3. <u>www.cancer.org/cancer/managing-cancer/side-effects.html</u>

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Immunotherapy for Kidney Cancer

Immunotherapy is the use of medicines to boost a person's own immune system to recognize and destroy cancer cells more effectively. Different types of immunotherapy can be used to treat kidney cancer.

- Immune checkpoint inhibitors
- Possible serious side effects of all checkpoint inhibitors
- Cytokines
- More information about immunotherapy

Immune checkpoint inhibitors

An important part of the immune system is its ability to keep itself from attacking normal cells in the body. To do this, it uses "checkpoint" proteins on immune cells, which act like switches that need to be turned on (or off) to start an immune response. Kidney cancer cells sometimes use these checkpoints to avoid being attacked by the immune system. But these drugs target the checkpoint proteins, which helps the immune system attack the cancer cells.

PD-1 and PD-L1 inhibitors

Pembrolizumab (Keytruda) and **Nivolumab (Opdivo)** are drugs that target PD-1, a protein on immune system cells (called T cells) that normally help keep these cells from attacking other cells in the body. **Avelumab (Bavencio)** targets PD-L1, a protein that binds to PD-1 that is found on some tumor cells and immune cells. By blocking either of these checkpoint proteins, these drugs boost the immune response against kidney cancer cells. This can often shrink tumors or slow their growth.

These drugs can be used in different situations to treat kidney cancer:

- Pembrolizumab can be given as an **adjuvant treatment** after surgery in people who are at higher risk of their cancer coming back, to help lower this risk. It is usually given for about a year after surgery.
- One of these drugs is often part of the first treatment for advanced kidney cancer, along with a targeted drug or with the CTLA-4 inhibitor ipilimumab (see below).
- One of these drugs can also be used if advanced kidney cancer starts growing again after other drug treatments have been tried. It might be given alone or along with another type of drug.

These drugs are given by infusion into a vein (IV), typically once every 2 to 6 weeks, depending on the drug.

Possible side effects of PD-1 and PD-L1 inhibitors

The most common side effects of these drugs include:

- Fatigue (feeling tired)
- Cough
- Nausea
- Itching
- Skin rash
- Loss of appetite
- Constipation
- Joint pain
- Diarrhea

See below for possible severe side effects of all checkpoint inhibitors. While it's not common, these drugs can also have more serious side effects - see below.

CTLA-4 inhibitor

Ipilimumab (Yervoy) is another drug that boosts the immune response, but it blocks CTLA-4, a different checkpoint protein on T cells that normally helps keep them in check.

Ipilimumab is not used by itself, but with nivolumab (a PD-1 inhibitor – see above).

Ipilimumab is given by intravenous (IV) infusion, usually once every 3 weeks for 4 treatments.

Possible side effects of CTLA-4 inhibitors

Side effects tend to be more common with this drug than with the PD-1 and PD-L1 inhibitors discussed above. The most common **side effects from ipilimumab** include:

- Fatigue
- Diarrhea

- Skin rash
- Itching

This drug can also have more serious side effects - see below.

Possible serious side effects of all checkpoint inhibitors

Serious side effects aren't common with these drugs, but they are possible.

Infusion reactions: Some people might have an infusion reaction while getting one of these drugs. This is like an allergic reaction, and can include fever, chills, flushing of the face, rash, itchy skin, feeling dizzy, wheezing, and trouble breathing. It's important to tell your doctor or nurse right away if you have any of these symptoms while getting this drug.

Autoimmune reactions: These drugs work by removing one of the safeguards on the body's immune system. Sometimes the immune system starts attacking other parts of the body, which can cause serious or even life-threatening problems in the lungs, intestines, liver, hormone-making glands (like the thyroid), kidneys, or other organs.

It's very important to report any new side effects during or after treatment to your health care team right away. If serious side effects do occur, you may need to stop treatment and take high doses of corticosteroids to suppress your immune system.

Cytokines

Cytokines are small proteins in the body that boost the immune system. Man-made versions of cytokines, such as interleukin-2 (IL-2), ¹might sometimes be used to treat kidney cancer in very specific cases. They can shrink kidney cancers in a small percentage of people.

Interleukin-2 (IL-2)

In the past, IL-2 was often used as a first-line treatment for advanced kidney cancer, and it may still be helpful for some people. But the newer immune checkpoint inhibitors (see above) and targeted drugs are more likely to be helpful.

IL-2 is given by infusion through a vein (IV). Giving high doses of IL-2 seems to offer the best chance of shrinking the cancer, but this can cause serious side effects, so it is not used in people who are in poor overall health.

Side effects of IL-2 can include flu-like symptoms, such as fever, chills, aches, severe tiredness, drowsiness, and low blood cell counts. In high doses, IL-2 can cause fluid to build up in the body so that the person swells up and can feel very sick.

Because these side effects can be severe, high-dose IL-2 is only given in the hospital at certain centers that are experienced with giving this type of treatment.

More information about immunotherapy

To learn more about how drugs that work on the immune system are used to treat cancer, see <u>Cancer Immunotherapy</u>².

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u>³.

Hyperlinks

- 1. www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html
- 2. <u>www.cancer.org/cancer/managing-cancer/side-effects.html</u>

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Chemotherapy for Kidney Cancer

Chemotherapy (chemo) uses anti-cancer drugs that are given into a vein (IV) or taken by mouth (as pills). These drugs enter your bloodstream and reach nearly all areas of the body, which makes this treatment potentially useful for cancer that has spread (metastasized) to organs beyond the kidney.

- When is chemotherapy used for kidney cancer?
- · Possible side effects of chemotherapy
- More information about chemotherapy

When is chemotherapy used for kidney cancer?

The most common <u>types of kidney cancer</u>¹ (renal cell carcinoma, or RCC), such as clear cell RCC, typically don't respond well to chemo, so it's not usually part of the treatment for these cancers. Targeted drugs and immunotherapy are the most common treatments for most advanced kidney cancers.

However, chemo can be helpful for some less common types of RCC, including collecting duct RCC and renal medullary carcinoma. Usually, a platinum drug (cisplatin or carboplatin) is combined with either gemcitabine or paclitaxel to treat these cancers. These drugs are given by infusion into a vein (IV).

Doctors give chemotherapy in cycles, with each period of treatment followed by a rest period to allow the body time to recover. Chemo cycles generally last a few weeks.

Possible side effects of chemotherapy

Chemo drugs can also affect other cells in the body, which can lead to certain side effects.

The <u>side effects of chemo</u>² depend on the which drugs are given, the doses used, and the length of treatment. Possible side effects of chemo can include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Diarrhea or constipation
- Increased chance of infections (due to low white blood cell counts)
- Easy bruising or bleeding (due to low blood platelet counts)
- Fatigue (feeling tired due to low red blood cell counts)

These side effects usually go away after treatment is finished. There are often ways to prevent or lessen them. For example, medicine can be given to help prevent or reduce nausea and vomiting.

Some chemo drugs can also cause other side effects. For example, drugs like cisplatin, carboplatin, and paclitaxel can damage nerves. This can sometimes lead to symptoms (mainly in the hands and feet) such as pain, burning or tingling, sensitivity to cold or heat, or weakness. This is called **peripheral neuropathy**.

Ask your health care team about the side effects your chemo drugs may cause.

More information about chemotherapy

For more general information about how chemotherapy is used to treat cancer, see <u>Chemotherapy</u>³.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u>⁴.

Hyperlinks

- 1. www.cancer.org/cancer/types/kidney-cancer/about/what-is-kidney-cancer.html
- 2. <u>www.cancer.org/cancer/managing-cancer/treatment-</u> <u>types/chemotherapy/chemotherapy-side-effects.html</u>
- 3. www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html
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Treatment of Kidney Cancer by Stage

The type of treatment(s) your doctors recommend will depend mainly on the <u>stage</u>¹ of the kidney cancer and on your overall health and decisions. Other factors, such as type and grade of the cancer, might also affect your treatment options.

This section sums up the options usually considered for each stage of renal cell

carcinoma (RCC), the most common type of kidney cancer.

- Treating stage I or II kidney cancer
- Treating stage III kidney cancer
- Treating stage IV kidney cancer
- Treating recurrent kidney cancer

Treating stage I or II kidney cancer

Stage I and II cancers are still only in the kidney.

Active surveillance

Some small (stage I) cancers might not need to be treated right away. Small tumors often grow slowly, and some might never cause serious problems. Because of this, active surveillance might be an option for some people with small kidney tumors. With this approach, the tumor is watched closely with regular imaging tests (such as CT scans or ultrasounds) and possibly other tests, and it's only treated if it grows or starts to show other concerning signs.

Surgery

If treatment is needed, these cancers are usually removed with surgery when possible.

- **Partial nephrectomy** (removing the part of the kidney containing the cancer) is often the treatment of choice for smaller tumors. This is especially true for people have reduced kidney function (or who might have it in the future).
- Radical nephrectomy (removing the entire kidney) is often favored if the tumor is larger, if it's in the central part of the kidney, or if there's more than one tumor in the kidney.

Some lymph nodes near the kidney are often removed as well. More lymph nodes might need to be removed if any of them look enlarged on imaging tests, or if there's a higher risk that the cancer might spread to the nodes.

Most often, no further treatment is needed after surgery.

If, after surgery, the cancer cells are found to have troubling features when evaluated in the lab (such as being very high grade), one option might be to get **adjuvant**

(additional) treatment to help lower the risk of the cancer coming back. Most often this is with the immunotherapy drug pembrolizumab (Keytruda), which is given for about a year.

Other treatment options

For people who aren't healthy enough to have surgery or who don't want surgery, other local treatments such as cryotherapy or radiofrequency ablation (RFA) can sometimes be used to destroy (ablate) the kidney tumor. Radiation therapy (particularly stereotactic body radiation therapy, or SBRT) may be another option. Although these types of treatments can have outcomes similar to surgery as far as the chances of the cancer spreading to other parts of the body, some studies show the cancer might be more likely to come back in the same area.

Treating stage III kidney cancer

Stage III cancers have grown into nearby large veins or tissues around the kidney, and/or they have spread to nearby lymph nodes.

Surgery

Surgery is typically the main treatment for these cancers. Most often, this is a **radical nephrectomy**, in which the entire kidney is removed. A **partial nephrectomy** (removing the part of the kidney containing the tumor) might also be an option if it's possible, especially in people with reduced kidney function or who have tumors in both kidneys.

Some lymph nodes near the kidney are often removed as well. More lymph nodes might need to be removed if any of them look enlarged on <u>imaging tests</u>², or if there's a higher risk that the cancer might spread to the nodes.

If the cancer has grown into the inferior vena cava (the large vein that brings blood from the lower part of the body back up to the heart), your surgeon may need to cut open this vein to remove all of the cancer. This may require putting you on bypass (a heart-lung machine), so that the heart can be stopped for a short time to remove the cancer from the vein.

For clear cell RCC, an option after surgery is to get **adjuvant** (additional) treatment to help lower the risk of the cancer coming back. Most often this is with the **immunotherapy** drug pembrolizumab (Keytruda), which is given for about a year.

Other treatment options

For people who can't have surgery for some reason, radiation therapy or another type of local treatment might be options.

Some stage III cancers can't be removed completely by surgery or destroyed with other treatments. These cancers might get the same treatment as stage IV cancers (see below), with targeted therapy drugs, immunotherapy, or a combination of these.

Treating stage IV kidney cancer

In stage IV kidney cancer, the main tumor has grown outside the kidney, or the cancer has spread to other parts of the body such as distant lymph nodes or other organs.

Treatment of stage IV kidney cancer depends mainly on how extensive the cancer is and on a person's general health.

For most people with stage IV kidney cancer, medicines such as immunotherapy and targeted drugs are the main treatments (see below). But in some cases, surgery may still be a part of treatment.

If both the kidney tumor and metastases appear to be removable

While it's not common, sometimes the main tumor appears to be removable and there is only limited spread to another area (such as to one or a few spots in the lungs). In these situations, surgery to remove both the kidney and the metastasis (the outside area of cancer spread) may be an option if a person is in good enough health. Other options to treat the metastatic tumors might include ablative treatments or radiation therapy.

If all of the tumors are removed (or destroyed), additional (adjuvant) treatment with the immunotherapydrug pembrolizumab might be considered. It is typically given for about a year.

If just the kidney tumor appears to be removable

If the kidney tumor can be removed but the cancer has spread extensively elsewhere, treatment options might include:

• Removing kidney with the tumor first. This type of surgery (known as a **cytoreductive nephrectomy**) isn't recommended for most people, but it might be

an option for otherwise healthy people in a <u>low-risk group</u>³. Surgery is then followed by drug treatments (immunotherapy and or targeted drugs) for most people.

 Giving drug treatments (immunotherapy and/or targeted drugs) first. This is likely to be preferred for most people, even if it looks like the cancer in the kidney can be removed. For some people, if the cancer shrinks a lot with this treatment, surgery, ablative treatments, or radiation therapy might be options to try to remove or destroy any remaining tumors.

If the kidney tumor isn't removable

If the kidney tumor can't be removed, the first treatment is usually with medicines such as immunotherapy and/or targeted therapy drugs. Often, one of each type of drug is part of the first treatment. Which ones are used depends to some extent on if the cancer is a clear cell RCC or a non-clear cell RCC. If one treatment doesn't work (or stops working), another one can often be tried.

For some less common types of non-clear cell RCC, such as collecting duct RCC or renal medullary carcinoma, chemotherapy is often the first treatment.

While it's not common, sometimes the first treatment might shrink the tumors enough so that surgery, ablative treatments, orradiation, might be options to try to get rid of any remaining tumors.

In other situations, surgery or other treatments might be used to help relieve symptoms from the cancer, such as pain or bleeding, rather than trying to get rid of the cancer completely. This type of treatment is called **palliative therapy**. (You can read more about palliative treatment for cancer in <u>Palliative (Supportive) Care⁴</u> or in <u>Advanced</u> <u>Cancer, Metastatic Cancer, and Bone Metastasis⁵</u>.) If you have advanced kidney cancer and your doctor suggests surgery, ablation, or radiation, be sure you understand what the goal of the treatment is.

No matter what type of treatment you're getting, having your <u>pain controlled</u>⁶ can help you maintain your quality of life. Treating the cancer itself can often help with this. Medicines to relieve pain can also be helpful, and they will not interfere with your other treatments. Controlling any pain you have can often help you be more active and continue your daily activities.

Because advanced kidney cancer is very hard to cure, <u>clinical trials</u>⁷ of new combinations of targeted therapy drugs, immunotherapy, or other new treatments are also options.

Treating recurrent kidney cancer

Cancer is called **recurrent** when it comes back after treatment. Recurrence can be local (near the area of the original tumor), or it may be in distant parts of the body.

Treatment of kidney cancer that comes back (recurs) after initial treatment depends on where it recurs and what treatments have been used, as well as a person's health and wishes for further treatment.

Local recurrence

For cancers that recur near the area of the original kidney tumor after surgery, further surgery orother localized treatments or radiation might be options. Even if not all of the cancer can be removed or destroyed, these treatments might still help relieve symptoms in some people. Other treatment options will most likely include immunotherapy and/ortargeted therapy drugs. <u>Clinical trials</u>⁸ of new treatments are an option as well.

Distant recurrence

Kidney cancer that recurs in distant parts of the body is treated like stage IV cancer (see above). Your options will depend on where the cancer is; if it's thought to be removable or not; which, if any, drugs you received as part of your first treatment (and how long ago you got them); and on your overall health and preferences.

For cancers that continue to grow or spread during treatment with immunotherapy or targeted therapy drugs, different drugs still might be helpful. Recurrent cancers can sometimes be hard to treat, so you might also want to ask your doctor about clinical trials.

For some people with recurrent kidney cancer, palliative treatments may be the best option. These treatments are intended to help control the cancer and relieve any symptoms it is causing. Options might include radiation therapy, ablative treatments, or even some type of surgery, if a person is healthy enough. Controlling symptoms such as pain is also an important part of treatment at any stage of the disease.

For more information, see <u>Understanding Recurrence</u>⁹.

Hyperlinks

- 1. <u>www.cancer.org/cancer/types/kidney-cancer/detection-diagnosis-</u> staging/staging.html
- 2. www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests.html
- 3. <u>www.cancer.org/cancer/types/kidney-cancer/detection-diagnosis-</u> staging/staging.html
- 4. <u>www.cancer.org/cancer/managing-cancer/palliative-care.html</u>
- 5. www.cancer.org/cancer/managing-cancer/advanced-cancer.html
- 6. <u>www.cancer.org/cancer/managing-cancer/side-effects/pain.html</u>
- 7. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-</u> <u>trials.html</u>
- 8. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-</u> <u>trials.html</u>
- 9. www.cancer.org/cancer/survivorship/long-term-health-concerns/recurrence.html

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Our team is made up of doctors and oncology certified nurses with deep knowledge of cancer care as well as editors and translators with extensive experience in medical writing.

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