Action Kidney Cancer

Papillary renal cell carcinoma (pRCC)

What is papillary renal cell carcinoma (pRCC)?

There are several different subtypes of RCC. RCC tumours are named according to how they look under the microscope. Papillary RCC tumours look like long thin finger-like growths (or papillae) under a microscope. Papillary renal cell carcinoma (pRCC) is a rare form of kidney cancer.

There are two types of papillary RCC: type 1 and type 2. The cells from these two types look different under the microscope. Type 1 papillary RCC is more common and grows slowly. Type 2 papillary RCC is more aggressive and grows quickly. Type 1 papillary RCC has a better outcome than type 2 papillary RCC. Papillary RCC can also develop sarcomatoid features, but this is very rare (see *Essential guide: Kidney cancer – Renal cell carcinoma* for information about sarcomatoid kidney cancer).

Usually only one kidney is affected by papillary RCC. However, papillary RCC can grow in both kidneys (bilateral kidney cancer).

Occurrence

RCC is the seventh most common cancer in UK adults, with around 13,300 new cases diagnosed per year between 2016-2018, and 4,700 deaths per year between 2015-2017. RCC accounts for 4% of all new cancer cases in the UK[1].

Papillary RCC is the second most common subtype of RCC and makes up about 10-15% of all RCC cases, which is around 1,300-2,000 new cases of papillary RCC diagnosed per year in the UK. Type 1 papillary RCC is more common than type 2. Papillary RCC is more common in men than in women[1].

Hereditary papillary renal cell carcinoma (HPRCC) is a rare form of papillary RCC that can be passed from generation to generation in a family. HPRCC increases the risk of type 1 papillary RCC. People with HPRCC tend to be younger (less than 45) and have an increased risk of multiple kidney tumours in one or both kidneys (also called bilateral kidney tumours). There are no other types of cancer or health problems known to be related to HPRCC.

Risk factors

A risk factor is anything that increases the 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, for example obesity.

- **Increasing age.** The risk of developing papillary RCC increases as people get older. The average age of someone diagnosed with papillary RCC is 64, with most cases occurring in people aged 55 and over
- **Weight.** People who are overweight and with a body mass index (BMI) of 25-30 increase their risk of developing kidney cancer by about one third. If a person is obese (BMI over 30) their risk of kidney cancer is double that of a person who is a healthy weight (BMI less than 25). Around 24% of all kidney cancers result from being overweight or obese
- **Cigarette smoking** can double the risk for some people and is found to be the cause of around 13% of kidney cancers. The higher the number of cigarettes smoked per day and the longer you have smoked, the greater the risk. It is thought that chemicals from tobacco in the blood stream damage the kidney tubules before being filtered out of the body in the urine
- **Gender.** Men who already have certain health conditions e.g., high blood pressure (hypertension) or advanced kidney disease (especially for those on long term dialysis) are more at risk of developing kidney cancer
- **Genetics** (passed down in your family) are a risk factor for a type of papillary RCC called hereditarypapillary renal cell carcinoma (HPRCC). Hereditary leiomyomatosis and renal cell cancer (HLRCC) is also a risk factor for papillary RCC.

Symptoms

Symptoms of papillary RCC 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 others may experience several:

- The most common symptom 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
- Persistent cough.

Often papillary RCC has no signs or symptoms in its early stages. In these cases, it is found by accident on a 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 25-30% of patients don't find out they have papillary RCC until their cancer has already spread (metastatic disease) and they

have symptoms such as blood in their urine, shortness of breath, coughing up blood (haemoptysis), bone pain, or bone fracture. Papillary RCC does not spread as easily as clear cell RCC and most commonly spreads to the lymph nodes, lungs, bone, and 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 papillary RCC

Making treatment decisions

Your surgeon and/or oncologist (cancer doctor) will discuss with you the treatments they think would be best for you. Sometimes they may offer you a choice of surgical treatments. In any case, you should be part of the decision-making process and your views and preferences are considered. You should have been given enough information to 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 always ask about anything that is unclear or worrying you. You can always ask for patient information to take away and read later at home.

Your clinician should explain to you:

- The type of treatment that is recommended for you and why
- How and when this will be carried out
- The advantages and disadvantages of this type of treatment
- Any other treatments that might be available
- Any significant risks or side effects of the recommended 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 (normal treatment). Taking part in a clinical trial can give you access to new treatments that are not routinely available.

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

- Will I need my whole kidney removed (a radical nephrectomy) or just part of my kidney removed (a partial nephrectomy)
- Is keyhole surgery possible (laparoscopic or robotic surgery)?
- What are the chances 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?
- How will I be followed up after surgery?

More information about preparing for an operation can be found on the NHS website. See also the *Help Sheet Going into hospital for surgery* on the Action Kidney Cancer website for tips and suggestions for items you might like to take into hospital.

What surgical treatments are available for papillary RCC?

Surgery is the main treatment for papillary RCC. The extent of the surgery will depend on the stage and grade of the cancer (see *Essential guide: Staging and grading of kidney cancer*) and the location of the tumour. Surgical removal of papillary RCC tumours is usually carried out by a urologist (a doctor who specialises in diagnosing and treating urinary, bladder and kidney problems). The operation is usually carried out under general anaesthetic.

You might be offered a biopsy of your tumour before surgery. A biopsy is the removal of a small piece of the tumour to look at the cells under a microscope. A biopsy will be able to tell you if the tumour is cancer or not. A biopsy will also be able to let you know the type of kidney cancer you have and the grade of the cancer (see *Essential guide: Staging and grading of kidney cancer*). Knowing the type and grade of your kidney cancer will help when choosing treatment options if your cancer comes back after surgery.

The most common surgical treatments for papillary RCC 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 or bleeding. 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 more information about the types of surgery available for kidney cancer.

Depending on the grade of your cancer, you may need further treatment, such as targeted therapy, immunotherapy, or radiotherapy (see below). This is called adjuvant therapy. Adjuvant therapy aims to reduce the risk of the cancer coming back after surgery to remove the tumour. Even if your surgery was successful at removing all visible cancer, microscopic cancer cells can sometimes remain. They cannot be seen by the naked eye and are undetectable with current methods.

An adjuvant immunotherapy treatment has been approved by the NHS for RCC patients who are at higher risk of the cancer returning after surgery. Targeted therapies have been tested as adjuvant therapies, but so far without success. Your oncologist or specialist nurse will discuss this with you.

What are the treatments for advanced papillary RCC?

Because papillary RCC is a very rare type of kidney cancer, there are no medicines that are licensed specifically for the treatment of papillary RCC that has spread. Currently, advanced, or metastatic papillary RCC is treated using the same medicines as for the more common form of kidney cancer, clear cell RCC, with varying degrees of success.

Several biological therapies are used for the treatment of advanced papillary RCC, including immunotherapies, targeted therapies and monoclonal antibodies.

Biological therapies are medicines made from natural substances found in the body. These are used to kill cancer cells or stop them from growing. Biological therapies can shrink or control the cancer and help people live longer. You will be given a biological therapy for kidney cancer that has already spread or for locally advanced kidney cancer that is at high risk of coming back after surgery.

Some people with advanced kidney cancer respond very well to biological therapies, and the treatment can control their cancer for several months or years. To improve survival, people are given these medicines one after the other (in sequence) when each medicine stops working. Some of these medicines are given together (in combination) with other medicines, again to extend survival. Research into the best combination or sequence of medicines for the treatment of kidney cancer is ongoing.

The medicines used for advanced papillary RCC include targeted therapies, such as vascular endothelial growth factor (VEGF) inhibitors (sometimes called tyrosine kinase inhibitors (TKIs) or monoclonal antibodies), mammalian target of rapamycin (mTOR) inhibitors, or immunotherapies. The success of these treatments is variable and clinical trials are ongoing to find an effective treatment for this type of kidney cancer.

Some medicines for the treatment of advanced papillary RCC might not be suitable for people with multiple serious diseases or conditions (co-morbidities). Also, you might decide you do not want to take medication for your cancer. You will need to discuss your options with your oncologist to make an informed decision about which treatment is right for you.

The following tables summarise the medicines available in the UK for the treatment of advanced papillary RCC, along with the common side effects for each treatment. These medicines are given alone or in combination with other treatments. 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	axitinib, cabozantinib, sunitinib, pazopanib, lenvatinib (taken with everolimus)	bevacizumab (taken with erlotinib or everolimus)	everolimus
How is it given?	Tablets taken daily, sometimes with breaks in treatment for 1-2 weeks	Bevacizumab is injected into a vein every 2 weeks. Erlotinib and everolimus are tablets taken daily	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	Fatigue, diarrhoea, decreased appetite, nausea, diabetes, mouth sores, skin rash, swelling in arms or legs (oedema), cough, and breathing problems

	Immunotherapy	
Medicine type	**Immune checkpoint inhibitors (PD/PD-L1)**	**Combination therapies**
Examples of this medicine	nivolumab, ipilimumab, pembrolizumab, avelumab	ipilimumab plus nivolumab, pembrolizumab plus lenvatinib, pembrolizumab plus axitinib,avelumab plus axitinib, nivolumab plus cabozantinib
How is it given?	Injected into a vein every 2 or 4 weeks	Immunotherapies are injected into a vein every 2-4 weeks. TKIs are tablets that are taken daily
How does it work?	Helps your immune system attack the cancer cells	Helps your immune system attack the cancer cells, prevents growth of cancer cells and blood vessels to the tumour
What are the more common side effects?	Fatigue, rash and itching of the skin, diarrhoea, pain in the muscles, bones and joints, nausea, cough, high temperature, vomiting, breathing difficulties, decreased appetite and inflammation such as colitis, pneumonitis, nephritis	Diarrhoea, constipation, fatigue, high blood pressure, pain in the muscles and bones, nausea, inflammation and ulceration of the membranes of the gut, hand-foot syndrome, inflammation of the mouth and lips, difficulty speaking, decreased appetite, taste changes (dysgeusia), low activity of the thyroid gland, rash, liver damage, cough, pain in the abdomen and headache

Please see the *Essential guide: Treatment for advanced renal cell carcinoma (RCC)* for management of side effects to cancer medicines, how these medicines are sequenced, access to medicines for RCC in the UK, and biomarkers.

New treatments for advanced papillary RCC

There have been several new medicines that have shown promise for the treatment of advanced papillary RCC. These medicines are targeted therapies that block the action of a protein involved in the growth and development of tumours.

A gene called MET makes a protein called MET tyrosine protein kinase (also called hepatocyte growth factor receptor), which stimulates the growth and development of tumours. MET tyrosine protein kinase is a key driver of the growth and development of papillary RCC. Various MET tyrosine protein kinase inhibitors, such as cabozantinib, crizotinib, and savolitinib have been tested in clinical trials for the treatment of advanced papillary RCC. Of these three medicines, cabozantinib was the most effective at improving survival and is the only one of these medicines that is licensed for the treatment of metastatic kidney cancer.

Combinations of various medicines have also been tested with varying degrees of success, such as savolitinib plus durvalumab, cabozantinib plus atezolizumab, and atezolizumab plus bevacizumab. None of these combinations have been licensed for use in advanced papillary RCC and are currently only available in clinical trials.

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 so 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, broad beam radiotherapy is not used very often to treat kidney cancer patients. Radiotherapy may be used to help control and

alleviate the symptoms of advanced RCC. 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. You will be able to talk to the radiographer via an intercom if you need them.

Stereotactic ablative radiotherapy (SABR, also called radiosurgery or gamma knife surgery or CyberKnife®) uses high doses of radiation directed at the cancer. It can be used to treat small numbers of metastases found in the liver and lung. In SABR, 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. Only a single treatment is required.

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 if 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.

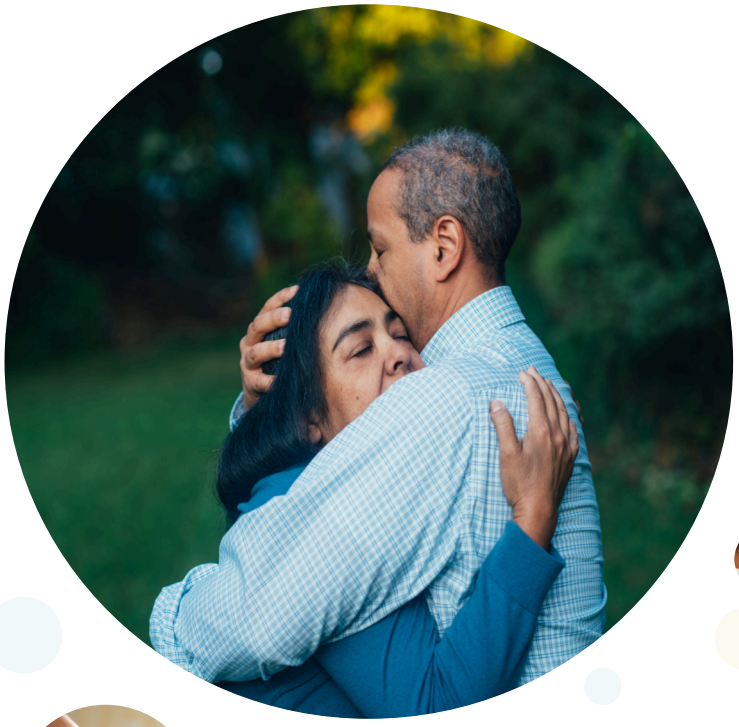
People with recurrent cancer often experience emotions such as disbelief, confusion, and fear. Patients are encouraged to talk with their healthcare team and other patients about these feelings and you can ask about support services and if there are cancer charities that can help you cope.

What if my cancer has already spread?

In advanced cases, papillary RCC 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 involved.

Sometimes, if there is metastatic spread to just the lymph nodes, lung, or liver, the metastatic tumours may be removed by surgery. If possible, removing as many of the metastatic tumours from, for example, the lung or liver might improve your overall survival.

Other treatments for patients with metastatic cancer include chemotherapy or radiotherapy depending on the location and extent of cancer spread. Patients are encouraged to talk through the treatment options with their doctor. At this stage, patients may also be recommended to consider participation in a clinical trial.



Further reading

- Action Kidney Cancer: https://www.actionkidneycancer.org
- National Institute of Health, National Center for Advancing Translational Science, Genetic and Rare Diseases Information Center: https://rarediseases.info.nih.gov/diseases/9572/papillary-renal-cell-carcinoma
- Healthline. Papillary renal cell carcinoma: Risks, treatments and more. https://www.healthline.com/health/papillary-renal-cell-carcinoma
- Shuch B, Hahn AW, Agarwal N. Current treatment landscape of advanced papillary renal cancer. J Clin. Oncol. 2017; 35 (26): https://ascopubs.org/doi/10.1200/JCO.2017.74.3328
- Steffens S, Janssen M, Roos FC, et al. Incidence and long-term prognosis of papillary compared to clear cell renal cell carcinoma – A multicentre study. Eur J Cancer. 2012; 48 (15): 2347-2352: https://www.ejcancer.com/article/S0959-8049(12)00376-0/fulltext
- Vikram R, Ng CS, Tamboli P, et al. Papillary Renal Cell Carcinoma: Radiologic-Pathologic Correlation and Spectrum of Disease. Radiographics. 2009; 29 (3): 741-757: https://pubs.rsna.org/doi/pdf/10.1148/rg.293085190
- European Association of Urology (EAU) Renal Cell Carcinoma guidelines, 3. Epidemiology, Aetiology and pathology. https://uroweb.org/guideline/renal-cell-carcinoma/#3

[1]Cancer Research UK, kidney cancer statistics 2014. http://www.cancerresearchuk.org/cancer-info/cancerstats/types/kidney/uk-kidney-cancer-statistics.

Please see the Action Kidney Cancer glossary for definitions of the medical and scientific terms used in this Action Kidney Cancer Essential Guide: https://actionkidneycancer.org/glossary/

Acknowledgements

Medical reviewer: Prof Dr Samra Turajlic BA MBBS MRCP PhD, Royal Marsden Hospital
Patient reviewer: Rose Woodward, Founder, Action Kidney Cancer
Patient reviewer: Julia Black, Charity Operations, Action Kidney Cancer
Medical writer: Sharon Deveson Kell BSc PhD MBA, Charity Operations, Action Kidney Cancer

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: October 2023
Next Review: October 2025