



5

## Metastatic Kidney Cancer

The underlined terms are listed in the glossary.

Kidney tumours can spread to other organs or distant lymph nodes. This is called metastatic disease. In metastatic disease, the kidney tumour is referred to as the primary tumour and the tumours in other organs are called metastases. Your doctor may recommend to treat metastatic disease with surgery, usually in combination with antiangiogenic therapy, also known as targeted therapy. In rare cases, immunotherapy is also used. For the treatment of metastases, radiotherapy may be recommended.

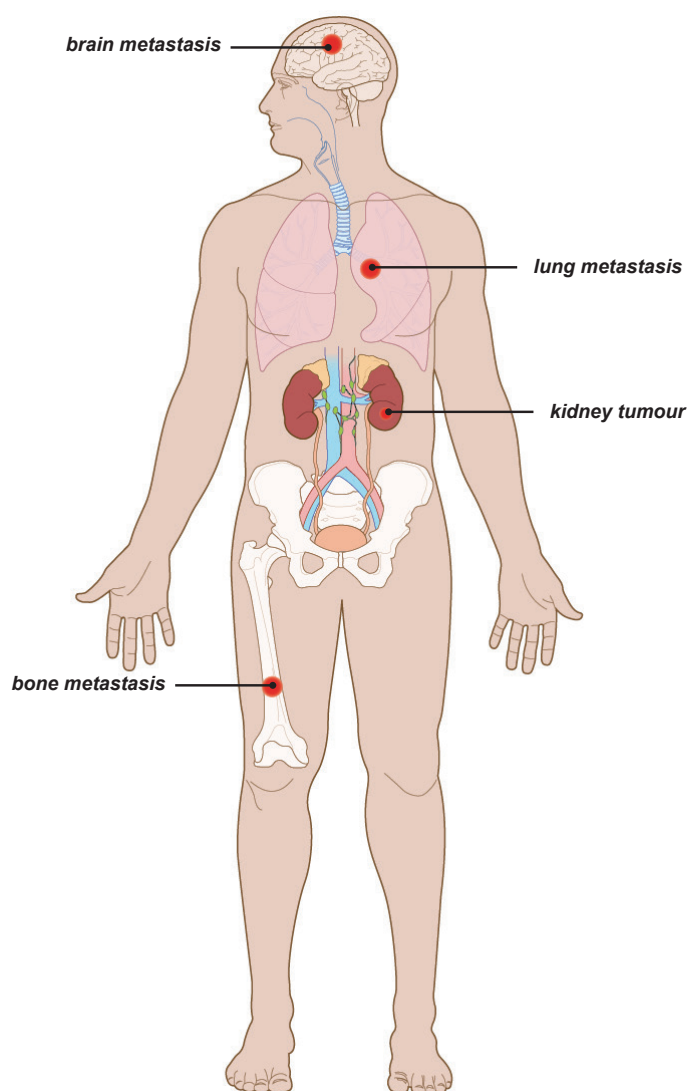
The treatment of metastatic disease aims to reduce the size of the primary tumour and the metastases. This will give you the chance to live longer and have fewer symptoms.

This section describes the different treatment options, which you should discuss with your doctor.

This is general information which is not specified to your individual needs. Keep in mind that situations can vary in different countries.

### What is metastatic kidney cancer?

If kidney cancer metastasizes, it generally spreads to the lungs, bones, distant lymph nodes, or the brain (**Fig. 1**). Metastases can be seen on a CT scan, either on initial diagnosis or during follow-up visits after treatment. They could also be detected because they cause symptoms. Metastatic disease may be asymptomatic or can cause different symptoms, according to where the cancer has spread. The most frequent symptoms are a persistent cough in case of lung metastasis, or bone pain if the cancer has spread to the bones.



**Fig.1: Metastatic kidney cancer can spread to the lungs, bones, or brain.**

## Treatment options

If you have metastatic disease, surgical removal of the kidney is recommended to reduce the size of the tumour and relieve symptoms. This surgery is called cytoreductive nephrectomy. The procedure is only possible if you are fit enough to undergo surgery. If successful, you can live longer and with fewer side effects.

If the metastases cause much pain or other symptoms, you may have further surgery to remove those metastatic tumours. Your doctor may recommend this if the tumours can be removed and you are fit for major surgery.

If the primary tumour is not very large or if your other kidney is not working well, your doctor may recommend cytoreductive partial nephrectomy. During this surgery, the doctor leaves as much as possible of the healthy kidney tissue intact.

In metastatic disease, surgery is generally combined with drug therapy. There are several types of drug treatment for kidney cancer:

- Antiangiogenic therapy, commonly described as targeted therapy
- Immunotherapy
- Chemotherapy, in combination with immunotherapy

The most commonly used drug treatment for kidney cancer is antiangiogenic therapy.

Your doctor may recommend drug treatment before surgery to shrink the tumour so it can be removed. In some cases, antiangiogenic therapy is used before surgery to see how the cancer responds to it. If it responds well, treatment continues after surgery. It is also possible that your doctor recommends drug treatment only after surgery.

If surgery is not possible, you will start treatment with drug therapies right away. These drugs influence the

mechanisms that tumours use to grow. Generally, antiangiogenic therapy is used. In rare cases you may be recommended immunotherapy. Drug therapy can relieve your symptoms and may shrink the primary tumour and the metastases.

If the metastases still cause symptoms after surgery or while you receive drug treatment, radiotherapy may help to relieve them further. These are some topics you should discuss with your doctor when planning your care pathway:

- Your medical history
- Your kidney function
- Whether you have one or more tumours in one or both of your kidneys
- Where the cancer has spread to
- The kind of treatment available at your hospital
- The expertise of your doctor. Ask your doctor about his or her experience with the recommended treatment option.
- Your personal preferences and values
- Support during treatment

## Cytoreductive nephrectomy

Cytoreductive nephrectomy is recommended for metastatic kidney cancer if you are fit for surgery and if the tumour can be removed. The aim is to remove as much of the tumour as possible. In order to do this, it may be necessary to remove surrounding organs such as the spleen or the pancreas, or parts of the intestines or the liver.

For cytoreductive nephrectomy you will receive general [anaesthesia](#). During the surgery, you will lay on your side or on your back, depending on the location and the size of the tumour.

### How is cytoreductive nephrectomy performed?

The standard of care is open cytoreductive nephrectomy. First, the size of the tumour is determined and the doctor checks which surrounding tissue or organs have been affected by it. The surgeon then cuts the abdominal wall to access the kidney directly. To prevent [tumour spillage](#), the surgeon keeps your kidney covered with a protective layer of [fatty tissue](#). The surgeon finally separates the [renal artery](#), [renal vein](#) and [ureter](#) from the kidney to remove the kidney.

### Cytoreductive partial nephrectomy

If the primary tumour in the kidney is not very large, or if your other kidney is not working well, your doctor may recommend cytoreductive partial nephrectomy. This is a rare procedure. The aim is to remove the part of the kidney that has been affected by the tumour, and leave as much as possible of the healthy kidney tissue intact. The procedure can be done through [open surgery](#) or [laparoscopy](#).

Another possibility is to treat the tumour with ablation therapy. Ablation therapy can be either radiofrequency ablation (RFA) or cryotherapy. The aim of these procedures is to kill tumour cells by heating (RFA) or freezing (cryotherapy). It can be done under local or general anaesthesia.

### **Metastasectomy**

Your doctor may recommend additional surgery to remove the metastatic tumours. This is only advised if it is technically possible to remove the metastases and if you are fit to undergo major surgery. This procedure can help if you are in a lot of pain or have other symptoms which cause discomfort.

### **How do I prepare for the procedure?**

Your doctor will advise you in detail about how to prepare for the procedure. You must not eat, drink, or smoke for 6 hours before surgery to prepare for the anaesthesia. If you are taking any prescribed medication, discuss it with your doctor. You may need to stop taking it several days before surgery.

### **What are the side effects of the procedure?**

After cytoreductive nephrectomy you may experience minor pain in the side of your body for some weeks.

Recommendations for 4-6 weeks after the surgery:

- Depending on your doctor's advice, drink 1-2 litres every day, especially water
- Do not lift anything heavier than 5 kilograms
- Do not do any heavy exercise
- Discuss any prescribed medication with your doctor

You need to go to your doctor or go back to the hospital right away if you:

- Develop a fever
- Have any blood loss
- Experience acute pain
- Have blood in the urine

### **What is the impact of the treatment?**

If cytoreductive nephrectomy is successful, it gives you the chance to live longer and you will have fewer side effects.

### **What will the follow-up be like?**

After cytoreductive nephrectomy for kidney cancer, your doctor will generally recommend drug treatment.

# Drug treatment for metastatic disease

Drug treatment is a common option for metastatic kidney cancer. There are several types of treatment:

- Antiangiogenic therapy, commonly described as targeted therapy
- Immunotherapy
- Chemotherapy, in combination with immunotherapy

These drugs influence the mechanisms that tumours use to grow. All decisions about the right therapy for you are taken after careful consideration of your general condition, your symptoms, and your prognosis. Further tests or scans are also used to see which treatment to select.

Generally, antiangiogenic therapy is recommended for kidney cancer. If you have a rare type of kidney cancer, your doctor may recommend chemotherapy treatment in combination with immunotherapy.

## Antiangiogenic therapy

These are a group of drugs which slow down tumour growth or possibly even shrink the tumour. They prevent the formation of new blood vessels which feed the cancer and allow it to grow. The formation of vessels is called **neovascularisation**, and the medical term for these drugs is antiangiogenic therapy. Antiangiogenic therapy is often referred to as targeted therapy because it mainly affects the cancer cells.

There are various types, each one targeting specific factors which influence tumour growth. Most types of antiangiogenic therapy are pills which you can take at home. A few are administered through an IV, for which you will need to go to the hospital. For kidney cancer treatment, common antiangiogenic drugs are:

- Sunitinib
- Pazopanib
- Axitinib
- Sorafenib
- Tivozanib
- Bevacizumab (combined with immunotherapy)

Antiangiogenic drugs which target a specific enzyme called mTOR are known as mTOR inhibitors. The mTOR enzyme is important for cell growth and cell survival. The following targeted drugs aim to shrink the tumour by attacking the enzyme:

- Temsirolimus
- Everolimus

Based on your individual prognosis and the characteristics of the tumour, your doctor will select the best antiangiogenic drug for your specific situation. If this particular drug is ineffective or does not relieve your symptoms, you can discuss with your doctor whether to try a different one.

Because these drugs influence the formation of new blood vessels throughout the body they cause many side effects.

**Fatigue** is a common side effect. This means you feel more tired than usual, you are out of energy, and it doesn't get better after you sleep. You may also experience pain in your joints, muscles and chest. Fatigue can be a side effect of the drugs, but it may also be caused by the tumour or the metastases.

It is common that you feel nauseous or sick during treatment. You may also have diarrhoea or constipation. If you have any of these symptoms let your medical team know. Your doctor may give you medicine to control these symptoms.

During treatment you may suffer from high blood pressure. Your blood pressure will be checked before the start of treatment and in the initial weeks. If necessary, your doctor will prescribe anti-hypertension drugs to control it. Antiangiogenic therapy may also cause erectile dysfunction.

These drugs can affect **thyroid** function. The thyroid is a gland which produces hormones and controls how your body uses energy. If there is a drop in the level of hormones the thyroid produces, you may feel tired,

cold, or gain weight. If the thyroid becomes overactive, you may feel hot and sweaty, restless, have problems concentrating and sleeping, or lose weight.

Sunitinib, pazopanib, axitinib, sorafenib, tivozanib and bevacizumab slow down wound healing, so you cannot start this treatment until your wounds from surgery have healed completely.

While taking these drugs you may experience shortness of breath, chest pain, and swollen ankles and feet. They may also cause blood clots which increases the risk of stroke or heart attack.

Your skin may be dry, become red, or you may develop a rash. In some cases your skin may turn yellow, which goes away once treatment finishes. You may experience numbness and tingling in your fingers and toes. Your hair may turn grey during the course of treatment. In the break between treatment courses some colour may come back. You could also develop hand-foot syndrome which causes blisters and redness on the palms of your hands and soles of your feet. If you experience this, your doctor may recommend to adjust or interrupt treatment.

The mTOR inhibitors temsirolimus and everolimus may cause other specific side effects, mainly related to your blood and your lungs.

The therapy can cause a temporary drop in the number of red or white blood cells, or blood platelets. A drop in white blood cells can increase the risk of infection. Lower levels of red blood cells can lead to tiredness and feeling out of breath. You could need a blood transfusion if the levels become too low. A drop in blood platelets can cause nosebleeds, bleeding gums after brushing your teeth, or lots of tiny red spots or bruises on your arms and legs, known as petechia.

You should contact your health care team if you have any of these side effects. Your doctor will check your blood counts regularly.

mTOR inhibitors may also affect your blood sugar levels and your cholesterol levels may rise. Your blood will be checked regularly.

Another possible symptom is soreness in the mouth. A mouthwash can help to relieve the symptoms, but avoid mouthwashes which contain alcohol, peroxide, iodine, or thyme because these can make the soreness worse. Ask your medical team for suggestions of brands you can use.

Your lungs could be affected by these drug therapies. Let your health care team know if you develop a cough during the course of treatment.

You can read more about how to cope with the side effects in the section *Dealing with the side effects of drug treatment*.

## Immunotherapy

Immunotherapy is a type of drug treatment which boosts the immune system to fight tumour cells. These therapies are used in specific cases only. If your general condition is good and if you have few metastases in the lungs, your doctor may recommend this treatment.

Two different types of immunotherapy are used to treat metastatic kidney cancer:

- Interferon-alpha (INF- $\alpha$ )
- Interleukin-2 (IL-2)

Your doctor may recommend interferon-alpha therapy if your tumour subtype is clear cell renal cell carcinoma, and the tumour has spread to the lungs only. Interferon is usually combined with the antiangiogenic drug bevacizumab. It is applied under the skin. Your doctor will discuss the treatment schedule with you. If your doctor recommends interleukin-2, you will need to stay in the hospital during the treatment because of the side effects.

Interferon-alpha and interleukin-2 can cause severe side effects. The most common include fatigue

and flu-like symptoms, such as fever and chills, headaches, and pain in the muscles and joints. Nearly everyone undergoing immunotherapy has these side effects at first. It usually gets better as your course of treatment continues. These symptoms appear 2 to 4 hours after your injection and last for about 12 hours. Paracetamol can help to relieve these symptoms.

Immunotherapy can also cause a temporary drop in the number of red or white blood cells, or blood platelets. A drop in white blood cells can increase the risk of infection. Lower levels of red blood cells can lead to tiredness and feeling out of breath. You could need a blood transfusion if the levels become too low. A drop in blood platelets can cause nosebleeds, bleeding gums after brushing your teeth, or lots of tiny red spots or bruises on your arms and legs, known as petechia. Itchy, dry skin, or rashes could also occur.

You should contact your health care team if you have any of these side effects. Your doctor will check your blood counts regularly.

Other symptoms include nausea and vomiting, diarrhoea, loss of appetite, and changes in taste or a metallic taste in your mouth. You could also experience a sore throat and pain when swallowing. Because these symptoms may lead to dehydration, weight loss, or malnutrition, be sure to let your doctor or nurse know if they do not go away.

During the course of treatment you may feel depressed, anxious, or have trouble sleeping. These feelings can be a side effect of immunotherapy, but they may also be a response to your diagnosis. You can ask your medical team about psychological support if you feel you need to have someone to talk to.

You can read more about how to cope with the side effects in the section *Dealing with the side effects of drug treatment*.

## Chemotherapy

Chemotherapy is a type of drug treatment which consists of one or more chemicals that are toxic to cells. It attacks any cell in the body that divides rapidly, which includes tumour cells but also hair-growth cells and bone marrow, among others. It is generally administered through an IV.

Chemotherapy is generally not effective for kidney cancer. For metastatic kidney cancer, chemotherapy with 5-fluorouracil can have an effect in combination with immunotherapy after complete removal of the primary tumour.

## Radiation therapy

Radiation therapy damages and kills the cancerous tissue. Kidney tumours are generally not very responsive to radiation therapy. Because of this, the therapy is only recommended to relieve symptoms caused by the primary tumour or metastases that cannot be removed by surgery. Treatment can be given in a single dose of radiation. You could also need to go to the hospital several times for a fractionated course of radiation therapy. In this case you receive one dose of radiation per day.

Radiation therapy for kidney cancer is generally recommended as part of a palliative care approach.

## Clinical trials

Your doctor may suggest you participate in a clinical trial. This is a type of study where new drugs are evaluated. It could also be a study on the sequence or dose of existing drug treatments.

Participating in a clinical trial has several advantages. It gives you the opportunity to be treated with drugs that are currently not widely available. These drugs have been tested before to ensure there are no further health risks. It could also be that you participate in a clinical trial to test the order in which different drugs can be used, or a new combination of drugs.

Your doctor will provide all information you might need before participating in a trial. Your symptoms and general condition will be monitored more often and more closely than during regular treatment.

It is important to know that you can stop your participation in a clinical trial at any time. You will not need to explain your reasons.

## Support for metastatic disease

Cancer has a great impact on your life, and the lives of your loved ones. It can cause feelings of anxiety, uncertainty, fear, or even depression. Undergoing treatment for cancer is intense and will affect your work and social life. To find support, approach your doctor or nurse. They will be able to give you contact information about patient organizations or others who can help you with psychological support, or practical matters such as financial advice.

### Preparing for a consultation

Preparing for a consultation can be very useful. It will help you and your doctor to better address your questions and concerns. Here are some things you can try:

- Write down the questions you would like to ask the doctor. This will help you remember things that you want to ask. Writing down questions can also help you organize your thoughts
- If you can, take someone with you to the visit. It is good to have someone to discuss what the doctor said and you probably remember different things
- Ask for information about your specific type of cancer

- Ask about your treatment options
- Find out what the possible side effects of treatment are and how you can cope with them
- If the doctor uses words you do not understand, ask for an explanation
- Tell your doctor what medicine you take and if you take any alternative medicine. Some of these medicines can affect the treatment

After the consultation you can:

- Search the Internet or go to the library for more information about your cancer. Be aware that not all the information you see online is of good quality. Your doctor, or your health care team, can point you to reliable websites
- Contact a patient organization, they can offer support and information
- Discuss with your health care team the possible financial consequences of your treatment. They might be able to direct you to people or places where you can get advice about your economic situation or even financial help
- If you want, you should ask for a second opinion from another specialist



## Support after surgery

In the first days or weeks after surgery you may need help with everyday activities. If you can, ask family, friends, or neighbours to help you with things like buying and carrying home food, cooking, cleaning, washing, and gardening. You can also ask your health care team for information about professional home care.

## Dealing with the side effects of drug treatment

If you need drug treatment for kidney cancer, you will experience unpleasant side effects. The side effects are common and management includes therapies to relieve them. It is important that you tell the doctor about the side effects you have. Write down your symptoms every day and try to describe them as precisely as possible. Note how often they occur and how much they affect your daily life. In some cases temporary treatment interruption, dose modification, or stopping the treatment can be considered.

It is common that you experience fatigue. This means you feel more tired than usual, you are out of energy, have trouble concentrating, and it doesn't get better after you sleep.

If you experience fatigue, it may help to:

- Write down things that give you energy, and give them priority during the day or week
- Get help with household tasks like washing, cleaning, or gardening
- Take short naps several times during the day
- Try to be as active as you can. A short walk every day is better than a long walk once a week
- When planning social activities like a trip or a visit, keep in mind you may need time to rest during the day. Discuss this with your family, friends, or caregiver so that you can plan ahead. It is important to tell them when you are feeling tired
- Discuss with your doctor if you plan to travel outside of your country. The doctor can give you advice about vaccinations or possible restrictions on certain medicines. Make sure to also check your travel insurance

Other common side effects include nausea, diarrhoea, high blood pressure, skin and mouth issues, and taste alterations. Some things you can do to cope are listed below.

During treatment, you may experience nausea caused by the therapy, tumour growth, or anxiety about your prognosis. The doctor can prescribe medicine to reduce the nausea.

It may also help if you:

- Eat smaller meals but eat more often throughout the day to make sure you still get enough nutrition
- Eat snacks
- Drink smaller amounts but drink more often to stay hydrated
- Try cold dishes if hot meals make you nauseous
- Ask someone to cook for you, if possible

Another common side effect of the treatment is diarrhoea. Diarrhoea can lead to dehydration and it is important to:

- Drink more than usual
- Avoid food that you think makes the diarrhoea worse
- Keep the anal area clean to prevent irritation
- Use moisturizer if you have anal irritation
- Ask the doctor to prescribe medicine to prevent diarrhoea

You may also experience a mild to moderate raise in your blood pressure, especially early on in your treatment. This is normal and can be managed with standard therapy. Your doctor will advise you if you need to monitor your blood pressure, and how often. If you feel dizzy or have a headache, let your doctor know as soon as possible.

Another possible side effect of drug therapy is dry skin or blisters on your hands and feet. To care for your skin you can:

- Use moisturizer to get your skin soft
- Wear loose-fitting shoes
- Gently pat your skin dry after bathing or washing
- Avoid sun exposure
- Use sunscreen
- Wear gloves when you do things like gardening because they may damage the skin in your hands
- Avoid cleaning products with strong chemicals
- Avoid the sauna

The surface in your mouth can get red and irritated during treatment. You can feel pain when you eat or when you brush your teeth. To prevent infections, it is important to make sure your mouth and teeth are clean. Make sure you:

- Brush your teeth carefully twice a day
- Use a soft toothbrush
- Use a mild toothpaste

Drug therapy may also cause changes in how food tastes to you. You may even begin to dislike certain foods you liked before. The best way to figure out what food you like is to try different things:

- Drink water before you eat to neutralize your taste
- If red meat tastes strange try white meat or fish, or the other way around
- If hot food tastes strange try it cold, or the other way around
- Try using more spices, or try using less
- Use a plastic fork and knife if the food tastes of metal

### **Lifestyle advice**

It is important to maintain a healthy lifestyle during treatment. Try to get physical exercise regularly. Find an activity that you enjoy doing. If you have doubts about what you can do ask your doctor to refer you to a physiotherapist.

Try to eat a balanced diet with a mix of vegetables, fruit and dairy. Also include starchy food like bread and potatoes, rice or pasta, and protein-rich food like meat, fish, eggs or legumes. Try to eat less sugar, salt, and fatty food. If you have any questions ask your doctor to refer you to a dietician.

### **Psychological support**

During treatment you may worry about your prognosis, the impact of cancer on your financial situation, or other issues.

If you feel the need to have someone to talk to, you can ask your doctor for a referral to a psychologist. A patient organization can also offer support.

Discuss with your health care team the possible financial consequences of your treatment. They might be able to direct you to people or places where you can get advice about your economic situation or even financial help. They can also help you find legal advice about your will and related matters.

Surgery and cancer treatment can affect your sexuality. For example, men may experience erectile dysfunction as a side effect of antiangiogenic therapy. Feelings of depression and fatigue can also have a negative effect on your sexual life. It is important that you talk to your partner about your feelings. There are many ways in which you can be intimate. If you do not want to be sexually active, be near each other, touch each other, give and take hugs, and just sit or lay down close to each other.

A cancer diagnosis can make you look at life in a different way and you may realize you now have different priorities. This will affect your work or relationships and can make you feel disoriented and uncertain. Talk to family, friends, or your spiritual advisor about your feelings and wishes. If you don't feel comfortable addressing these issues with those close to you, you can ask your health care team for a referral to a psychologist. The psychologist can give you the tools to deal with these feelings.

## Support for family and friends

A cancer diagnosis not only affects the patient, but also the people around them. As a loved one, you can offer support in many different ways. Sometimes you can help with practical things like laundry, gardening, or grocery shopping.

It may also be helpful to go to the doctor together. You could offer to drive to the visit or help formulate questions to ask during consultation. Being there for the consult can also be good. You may remember different things or focus on other details, which you can later discuss together. You could also ask the doctor how the treatment may impact your lives in terms of caregiving and psychological effects.

The diagnosis and treatment can be very emotional for everybody involved. Cancer treatment is intense and your life may change suddenly. Questions about prognosis, effects of the treatment, and death will come up. As a friend or a loved one you can be there and listen. You don't need to have the answers.

If you feel you need somebody to talk to, approach your family doctor or the medical team to get support. Patient organizations also offer support for family members or friends of people who have been diagnosed with cancer.

These organizations can also help with more practical matters such as financial support and legal advice.

### This information was updated in May 2014.

This leaflet is part of EAU Patient Information on Kidney Cancer. It contains general information about this disease. If you have any specific questions about your individual medical situation you should consult your doctor or other professional healthcare provider. No leaflet can replace a personal conversation with your doctor.

This information was produced by the European Association of Urology (EAU) in collaboration with the EAU Section of Uro-Oncology (ESOU), the Renal Cell Carcinoma Working Group of the Young Academic Urologists (YAU), and the European Association of Urology Nurses (EAUN).

The content of this leaflet is in line with the EAU Guidelines.

You can find this and other information on urological diseases at our website: <http://patients.uroweb.org>

### Series contributors:

Dr. Bülent Akdoğan	Ankara, Turkey
Dr. Sabine D. Brookman-May	Munich, Germany
Prof.Dr. Martin Marszalek	Vienna, Austria
Dr. Andrea Minervini	Florence, Italy
Prof. Haluk Özen	Ankara, Turkey
Dr. Alessandro Volpe	Novara, Italy
Ms. Bodil Westman	Stockholm, Sweden