Supported by the Merck-Pfizer alliance,
who had no input into the content of this guide

Action Kidney Cancer

Renal medullary carcinoma (RMC)

What is renal medullary carcinoma (RMC)?

Renal medullary carcinoma (RMC) is an extremely rare and aggressive form of kidney cancer. It is almost exclusively found in young people who carry the sickle cell gene. The sickle cell gene is particularly common in people with an African, Caribbean, or Mediterranean family background and can cause a group of inherited conditions that affect the red blood cells, causing anaemia. RMC is almost always associated with sickle cell trait or disease.

Kidney tissue is made up of very small tubes (called tubules) that filter and clean the blood. These tubules are lined with a tissue called epithelium. Epithelium lines the cavities and surfaces of all organs and structures throughout the body, and forms many glands, such as salivary glands. RMC grows in the epithelium that lines the renal pelvis (or collecting duct) of the kidney. The renal pelvis is the funnel-like dilated beginning of the ureter where it joins the kidney (see *Essential guide: The Kidneys for more information*).

There are several different subtypes of kidney cancer. These subtypes are named according to the type of the epithelial cell where the cancer starts to grow or how they look under the microscope. Medullary cells are fatty cells that fill the spaces between the functional cells of the renal pelvis to provide a supportive framework around the collecting ducts. They also help regulate water levels in the blood.

Usually only one kidney is affected by RMC, and in 75% of cases the tumour grows in the right kidney. Patients tend to be young with an average age of 24, and more than twice as many men develop RMC than women. For most patients, the cancer has already spread by the time the disease is diagnosed.

Occurrence

Renal cell carcinoma (RCC) is the seventh most common cancer in UK adults, with around 13,000 new cases diagnosed per year between 2015-2017, and 4,500 deaths per year from RCC in the same years. RCC accounts for 3% of all new cancer cases in the UK.

RMC is an extremely rare subtype of RCC and only a few hundred cases have been diagnosed worldwide since it was first described in 1995.

Risk factors

A risk factor is anything that is associated with an increased chance of developing cancer. Some people with several risk factors never get cancer, while others with no known risk factors do. However, knowing your risk factors and talking about them with your doctor may help you make more informed lifestyle and health care choices. A cause is a factor that has been proven to give rise to kidney cancer.

- **Age.** Patients with RMC tend to be young, with an average age of 24 years
- **Gender.** Men are more than twice as likely to be at risk of developing RMC than women
- **Genetics** (passed down in your family). RMC is almost exclusively found in young people who carry the sickle cell gene, and rarely in people with sickle cell disease. Note: most people with the sickle cell gene are otherwise healthy and do not know they have this blood disorder. There is currently no evidence to suggest that family members of a patient with RMC are at increased risk for developing RMC themselves. Although people with sickle trait and disease should take early signs and symptoms of possible RMC very seriously and have themselves checked by their GP.
- **Race.** The sickle cell gene is particularly common in people with an African, Caribbean, or Mediterranean family background.

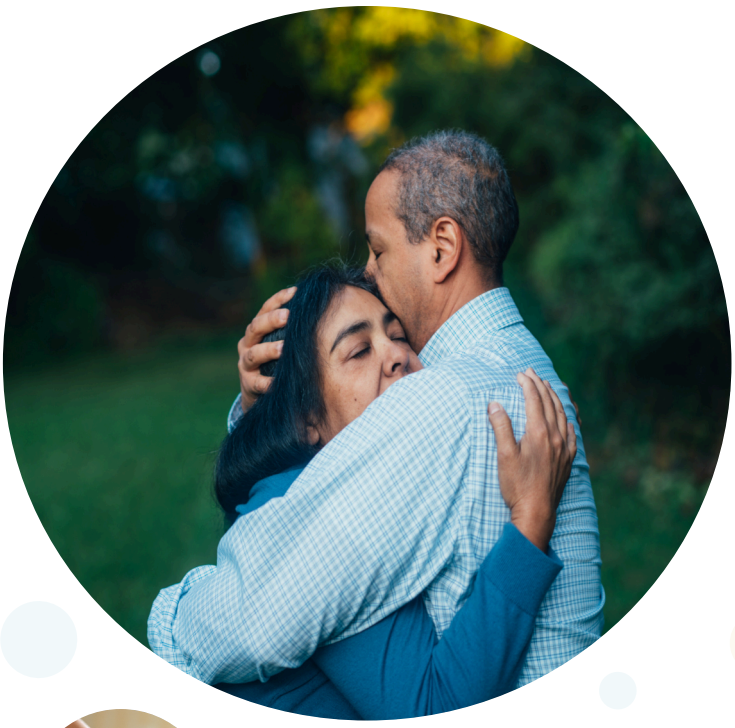
Symptoms

Symptoms of RMC are often like those caused by urinary tract infections or stones in the bladder or kidneys. However, it is important to have any of the symptoms mentioned below checked by your doctor, because the earlier the cancer is diagnosed, the more likely it is to be treated. Some people do not show any of these symptoms, while other people may experience several of them:

- The most common first sign is blood in the urine (haematuria), which may appear suddenly and may come and go. The urine may look pink, red, or brown and you may see streaks of blood or blood clots. It is important to have blood in the urine checked by your doctor immediately. Sometimes the blood cannot be seen (microscopic haematuria) and is picked up when you have your urine tested
- A lump in the tummy (abdomen) or the side of the body between the ribs and hips (also called the flank)
- Pain or cramps in the flank/mid back
- Painful spasms in the area around the bladder caused by blood clots
- Raised temperature for an unknown reason that doesn't go away
- Extreme tiredness (fatigue) and lack of energy
- Unexplained weight loss

Often RMC has no signs or symptoms in its early stages. In these cases, it is found by accident on an ultrasound or CT scan carried out for other reasons or to investigate symptoms, such as high blood pressure, weight loss, high temperature, problems with muscles or nerves in the body, or abnormal blood tests.

Around 90% of patients don't find out they have RMC until their cancer has already spread (metastatic disease) and they have symptoms such as weight loss, shortness of breath, coughing up blood (haemoptysis), bone pain, or bone fracture. RMC most commonly spreads to the lymph nodes (85% of patients), lungs



(46%), liver (15%) and bone (15%), but almost never spreads to the brain.

For information about the kidneys, diagnosis of kidney cancer and staging and grading of kidney cancer, please see Essential guide: The kidneys, *Essential guide: Diagnosis and tests for kidney cancer* and *Essential guide: Staging and grading of kidney cancer*.

Treatments for renal medullary carcinoma

Making treatment decisions

Your surgeon and oncologist will discuss with you the treatments they think would be best for you (please see the treatment options detailed below). Sometimes they may offer you a choice of surgical treatments. Your healthcare team should always make sure you are part of the decision-making process and that your views and preferences have been considered. You should make sure you have been given enough information and you understand the options, before you give permission for the treatment to start. Don't be embarrassed about asking people to explain things again and remember to ask about any particular aspects that are worrying you.

You should be told:

- The type of treatment that is recommended for you
- How and when this will be carried out
- The advantages and disadvantages of this type of treatment
- Any possible other treatments that might be available
- Any significant risks or side effects of the treatment.

When making treatment decisions, you might also be encouraged to consider a clinical trial as an option. A clinical trial is a research study to test a new treatment or procedure to evaluate whether it is safe, effective, and possibly better than the standard of care (standard treatment).

Treatment options depend on several factors, including the type and stage of your cancer (see *Essential guide: Kidney cancer – Renal cell carcinoma (RCC)* and *Essential guide: Staging and grading of kidney cancer*), possible side effects to the treatment, your preferences and your overall health (see below).

Before your operation, you will have a talk with your surgeon about what treatment options are available for you. You might like to ask:

- Will I need a partial or complete (radical) nephrectomy (removal of the kidney)?
- Can I have keyhole surgery (laparoscopic or robotic surgery)?
- Is it likely that I might need a complete nephrectomy even if a partial nephrectomy is planned?
- Is this surgery curative?
- What other related procedures or treatments might I need?

What surgical treatments are available for renal medullary carcinoma?

If scans show that the cancer is confined within the kidney and has not spread to other parts of the body, then surgery can be considered to remove the kidney along with the tumour. The extent of the surgery will depend on the stage and grade of the cancer (see *Essential guide: Staging and grading of kidney cancer)*, the location of the tumour and the general health of the patient.

Surgical removal of RMC tumours is usually carried out by a urologist (a surgeon who specialises in diagnosing and treating urinary, bladder and kidney problems). The operation is usually carried out under general anaesthetic.

The most common surgical treatments for kidney tumours are as follows:

Radical nephrectomy where the whole kidney with the tumour is removed. Sometimes it is necessary to also remove the surrounding tissues, nearby lymph nodes and the bladder if the cancer has spread into these areas.

Partial nephrectomy (nephron-sparing surgery) where only the area of the kidney affected by the tumour is removed so that the rest of the kidney can still work to clean the blood and regulate the body. This operation can be a good option for patients with a small tumour that has not spread. It is also used for people with one kidney or those with poor kidney function.

Radical and partial nephrectomy can be carried out as open surgery or using keyhole (laparoscopic) surgery.

Laparoscopic or keyhole surgery is a less invasive form of surgery that results in less scarring and faster recovery times than traditional open surgery. Laparoscopic surgery can be assisted by a robot (robot-assisted laparoscopic surgery) to improve accuracy.

If your cancer has spread to other parts of the body, surgery may still be useful to relieve symptoms such as pain, bleeding or to help control the chemical balance in the blood. This sort of surgery does not usually offer a cure so it is important to think carefully about the risks and benefits it may bring. Sometimes, if there is spread to just the lungs or liver, the metastatic tumours can be removed by surgery as well. Removing the metastases can also improve survival time.

See *Essential guide: Surgery for kidney cancer* for information about the types of surgery available for kidney cancer.

Most RMCs will need further treatment. However, many of the therapies that are used for other kidney cancers are not effective against RMC. Advanced RMC is often treated with chemotherapy or targeted therapy (see below). Your oncologist or specialist nurse will discuss this with you.

What are the treatments for advanced renal medullary carcinoma?

Because RMC is an extremely rare type of kidney cancer, there are no medicines that are licensed specifically for the treatment of RMC that has spread. Currently, most treatments, although licensed for the treatment of advanced kidney cancer in the UK, remain experimental for RMC. You might be offered chemotherapy, targeted therapy or sometimes a combination of both types of medicine.

Chemotherapy

If your cancer has spread into other organs or tissue, you might have chemotherapy to reduce the spread of your cancer. Your oncologist might also recommend chemotherapy if you are not able to have the tumour removed for other health reasons. You could also be offered chemotherapy to shrink the tumour and treat any microscopic tumours from the lungs or other organs before surgery. This is called neoadjuvant therapy.

Chemotherapy may also be given after surgery to prevent the cancer from coming back. This is called adjuvant chemotherapy. Chemotherapy is the use of toxic drugs to kill cancer cells (cytotoxic drugs). The chemotherapy drugs are given by an injection into a vein (intravenous) in the arm. They are systemic drugs that circulate around the body in the blood stream and act by disrupting the growth of cancer cells.

Several chemotherapy drugs have been tested for the treatment of RMC, either alone or in combination. The type of chemotherapy you will be offered depends on the stage and grade of your cancer, as well as your general health and if you have any other medical conditions that could make the side effects to chemotherapy worse.

Chemotherapy drugs are given over a few consecutive days; this is called a cycle of chemotherapy. Several cycles will be repeated every few weeks over a period of several months; this is called a course of chemotherapy.

A variety of cytotoxic drugs has been tested for the treatment of RMC, including carboplatin, cisplatin, cyclophosphamide, doxorubicin, gemcitabine, methotrexate, topotecan and vinblastine.

Those drugs destroy cancer cells by interfering with cancer DNA or certain proteins. The treatments maybe used as a single treatment or combination and are administered via a short tube into a vein in your arm or sometimes via a longer tube into a large vein in the chest.

Side effects to chemotherapy depend on the drug used and the patient, and may include fatigue, anaemia, nausea, vomiting, diarrhoea, sore mouth, loss of appetite, hair loss and risk of infection. However, most of these side effects usually can be treated effectively and go away when treatment with the drug stops.

The effectiveness of some chemotherapy drugs might be reduced by dietary or herbal supplements, such as fish oil preparations or grapefruit. It is therefore important to let your doctor know if you are taking any dietary supplements or complementary therapies before you start treatment.

It is dangerous to become pregnant or to father a child while taking chemotherapy drugs, as they may harm the developing baby. It is therefore important to use effective contraception during treatment and for a few months after treatment. Please discuss this issue with your oncologist or nurse.

Targeted therapy

The treatments used for RMC include targeted therapies, such as vascular endothelial growth factor (VEGF) inhibitors (such as sunitinib or bevacizumab) or mammalian target of rapamycin (mTOR) inhibitors (such as everolimus). These treatments are called targeted therapies because they target specific proteins that are important for the survival of cancer cells.

The following tables summarise the targeted therapies available in the UK for the treatment of advanced RMC, along with the common side effects for each treatment. These medicines are given alone or in combination with chemotherapy. Most are used as the first treatment after surgery; however, they can be given as second-or third-line treatments.

	Targeted therapy		
Type of medicine	**Vascular endothelial growth factor (VEGF) inhibitors: Tyrosine kinase inhibitors (TKI)**	**Vascular endothelial growth factor (VEGF) inhibitors:Monoclonal antibodies (MAb)**	**Mammalian target of rapamycin (mTOR) inhibitors**
Examples of this medicine	sunitinib	bevacizumab	everolimus
How is it given?	Tablets on a daily basis, sometimes with breaks in treatment for 1-2 weeks	Bevacizumab is injected into a vein every 2 weeks.	Daily tablet
How does it work?	Prevents growth of cancer cells and blood vessels to the tumour	Prevents growth of cancer cells and blood vessels to the tumour	Prevents growth of cancer cells
What are the more common side effects?	Fatigue, diarrhoea, nausea and vomiting, stomach pain, weight loss, high blood pressure, tenderness and sensitivity in the hands and feet (hand - foot syndrome), skin rash, mouth sores, taste changes, pain and swelling in arms or legs (oedema), chest pain and breathing problems	Headache, back pain, diarrhoea, loss of appetite, cold symptoms (stuffy nose, sneezing, sore throat, dry or watery eyes), dry or flaky skin, hair loss, changes in your sense of taste, jaw pain, swelling, numbness, loose teeth and gum infection, thrombosis and bleeding	Fatigue, diarrhoea, decreased appetite, nausea, diabetes, mouth sores, skin rash, swelling in arms or legs (oedema), cough, and breathing problems

New treatments for advanced renal medullary carcinoma

Treatment options for RMC are few, and those that are available have limited success. Researchers and oncologists have tested various cancer treatments to improve the survival of their patients. Case reports showed activity for treatments with topoisomerase II inhibitors, the proteasome inhibitor bortezomib and immune checkpoint inhibitors. But these treatments are not standard, and their use has to be discussed with every patient on a case-by-case basis.

Some medicines might not be suitable for people with multiple serious diseases or conditions (co-morbidities). You will need to discuss your suitability for medication with your oncologist to make an informed decision about which option to choose.

Radiotherapy

Radiotherapy uses high energy X-rays to destroy cancer cells. For patients who are unable to have surgery, it can be used to shrink tumours and control symptoms. It can also be used if the cancer has spread to other areas of the body, such as the brain, lungs, liver or bone, or for the treatment of cancer that has come back.

Because kidney cancer cells are not very sensitive to radiation, radiotherapy is not used very often to treat kidney cancer patients. Radiotherapy may be used to help control and alleviate the symptoms of advanced RMC. It can be used to shrink a large tumour and relieve pressure on nearby organs, and the subsequent pain and discomfort this causes. Shrinking the tumour may also relieve the pressure on nerves that may be causing pain (neuropathic pain).

Treatment is given in the hospital radiotherapy department and will be tailored to you. Some people have daily treatments (or fractions) from Monday to Friday for several weeks. Some people may need only one or two treatment fractions. The treatment only takes a few minutes and does not hurt.

Stereotactic body radiotherapy (SBRT) uses high doses of radiation directed at the cancer. It can be used to treat single metastases found in the liver and lung. In SBRT, radiotherapy is directed at the area of the body containing the tumour to kill the cancer cells and avoid as much healthy tissue as possible.

Side effects to radiotherapy can include fatigue, nausea and vomiting, and sore or red skin. They take a while to build up and usually persist for a few days after the treatment has finished. Your radiographer will be able to tell you what to expect and how to cope.

What happens if my cancer comes back?

When your treatment has been completed and you are in remission (your symptoms have gone away), talk with your oncologist about what happens next and how you will be monitored for recurrence of the cancer. Many patients feel worried or anxious that the cancer will return.

If the cancer does return, you will undergo further tests to learn as much as possible about the recurrence. You and your oncologist will then talk about your treatment options, such as further surgery or drug treatment.

People with recurrent cancer often experience emotions such as disbelief, confusion and fear. Patients are encouraged to talk with their healthcare team about these feelings and ask about support services to help them cope.

What if my cancer has already spread?

In advanced cases, RMC may spread to the lymph nodes, liver, lungs, and bones. If your cancer has already spread to other parts of the body, surgery may still be useful to relieve symptoms such as pain and bleeding, or to help control the chemical balance in the blood. Surgery after the cancer has spread does not usually cure the cancer, so it is important to think carefully about the risks and benefits it may bring.

Sometimes, if there is metastatic spread to just the lymph nodes, lung or liver, this can be removed by surgery as well. Removing as many of the metastatic tumours from, for example, the lung or liver may improve your overall survival in rare cases.

Other treatments for patients with metastatic cancer include chemotherapy, targeted therapy or radiotherapy depending on the location and extent of cancer spread. Patients are encouraged to talk through the treatment options with their doctor.

Further reading

Further information and support can be obtained from the following patient organisations:

- In the UK, The Ricky Casey Trust: https://therickycaseytrust.org.uk/
- In the USA, the Chris “CJ” Johnson Foundation: https://chrisjohnsonfoundation.org/Action Kidney Cancer
- Action Kidney Cancer - https://www.actionkidneycancer.org

- National Organization for Rare Disorders. Renal Medullary Carcinoma. https://rarediseases.org/rare-diseases/renal-medullary-carcinoma/
- Shetty A and Matrana M. Renal Medullary Carcinoma: A Case Report and Brief Review of the LiteratureOCHSNER J. 2014 Summer; 14(2): 270–275. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4052598/
- Goenaga-Vazquez Y, Colon G, Barrios N, et al. Renal medullary carcinoma: a nearly fatal malignancy specifically affecting patients with a so-called benign condition. CEN Case Report. 2018 May; 7(1): 121–126. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5886939/

Acknowledgements

Medical reviewer: Dr Andreas Schmitt, Royal Marsden Hospital
Patient reviewer: Rose Woodward, Founder
Patient reviewer: Julia Black, Charity Operations
Medical writer: Sharon Deveson Kell BSc PhD MBA, Medical Affairs

Terms and Conditions governing the use of this Action Kidney Cancer Essential Guide

- This guide is intended for use with the advice of the healthcare professionals responsible for your treatment and care. This guide does not support any particular course of treatment over another.
- If you have any worries or concerns about your treatment or care, please discuss these with your healthcare professional
- You may use this information for educational, non-commercial and personal use only
- Please retain all copyright, trademarks disclaimers and proprietary notices on this guide
- Please do not modify, reproduce, display, or distribute this guide without prior written consent from Action Kidney Cancer
- This guide is one of a series of guides about the care and treatment of people with kidney cancer.

Factsheet Updated: April 2021
Next Review: April 2023