



What is **Bladder Cancer**?

Let us answer some of your questions.

ESMO Patient Guide Series

An ESMO guide for patients

Patient information based on ESMO Clinical Practice Guidelines

This guide has been prepared to help you, as well as your friends, family and caregivers, better understand bladder cancer and its treatment. It contains information on the causes of the disease and how it is diagnosed, up-to-date guidance on the types of treatments that may be available and any possible side effects of treatment.

The medical information described in this document is based on the ESMO Clinical Practice Guideline for bladder cancer, which is designed to help clinicians with the diagnosis and management of bladder cancer. All ESMO Clinical Practice Guidelines are prepared and reviewed by leading experts using evidence gained from the latest clinical trials, research and expert opinion.

The information included in this guide is not intended as a replacement for your doctor's advice. Your doctor knows your full medical history and will help guide you regarding the best treatment for you.

Words highlighted in **colour** are defined in the glossary at the end of the document.

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Bladder cancer: A summary of key information

The following information will be discussed in detail in this guide.

Introduction to bladder cancer

- Bladder cancer forms in cells lining the bladder. The most common type of bladder cancer is urothelial carcinoma; this guide will focus exclusively on urothelial carcinoma.
- There are several known risk factors for bladder cancer, including tobacco smoking, exposure to
 chemicals or ionising radiation and recurrent urine infections. Smoking is the most important risk factor,
 accounting for half of all cases. However, some people who develop bladder cancer have none of the known
 risk factors.
- Bladder cancer is the 10th most common cancer worldwide. Bladder cancer is more common in men than
 women and its incidence increases with age.

Diagnosis of bladder cancer

- The most common symptom of bladder cancer is blood in the urine without any pain. Other symptoms may
 include frequent, sudden or painful urination, weight loss and pain in the back, lower abdomen or bones.
- A diagnosis of bladder cancer is usually based on the results of a cystoscopy, which can show if there is a tumour in the bladder, and a biopsy to confirm the presence of cancer cells.
- Bladder cancer is categorised according to how far it has spread. Non-muscle-invasive bladder cancer
 (NMIBC) is limited to the inner lining of the bladder, muscle-invasive bladder cancer (MIBC) has spread
 into or through the muscle layer of the bladder and advanced/metastatic bladder cancer has grown beyond
 the bladder and may have spread to another part of the body. This information is used to help decide the
 best treatment.
- Patients with advanced/metastatic bladder cancer may be tested for the presence of a protein called programmed death-ligand 1 (PD-L1), as this can help to decide if certain types of immunotherapy could be beneficial. Patients with advanced/metastatic bladder cancer may also be tested for mutations in fibroblast growth factor receptor (FGFR) genes, as this can indicate suitability for treatment with a specific targeted therapy.

Treatment options for bladder cancer

- Treatment for bladder cancer depends on the size, location and stage of the tumour, and the general health
 of the patient.
- Patients should be fully informed and involved in decisions about treatment options.

Non-muscle-invasive bladder cancer

- NMIBC is typically removed surgically via transurethral resection of the bladder tumour (TURBT).
- Patients with low-risk NMIBC usually have one dose of intravesical chemotherapy immediately after TURBT.
- Patients with intermediate-risk NMIBC receive additional doses of intravesical chemotherapy or intravesical bacillus Calmette-Guerin (BCG) for up to 1 year after TURBT to reduce the risk of recurrence.
- Patients with high-risk NMIBC typically receive intravesical BCG treatment for up to 3 years after TURBT. Patients who are at very high risk of the cancer returning, or who have not responded to BCG treatment, may be offered a radical cystectomy, in which the whole bladder is removed surgically.

Muscle-invasive bladder cancer

- Patients with MIBC typically undergo a radical cystectomy.
- Chemotherapy is usually given as neoadjuvant therapy before radical cystectomy. Patients who are
 not fit enough to tolerate chemotherapy can undergo surgery without any neoadjuvant therapy.

Advanced or metastatic bladder cancer

- The standard first-line treatment for advanced/metastatic bladder cancer is chemotherapy followed by maintenance immunotherapy. Patients with high PD-L1 levels may be offered first-line treatment with immunotherapy alone, but this is less common.
- Second-line treatment after first-line chemotherapy may include immunotherapy, regardless of PD-L1 levels. Patients with FGFR mutations may be offered a targeted therapy that acts on FGFR as a second-line option.
- Second-line treatment after first-line immunotherapy may include targeted therapy or chemotherapy.
- Targeted therapy is the standard treatment for patients experiencing cancer progression after receiving both chemotherapy and immunotherapy.

Long-term impact

- Bladder cancer, and the treatments for it, can have a long-term impact on quality of life. After a radical
 cystectomy, patients must pass urine in a different way and may have to learn how to care for a stoma.
- These changes may affect self-esteem and can have an impact on relationships and sex. Many patients find
 it helpful to talk to other people about their feelings and experiences; this can include family and friends,
 or a trained professional such as a therapist. Talking to other people who have had treatment for bladder
 cancer can also help, and patient support groups can connect patients with fellow survivors.

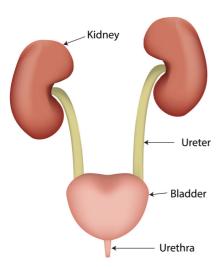
Follow-up during/after treatment

- The timings of follow-up appointments vary between countries and practices. Follow-up appointments may
 include a clinical examination, cystoscopy and/or computed tomography scan.
- Patients who experience a recurrence of their cancer can usually have further treatment. The treatment will
 depend on the extent of the recurrence, previous treatments received and the overall health of the patient.
- Support groups can help patients and their families to better understand bladder cancer and to learn how to cope with all aspects of the disease, from diagnosis to long-term effects.
- The World Bladder Cancer Patient Coalition is a global community of bladder cancer patient organisations: https://worldbladdercancer.org/

What is bladder cancer?

Bladder cancer is a type of cancer that develops in the lining of the bladder. The bladder is part of the **urinary tract**, which filters waste products from the blood and produces urine. As well as the bladder, the **urinary tract** includes the kidneys, **ureters** and **urethra**.

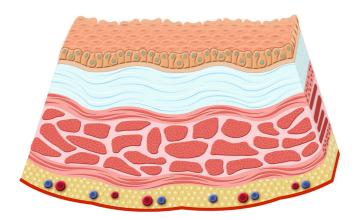
The kidneys filter the blood and produce urine, which is carried to the bladder by the **ureters**. The bladder stores urine until it is emptied via the **urethra**.



Anatomy of the urinary tract.

The bladder has four layers:

- Urothelium lines the bladder and stretches as the bladder fills up; it also prevents the urine being absorbed back into the body
- 2) Lamina propria a thin layer of connective tissue
- 3) Muscularis propria a layer of muscle tissue
- 4) Fatty connective tissue separates the bladder from other body organs



Layers of the bladder.

Most types of bladder cancer are **urothelial carcinomas**, which develop from the cells of the **urothelium** then grow and spread into the other layers. Rarer types of bladder cancer include **squamous cell carcinoma** (in the flat, skin-like tissues that line the bladder) and **adenocarcinoma** (in mucus-producing cells).

This guide will focus on **urothelial carcinoma**.

Urothelial carcinoma is the most common type of bladder cancer

What are the symptoms of bladder cancer?

The most common symptom of bladder cancer is blood in the urine without any pain (*Powles et al., 2022*). Other symptoms may include:

- Painful urination
- Urinating very often
- Urinating very suddenly
- Weight loss
- Pain in the back, lower abdomen or bones
- Feeling tired and unwell

You should see your doctor if you experience any of these symptoms. However, it is important to remember that these symptoms can also occur in people who do not have bladder cancer; they may be caused by other conditions, for example a urine infection.



Any symptoms of bladder cancer should be checked by a doctor

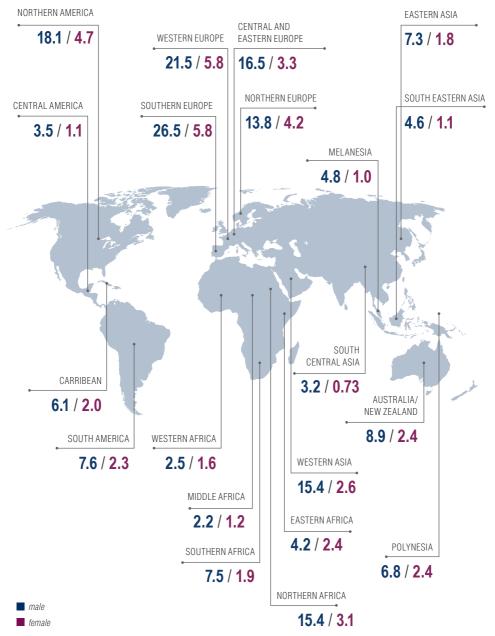
How common is bladder cancer?

Bladder cancer is the 10th most common cancer worldwide, with more than 573,000 new cases and 210,000 deaths in 2020. The highest incidence rates in Europe are in the south (Greece, Spain, Italy) and west (Belgium, the Netherlands) (*Powles et al., 2022; Ferlay et al., 2020*).

Bladder cancer is more common in older people, with most new cases occurring in people aged 75 years and older. It is more common in men than in women.

Bladder cancer is the 10th most common cancer worldwide and is more common in men than women

The map shows estimated numbers of new cases of bladder cancer diagnosed in 2020 per 100,000 people of each region's population (Ferlay et al., 2020).



What causes bladder cancer?

Several **risk factors** for developing bladder cancer have been identified. It is important to remember that having a **risk factor** increases the risk of cancer developing but it does not mean that you will definitely get cancer. Likewise, not having a **risk factor** does not mean that you definitely won't get cancer.



Several risk factors have been identified for bladder cancer

FACTORS THAT MAY INCREASE RISK

Tobacco smoking

Exposure to aromatic amines

Exposure to ionising radiation

Recurrent or long-lasting urine infections

Previous treatment for bladder cancer

Other medical conditions, such as systemic sclerosis or kidney transplant

Family history of bladder cancer

Obesity

There are various **risk factors** associated with developing bladder cancer although each factor may not apply to everyone who develops the disease.

The most important **risk factor** for developing bladder cancer is tobacco smoking, which accounts for around 50% of cases (*Powles et al.*, 2022). People who smoke have a four-fold greater risk of developing bladder cancer than people who have never smoked. People with the highest risk are those who smoke heavily, started smoking at a young age or have smoked for a long time.

Around half of bladder cancers are caused by smoking

Occupational exposure to chemicals such as **aromatic amines** and occupational or medical exposure to **ionising radiation** via previous **radiotherapy** for pelvic cancer are also important **risk factors** for bladder cancer (*Powles et al.*, 2022). It is important to understand, however, that many people who develop bladder cancer have none of the known **risk factors**.

How is bladder cancer diagnosed?

A diagnosis of bladder cancer is based on the results of the following examinations and tests:

Clinical examination

If you have symptoms of bladder cancer, your doctor may carry out a general clinical examination and feel around your abdomen. You are likely to have a urine test to see if your symptoms could be due to a urine infection, and to check for the presence of cancer cells. Your doctor may also do an internal examination via the rectum or vagina to check if everything feels normal around your bladder.



Clinical examination and a urine test can indicate if further tests are needed

Cystoscopy

Your doctor may recommend that you have a **cystoscopy**. This procedure allows the doctor to see inside your bladder using a light and camera attached to a thin tube that is inserted into your bladder via the **urethra**.

You may be awake or asleep during the **cystoscopy** depending on which type of procedure you have. Flexible **cystoscopy** uses a soft, bendy tube and is done under **local anaesthetic**, whereas rigid **cystoscopy** involves a hard, straight tube and is usually done under **general anaesthetic**.

During a **cystoscopy**, your doctor can take samples (biopsies) of the bladder lining to check for cancer cells.

Bladder cancer is usually diagnosed by taking biopsies of the bladder lining

How will my treatment be determined?

Your treatment will largely depend on the stage of your cancer.

Staging

Staging is used to describe the extent of the cancer overall; this includes its size and position and whether it has spread from where it started.

If your **cystoscopy** shows that you have bladder cancer, you may have a **computed tomography (CT)** scan and/or **magnetic resonance imaging (MRI)** scan of your **urinary tract. CT** is a type of **X-ray** technique that lets doctors see your internal organs in detail by showing very thin slices of the body. **MRI** uses magnetic fields and radio waves to produce detailed images of the inside of the body.

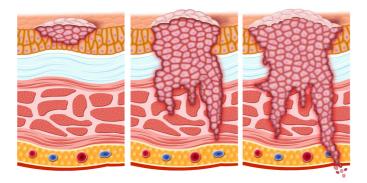


The CT and/or MRI scans allow the doctor to assess the location and size of the cancer. You may also undergo imaging of your chest, abdomen and pelvis to check for any signs that the cancer has spread (*Powles et al., 2022*).

After diagnosis, imaging scans can show if the cancer has spread to other parts of the body

The results of your **biopsies** and/or imaging scans will confirm what type of bladder cancer you have (**urothelial carcinoma** or one of the rarer types) and how far your cancer has spread. Your doctor will categorise your disease as one of the following:

- Non-muscle-invasive bladder cancer (NMIBC) is early-stage bladder cancer in which the cancer cells
 are only in the inner lining of the bladder and have not grown into the deeper muscle layer. This type of
 bladder cancer is further categorised as low risk, intermediate risk or high risk, depending on how likely it is
 that the cancer will spread further, or come back after treatment.
- Muscle-invasive bladder cancer (MIBC) has spread into or through the muscle layer of the bladder.
- Advanced or metastatic bladder cancer has grown beyond the bladder and may have spread to another
 part of the body. Tumours found in other parts of the body away from the original tumour site are called
 metastases



Stages of bladder cancer.

MIBC, muscle-invasive bladder cancer; NMIBC, non-muscle-invasive bladder cancer.

Your treatment will vary depending on whether you have NMIBC, MIBC or advanced/metastatic bladder cancer.

Molecular pathology

If you have advanced/metastatic disease, you may be tested for the expression of a protein called programmed death-ligand 1 (PD-L1). PD-L1 can stop the body's immune system from recognising and killing cancer cells. Therefore, if you are found to have a high level of PD-L1, you may be offered treatment with certain types of immunotherapy that block PD-L1 and allow the body's immune system to kill the cancer cells.

You may also be tested for **mutations** in *fibroblast growth factor receptor* (*FGFR*) genes. *FGFR* genes make proteins that are involved in cell division and formation of new blood vessels. A **mutation** in one of the *FGFR* genes can cause an *FGFR* protein to become overactive in bladder cancer; therefore, the presence of an *FGFR* mutation may mean that you are suitable for treatment with a specific **targeted therapy** that inhibits the *FGFR* protein (*Powles et al.*, 2022).

TNM staging

Staging to determine the size and spread of the cancer is described using a sequence of letters and numbers. For bladder cancer, there are five stages designated with Roman numerals 0 to IV. Generally, the lower the stage, the better the **prognosis**. The TNM staging system considers:

- How big the cancer is, or tumour size (T).
- Whether the cancer has spread to nearby lymph nodes (N).
- Whether it has spread to distant sites, or metastases (M).

Staging helps to determine the most appropriate treatment for bladder cancer

The staging system for bladder cancer is described in the table below (Powles et al., 2022). This may seem complicated, but your doctor will be able to explain which parts of the table correspond to your cancer.

STAGE OA.	T	Non-invasive papillary carcinoma (Ta)
The cancer is only in the inner layer of the bladder		No regional lymph node metastasis (NO)
lining (Ta-N0-M0)		No distant metastasis (M0)
STAGE Ois.		Carcinoma in situ: 'Flat tumour' (Tis)
There are very early, high-grade cancer cells only in the inner layer		No regional lymph node metastasis (N0)
of the bladder lining (Tis-N0-M0)		No distant metastasis (M0)
STAGE I.		Tumour invades the subepithelial connective tissue (T1)
The cancer has started to grow into the connective tissue		No regional lymph node metastasis (N0)
beneath the bladder lining (T1-N0-M0)		No distant metastasis (M0)
STAGE II.		Tumour invades superficial muscle (inner half) (T2a)
The cancer has grown through the connective		Tumour invades deep muscle (outer half) (T2b)
tissue layer into the muscle of the bladder		No regional lymph node metastasis (N0)
wall (T2a to T2b-N0-M0)	M	No distant metastasis (M0)
STAGE IIIA.		• Tumour invades subepithelial connective tissue (T1)
The cancer has grown		• Tumour invades superficial muscle (inner half) (T2a)
through the muscle into the fat layer and		Tumour invades deep muscle (outer half) (T2b)
may have spread to		• Tumour invades perivesical tissue microscopically (T3a)
the prostate, womb or vagina. It might also		• Tumour invades perivesical tissue macroscopically (extravesical mass) (T3b)
have spread to a nearby		• Tumour invades prostate stroma, seminal vesicles, womb or vagina (T4a)
lymph node (T3a to T4a-N0-M0 or T1 to		No regional lymph node metastasis (N0)
T4a-N1-M0)		Metastasis in a single lymph node in the pelvis (N1)
	M	No distant metastasis (M0)

STAGE IIIB.		Tumour invades subepithelial connective tissue (T1)
		• Tumour invades superficial muscle (inner half) (T2a)
		Tumour invades deep muscle (outer half) (T2b)
		Tumour invades perivesical tissue microscopically (T3a)
		Tumour invades perivesical tissue macroscopically (extravesical mass) (T3b)
spread to nearby lymph		• Tumour invades prostate stroma, seminal vesicles, womb or vagina (T4a)
nodes (T1 to T4a-N2 to N3-M0)		Metastasis in multiple regional lymph nodes in the pelvis (N2)
The may		Metastasis in common iliac lymph node(s) (N3)
		No distant metastasis (M0)
STAGE IVA.	T	Tumour invades subepithelial connective tissue (T1)
		• Tumour invades superficial muscle (inner half) (T2a)
		• Tumour invades deep muscle (outer half) (T2b)
or pelvis or to distant lymph nodes		Tumour invades perivesical tissue microscopically (T3a)
		• Tumour invades perivesical tissue macroscopically (extravesical mass) (T3b)
		Tumour invades prostate stroma, seminal vesicles, womb or vagina (T4a)
		Tumour invades pelvic wall or abdominal wall (T4b)
		No regional lymph node metastasis (NO)
		Metastasis in a single lymph node in the pelvis (N1)
		Metastasis in multiple regional lymph nodes in the pelvis (N2)
		Metastasis in common iliac lymph node(s) (N3)
		No distant metastasis (M0)
		Non-regional lymph node metastasis (M1a)
STAGE IVB.	Т	Tumour invades subepithelial connective tissue (T1)
		• Tumour invades superficial muscle (inner half) (T2a)
		• Tumour invades deep muscle (outer half) (T2b)
		Tumour invades perivesical tissue microscopically (T3a)
		• Tumour invades perivesical tissue macroscopically (extravesical mass) (T3b)
		Tumour invades prostate stroma, seminal vesicles, womb or vagina (T4a)
		Tumour invades pelvic wall or abdominal wall (T4b)
		No regional lymph node metastasis (NO)
		Metastasis in a single lymph node in the pelvis (N1)
		Metastasis in multiple regional lymph nodes in the pelvis (N2)
		Other distant metastases (M1b)
	M	 Metastasis in multiple regional lymph nodes in the pelvis (N2) Metastasis in common iliac lymph node(s) (N3)

What are the treatment options for bladder cancer?

Your treatment will depend upon the size, location and stage of your **tumour**, as well as your general health and level of fitness. The choice of treatments will be discussed with you and your preferences will be taken into account. Your treatment will be discussed by a **multidisciplinary team**, which means that experts in different areas of cancer treatment (e.g. oncologists, urologists, surgeons, radiologists and nurses) come together to share their expertise in order to provide the best patient care.

It is important that patients are fully involved in the treatment decision-making — when there are several treatments available, doctors should involve patients in making decisions about their care so that they can choose the care that meets their needs and reflects what is important to them. This is called 'shared decision-making'.



It is important that patients are fully involved in discussions and decisions about their treatment

Your doctor will be happy to answer any questions you have about your treatment. Four simple questions that may be helpful when talking with your doctor or any healthcare professional involved in your care are shown below.

"What treatment options do I have?"

"What are the possible advantages and disadvantages of these treatment options?"

"How likely am I to experience benefits or side effects?"

"Are there any clinical trial options?"

Your doctor may recommend one or more of the following approaches for treating bladder cancer:

Surgical resection

The aim of **resection** is to remove the cancer along with a healthy **margin** of tissue to help stop it from coming back. The type of surgical **resection** depends on the stage of the cancer.

Surgery options for bladder cancer include:

 Transurethral resection of the bladder tumour (TURBT) in which the tumour is removed via the urethra. This type of surgery is typically used to remove early-stage bladder cancer and can be done at the same time as a cystoscopy. It is usually done under general anaesthetic.



Cystectomy, in which all (radical cystectomy) or part (partial cystectomy) of the bladder is removed.
 This type of surgery is used to remove MIBC and high-risk NMIBC and is done under general anaesthetic.

The type of surgery depends on the stage of the cancer

During a radical **cystectomy**, nearby **lymph nodes** and some other close organs may also be removed (e.g. the prostate gland in men and the womb and fallopian tubes in women). This is to ensure all of the cancer is removed with a healthy **margin**.

When the bladder is removed, an alternative method of collecting and passing urine must be created by the surgeon. Methods used include:

- Urostomy: The surgeon creates a new opening (called a stoma) in your abdomen for the urine to pass through. The urine is then collected in a waterproof bag that attaches over the stoma. This is the most common procedure following a radical cystectomy.
- Continent urinary diversion: The surgeon uses a part of your bowel to create a pouch to collect urine inside
 the body, which is then connected to a stoma on your abdomen through which the urine can be emptied.
- Neobladder: The surgeon creates a new bladder using a part of your bowel, which is then connected up to the ureters and urethra.
- Recto sigmoid pouch: The surgeon alters your rectum to make a pouch to collect urine. You will then pass
 urine from your rectum along with your bowel movements.

Changes in the way you urinate are a significant side effect of **cystectomy** that can have long-term effects on your physical and emotional well-being (see section 'Long-term side effects' for more information).

Chemotherapy

Chemotherapy destroys cancer cells and is used in the treatment of both early-stage and advanced/metastatic bladder cancer. In NMIBC, the chemotherapy can be applied directly to the bladder through a thin tube via your urethra. This is called intravesical chemotherapy. Mitomycin C is a type of chemotherapy that is often used for intravesical chemotherapy.

In MIBC and advanced/metastatic bladder cancer, chemotherapy is administered intravenously so it can travel throughout the whole body. Cisplatin is the most common chemotherapy used for MIBC, while options for advanced/metastatic disease include cisplatin, carboplatin and gemcitabine.

It is important to understand that not all of these agents are suitable for all patients. Some patients may not be well enough to tolerate treatment with certain **chemotherapy regimens**, so your doctor will take



your general health and fitness into consideration when deciding on the best treatment for you.

Chemotherapy is frequently used in the treatment of bladder cancer

Radiotherapy

Radiotherapy uses ionising radiation to damage the DNA of cancerous cells, causing them to die. In the treatment of bladder cancer, radiotherapy may be used alone or in combination with chemotherapy.

Immunotherapy

Immunotherapies are treatments that block processes which reduce the body's immune response to cancer. The immunotherapies thereby help to reactivate the body's immune system to detect and fight the cancer.

Bacillus Calmette-Guerin (BCG) is a vaccine that is thought to activate immune cells in the bladder lining, which can then kill cancer cells. **Intravesical BCG** is used in early-stage bladder cancer and is applied to the bladder through a thin tube via the **urethra**.

Pembrolizumab, atezolizumab and avelumab are intravenous immunotherapies that act on processes relating to PD-L1 and are used in the treatment of advanced/metastatic bladder cancer. Sometimes, the use of pembrolizumab and atezolizumab will depend on PD-L1 levels, but often these drugs can be used regardless of PD-L1 expression (Powles et al., 2022).

Novel immunotherapies are now available for the treatment of bladder cancer

Targeted therapy

Targeted therapies are drugs that block specific biological processes in cancer cells that encourage them to grow. Erdafitinib is an FGFR inhibitor that is only used in patients with an FGFR mutation. Enfortumab-vedotin (EV) is a monoclonal antibody (enfortumab) linked to a chemotherapy drug (vedotin) that is used in the treatment of advanced/metastatic bladder cancer.

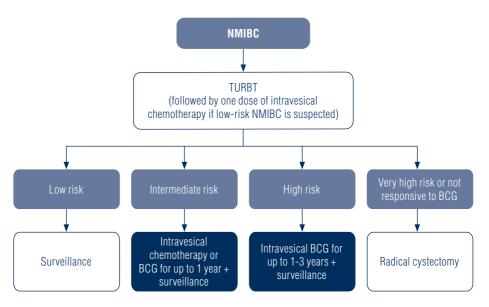
What are the treatment options for NMIBC?

NMIBC is typically treated with **TURBT** (*Powles et al., 2022*). Patients with low-risk **NMIBC** usually have one dose of **intravesical chemotherapy** (such as **mitomycin C**) immediately after **TURBT**, and then undergo regular surveillance via **cystoscopy** to check for any signs of the cancer returning.

In intermediate-risk **NMIBC**, additional doses of **intravesical** therapy are usually given after **TURBT** to reduce the risk of **recurrence**. This may be **intravesical chemotherapy** for up to 1 year, or six **BCG** doses at weekly intervals followed by further doses at 3, 6 and 12 months.

Patients with high-risk NMIBC typically receive intravesical BCG treatment for 1-3 years after TURBT, usually given as nine BCG doses at weekly intervals followed by further doses at 3-6 month intervals.

In patients who are considered to be at very high risk of the cancer returning, and in those who have not responded to **BCG** treatment, a radical **cystectomy** may be offered.



Overview of treatment options for NMIBC.

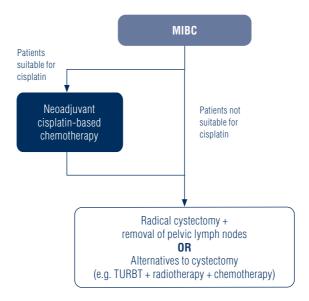
BCG, Bacillus Calmette-Guerin; NMIBC, non-muscle-invasive bladder cancer; TURBT, transurethral resection of the bladder tumour.

What are the treatment options for MIBC?

Radical **cystectomy** is the most common treatment for **MIBC** (*Powles et al., 2022*). The surgery also includes removal of the pelvic **lymph nodes**.

Cisplatin-based **chemotherapy** is usually given as a first step to shrink the **tumour** before radical **cystectomy**. This is known as **neoadjuvant chemotherapy**. Patients who are not fit enough to tolerate **cisplatin** treatment usually undergo surgery without any **neoadjuvant** therapy.

For patients who are unable or unwilling to undergo radical **cystectomy**, alternatives are available, such as a combination of **TURBT**, **radiotherapy** and **chemotherapy**.



Overview of treatment options for MIBC.

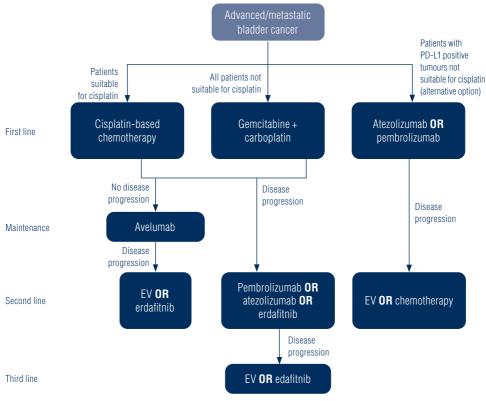
MIBC, muscle-invasive bladder cancer; TURBT, transurethral resection of the bladder tumour.

What are the treatment options for advanced or metastatic bladder cancer?

The standard **first-line** treatment for advanced/**metastatic** disease is **cisplatin**-based **chemotherapy** followed by **maintenance** treatment with the **immunotherapy avelumab** (as long as the cancer did not progress during the **chemotherapy**) (*Powles et al., 2022*). Patients who are not suitable for **cisplatin** may be offered **gemcitabine** + **carboplatin** as an alternative, followed by **avelumab**. Some patients who are not suitable for **cisplatin** and are found to have high **PD-L1** levels may be offered **first-line** treatment with the **immunotherapies atezolizumab** or **pembrolizumab**, but this is less common than the **chemotherapy** options.

If the cancer progresses after **chemotherapy**, **second-line** treatment may involve **pembrolizumab** or **atezolizumab**, regardless of **PD-L1** levels. Patients with **FGFR mutations** may be offered **erdafitinib**. If the cancer progresses after **first-line immunotherapy**, **second-line options** include **EV** or **chemotherapy**.

EV is the standard treatment for patients experiencing cancer progression after receiving both **chemotherapy** and **immunotherapy**, but **erdafitinib** may be offered to patients with **FGFR** mutations.



Treatment options for advanced or metastatic bladder cancer.

FV enfortumah-vedotin

Clinical trials

Your doctor may ask you whether you would like to take part in a **clinical trial**. This is a research study conducted with patients in order to (ClinicalTrials.gov, 2019):

- Test new treatments.
- Look at new combinations of existing treatments or change the way they are given to make them more effective or reduce side effects.
- Compare the effectiveness of drugs used to control symptoms.

Clinical trials help to improve knowledge about cancer and develop new treatments, and there can be many benefits to taking part. You will have to undergo various tests before entering a trial and be carefully monitored during and after the study. Although the new treatment



may offer benefits over existing therapies, it's important to bear in mind that some new treatments are found not to be as good as existing treatments or to have side effects that outweigh the benefits *ClinicalTrials.gov. 2019*).

Clinical trials help to improve knowledge about diseases and develop new treatments – there can be many benefits to taking part

You have the right to accept or refuse participation in a **clinical trial** without any consequences for the quality of your treatment. If your doctor does not ask you about taking part in a **clinical trial** and you want to find out more about this option, you can ask your doctor if there is a trial for your type of cancer taking place nearby (*ClinicalTrials.gov. 2019*).

The European Medical Association has a register of all European **clinical trials**. You can find it here: https://www.clinicaltrialsregister.eu/

Additional interventions

Patients may find that supplementary care helps them to cope with their diagnosis, treatment and the long-term effects of treatment for bladder cancer

Your cancer, and the treatment you receive for it, can cause complications that require further interventions. During the course of your cancer, anti-cancer treatments should be supplemented with interventions that aim to prevent the complications of disease and treatment, and to maximise your quality of life. These interventions may include supportive, palliative, survivorship and end-of-life care, which should all be coordinated by a multidisciplinary team (Jordan et al., 2018).

Ask your doctor or nurse about which additional interventions are available; you and your family may receive support from several sources, such as a physiotherapist, social worker, priest or other spiritual advisor, complementary therapist or occupational therapist.

Supportive care

Supportive care involves the management of cancer symptoms and the side effects of therapy. Having regular **cystoscopies** to check that the cancer has not returned can result in irritation to the bladder (e.g. pain when urinating or having to urinate frequently) and urine infections. Your doctor or nurse will be able to help you to cope with these effects and may be able to prescribe medicines to help. If you have undergone a radical **cystectomy**, you will get support from a specialist nurse to help you deal with the changes in the way you urinate (see section 'What are the possible side effects of treatment?' for more information).

Palliative care

Palliative care is a term used to describe care interventions in advanced disease, including the management of symptoms as well as support for coping with **prognosis**, making difficult decisions and preparation for end-of-life care. Palliative care in patients with bladder cancer may include treatment for urinary incontinence, pain and breathlessness (dyspnoea) (Pais et al., 2020).

Survivorship care

Support for patients surviving cancer includes social support, education about the disease and rehabilitation. For example, psychological support can help you to cope with any worries or fears.

Psychosocial problems impacting on your quality of life may include concerns about the physical changes to your body after surgery, the cancer returning and the long-term effects of your treatment (see section 'Long-term side effects' for more information). Patients often find that social support is essential for coping with the cancer diagnosis, treatment and emotional consequences. A survivor care plan can help you to recover wellbeing in your personal, professional and social life. For further information and advice on survivorship, see ESMO's patient guide on survivorship



(https://www.esmo.org/for-patients/patient-guides/survivorship).

End-of-life care

End-of-life care for patients with incurable cancer primarily focusses on making the patient comfortable and providing adequate relief of physical and psychological symptoms, for example **palliative** sedation to induce unconsciousness can relieve severe pain, **dyspnoea** or delirium *(Chemy, 2014)*. Discussions about end-of-life care can be upsetting, but support should always be available to you and your family at this time. Your doctor or nurse will help to guide you through the options available.

What are the possible side effects of treatment?

As with any medical treatment, you may experience side effects from your anti-cancer treatment. The most common side effects for each type of treatment are highlighted below, along with some information on how they can be managed. You may experience side effects other than those discussed here. It is important to talk to your doctor about any potential side effects that are worrying you.

Doctors classify side effects from any cancer therapy by assigning each event a 'grade', on a scale of 1–4, by increasing severity. In general, grade 1 side effects are



considered to be mild, grade 2 moderate, grade 3 severe and grade 4 very severe. However, the precise criteria used to assign a grade to a specific side effect varies depending on which side effect is being considered. The aim is always to identify and address any side effect before it becomes severe, so you should always report any worrying symptoms to your doctor as soon as possible.

It is important to talk to your doctor about any treatment-related side effects that are worrying you

Fatigue is very common in patients undergoing cancer treatment and can result from either the cancer itself or the treatments. Your doctor can provide you with strategies to limit the impact of **fatigue**, including getting enough sleep, eating healthily and staying active (Cancer.Net, 2020). Loss of appetite and weight loss frequently occur in patients with cancer, and significant weight loss, involving loss of both fat and muscle tissue, can lead to weakness, reduced mobility and loss of independence, as well as anxiety and depression (Escamilla and Jarrett, 2016). Your doctor may refer you to a **dietician** who can look at your nutritional needs and advise you on your diet and any supplements that you might need.

Surgery

Most patients recover quickly from **TURBT**. You may experience blood in your urine and/or a burning sensation when urinating in the first few days after the procedure, but this is normal. You should contact your doctor or nurse if the bleeding gets worse or if you have severe pain when urinating. You will be asked to drink plenty of fluids to flush out your bladder and prevent urine infections.

Cystectomy is a major operation and it will take some time to recover – you will have to stay in hospital for at least a few days. It is normal to experience pain for the first week or so and your doctor or nurse will be able to give you painkillers to help keep you feeling comfortable. You may have an **intravenous** drip to keep you hydrated in the first few days. You will gradually be able to drink and eat a light diet and you will be encouraged to move around as soon as possible after your operation to speed up your recovery; however, it is normal to feel tired for several weeks after surgery.

If you have had a radical **cystectomy**, your surgeon will have created a new way for you to store and pass urine (see section 'Surgical resection' for more information). If you have a **stoma** you will be taught how to care for it. If you have a **neobladder**, you will need to learn how to use the muscles in your abdomen to empty your new bladder, as it won't feel the same as your original bladder. For example, you will have to remember to go to the toilet regularly as the new bladder will not have the nerve supply that tells you when it is full. Following surgery to create a recto sigmoid pouch, you will have to learn how to gain control of the muscles controlling the new pouch. These changes to your physical function will take some time to get used to and can affect your body image and relationships (see section 'Long-term side effects' for more information).

Cystectomy is a major operation and can have longterm health implications

Radiotherapy

Radiotherapy to the bladder may cause inflammation, which can lead to frequent urination and/or pain during urination. The inflammation will reduce after the radiotherapy is finished, but you should drink plenty of fluids in the meantime

Other common side effects of **radiotherapy** for bladder cancer include **fatigue** and diarrhoea. **Fatigue** from **radiotherapy** usually starts during treatment and can last for a few weeks after. Diarrhoea can occur when **radiotherapy** causes inflammation in the lining of the bowel; your doctor or nurse may recommend that you follow a low fibre diet or take medication to reduce the diarrhoea. Diarrhoea usually gets better a few weeks after **radiotherapy** has finished.

Radiotherapy may also cause the skin in the treatment area to become red/dark and sore (like mild sunburn). You may be given cream to soothe the skin, and the soreness usually disappears a few weeks after finishing treatment.

Chemotherapy

Side effects from **chemotherapy** vary depending upon the drugs and doses used — you may get some of those listed below but you are very unlikely to get all of them. You may also experience some side effects that are not listed below. The main areas of the body affected by **chemotherapy** are those where new cells are being quickly made and replaced (**bone marrow**, **hair follicles**, the digestive system, the lining of your mouth). Some patients find that their sense of taste is affected — changes in **enzymes** in your mouth can lead to a metallic taste and blisters. Reductions in your levels of **neutrophils** (a type of white blood cell) can lead to **neutropenia**, which can make you more susceptible to infections. Most side effects of **chemotherapy** are temporary and can be controlled with drugs or lifestyle changes — your doctor will help you to manage them (*Macmillan*, 2018). The table below lists the most important side effects of **chemotherapy** drugs that may be used in the treatment of bladder cancer

CHEMOTHERAPY DRUG	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Carboplatin (Carboplatin SPC, 2020)	Anaemia Decreased fertility in men Leukopenia Nausea / vomiting Neutropenia Thrombocytopenia	Your blood cell counts will be monitored frequently throughout your treatment in order to detect any anaemia, leukopenia, neutropenia or thrombocytopenia — your doctor may adjust your treatment according to test results, and will advise you on how to prevent infections Your doctor or nurse will be able to help you prevent or manage any nausea or vomiting Treatment can cause reduced/abnormal sperm production, which can result in irreversible infertility in some patients. Advice on sperm banking should be provided by your doctor prior to starting treatment. Reliable contraception should also be used during and for at least 6 months after treatment

CHEMOTHERAPY DRUG	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Cisplatin (Cisplatin SPC, 2021)	Anaemia Decreased fertility in men Hyponatraemia Kidney disorders: kidney failure, nephrotoxicity Leukopenia Peripheral neuropathy Thrombocytopenia Tinnitus / changes in hearing	Your blood cell counts will be monitored frequently throughout your treatment in order to detect any anaemia, leukopenia or thrombocytopenia — your doctor may adjust your treatment according to test results, and will advise you on how to prevent infections Report any signs of peripheral neuropathy (tingling or numbness in your hands or feet) to your doctor or nurse You will have tests before and during treatment to check how well your kidneys are functioning. You will be asked to drink plenty of fluids (1.5—2 litres per day) to prevent your kidneys from becoming damaged. You should avoid drinking alcohol, as this can result in dehydration and kidney dysfunction Tell your doctor if you notice any changes in your hearing or experience ringing in your ears (tinnitus). Changes in hearing can occasionally be permanent Treatment can cause reduced/abnormal sperm production, which can result in irreversible infertility in some patients, although this is uncommon. Advice on sperm banking should be provided by your doctor prior to starting treatment Hyponatraemia may occur as a result of changes in kidney function or diarrhoea. It is important to drink plenty of fluids and tell your doctor or nurse if you experience any lethargy or confusion (symptoms of hyponatraemia)
Gemcitabine (Gemcitabine SPC, 2019)	Anaemia Blood in urine Decreased fertility in men Dyspnoea Flu-like symptoms Increased liver enzymes Leukopenia Oedema Protein in urine Rash Thrombocytopenia	Your blood cell counts will be monitored frequently throughout your treatment in order to detect any anaemia, leukopenia or thrombocytopenia your doctor may adjust your treatment according to test results and will advise you on how to prevent infections Dyspnoea is usually mild and passes rapidly without treatment Treatment can cause reduced/abnormal sperm production, which can result in irreversible infertility in some patients, although this is uncommon. Advice on sperm banking should be provided by your doctor prior to starting treatment Your liver and kidney function will be monitored during treatment Let your doctor or nurse know if you experience swelling, rash or flu-like symptoms, so that they can decide how to manage these

CHEMOTHERAPY DRUG	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Intravesical mitomycin C (Mitomycin C SPC, 2021)	Bladder irritation Blood in urine Dermatitis Frequent urination Hand-foot syndrome Painful urination Pruritus Rash Urine infection	To prevent and treat hand-foot syndrome, you can try keeping hands and feet cool by exposing them to cool water (soaks, baths or swimming), avoiding excessive heat/hot water and keeping them unrestricted (no socks, gloves or shoes that are tight fitting). Your treatment schedule may need to be adjusted if you experience severe hand-foot syndrome but in most cases, symptoms will be mild and treatable with creams and ointments and will subside once you have finished treatment
		Let your doctor or nurse know if you experience any symptoms of a urine infection (pain, blood in urine), so that they can decide how to manage these and give you antibiotics if you need them Your doctor or nurse will be able to help you manage any skin irritation

Important side effects associated with individual chemotherapy drugs used in the treatment of bladder cancer.

The most recent Summary of Product Characteristics (SPC) for any individual drug can be located at: http://www.ema.europa.eu/ema/.

Immunotherapy

Common side effects in patients treated with **immunotherapy** include effects on the **gastrointestinal system** and **thyroid** dysfunction. Many of the side effects from **immunotherapy** can be effectively managed if they are recognised and treated early.

It is important to be aware that **immunotherapy** can cause **autoimmunity**, in which the immune system incorrectly identifies its own tissues as foreign bodies and attacks them. **Autoimmunity** can cause inflammation that may affect any organ in the body. In some cases, this side effect can be life-threatening; therefore, it is essential that you alert your doctor or nurse immediately if you notice any side effects or if you feel at all unwell when being treated with an **immunotherapy** drug.

The table below lists the most important specific side effects of the **immunotherapy** drugs used in the treatment of bladder cancer.

For further information and advice on **immunotherapy** side effects, see ESMO's patient guide on **immunotherapy**-related side effects and their management (https://www.esmo.org/for-patients/patient-guides/immunotherapy-side-effects).



IMMUNOTHERAPY	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Atezolizumab (Tecentriq SPC, 2022)	Cough Decreased appetite Diarrhoea Dyspnoea Headache Nausea / vomiting Urine infection	Effects on the gastrointestinal system (e.g. nausea, vomiting, diarrhoea) may result in loss of appetite. Your doctor or nurse will be able to help you to prevent or manage these side effects Tell your doctor or nurse if you experience a persistent cough. Troublesome dyspnoea can be treated with drugs Let your doctor or nurse know if you experience headaches or any symptoms of a urine infection, so that they can decide how to manage these
Avelumab (Bavencio SPC, 2022)	Abdominal pain Anaemia Arthralgia Back pain Constipation Cough Decreased appetite Diarrhoea Dyspnoea Fatigue Fever Infusion-related reactions Nausea / vomiting Oedema	Your blood cell counts will be monitored frequently throughout your treatment in order to detect any anaemia — your doctor may adjust your treatment according to test results Effects on the gastrointestinal system (e.g. nausea, vomiting, diarrhoea, constipation, abdominal pain) may result in loss of appetite and fatigue. Your doctor or nurse will be able to help you to prevent or manage these side effects Tell your doctor or nurse if you experience a persistent cough. Troublesome dyspnoea can be treated with drugs Let your doctor or nurse know if you experience any fever, swelling, pain, joint stiffness or symptoms at the injection site, so that they can decide how to manage these
Intravesical BCG (OncoTICE SPC, 2021)	Blood in urine Fatigue Fever Flu-like illness Frequent urination Painful urination Urine infection	Any flu-like symptoms, including fever and fatigue, should be reported to you doctor or nurse so they can monitor you for systemic BCG infection, which may need to be treated with anti-tuberculosis drugs Let your doctor or nurse know if you experience any symptoms of a urine infection (pain, blood in urine), so that they can decide how to manage these and give you antibiotics if you need them

IMMUNOTHERAPY	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Pembrolizumab (Keytruda SPC, 2022) Constipation Cough Decreased appetite Diarrhoea Dysphonia Fatigue Hand-foot syndrome Hypertension Increased liver enzymes Nausea Thyroid effects	Effects on the gastrointestinal system (e.g. nausea, diarrhoea, constipation) may result in loss of appetite and fatigue. Your doctor or nurse will be able to help you to prevent or manage these side effects To prevent and treat hand-foot syndrome, you can try keeping hands and feet cool by exposing them to cool water (soaks, baths or swimming), avoiding excessive heat/hot water and keeping them unrestricted (no socks, gloves or shoes that are tight fitting). Your treatment schedule may need to be adjusted if you experience severe hand-foot syndrome but in most cases, symptoms will be mild and treatable with creams and ointments and will subside once you have finished treatment	
		Your thyroid and liver function will be monitored before and during treatment — your doctor may adjust your treatment according to test results Your blood pressure will be monitored during treatment and anti-hypertensive treatment will be given if necessary Let your doctor know if you experience a persistent cough or if you develop problems with speaking (dysphonia) so that they can decide how to manage these

Important side effects associated with individual immunotherapy drugs in the treatment of bladder cancer. The most recent Summary of Product Characteristics (SPCs) for any individual drug can be located at: http://www.ema.europa.eu/ema/.

Targeted therapies

Common side effects in patients treated with **targeted therapies** include skin reactions and effects on the **gastrointestinal system** (e.g. nausea, diarrhoea). Many of the side effects from **targeted therapies** can be prevented or managed effectively. Always tell your doctor or nurse as soon as possible if you notice any side effects from taking a **targeted therapy**.

The table below lists the most important specific side effects of **targeted therapies** used in the treatment of bladder cancer.

TARGETED THERAPY	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Enfortumab-vedotin (Padcev SPC, 2022)	Alopecia Anaemia Decreased appetite Decreased weight Diarrhoea	Your blood cell counts will be monitored frequently throughout your treatment in order to detect any anaemia – your doctor may adjust your treatment according to test results
	 Diarritoea Dry eye Dry skin Dysgeusia Fatigue Hyperglycaemia Increased liver enzymes Nausea / vomiting Peripheral neuropathy Pruritus Rash 	Effects on the gastrointestinal system (e.g. diarrhoea, nausea, vomiting, dysgeusia) may result in loss of appetite and fatigue. Your doctor or nurse will be able to help you to prevent or manage these side effects
		Your liver function and blood sugar levels will be monitored before and during treatment – your doctor may adjust your treatment according to test results
		Report any signs of peripheral neuropathy (tingling or numbness in your hands or feet) to your doctor or nurse
		Let your doctor or nurse know if you experience any hair loss, skin reactions or eye irritation, so that they can decide how to manage these

TARGETED THERAPY	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Erdafitinib (Balversa PI, 2022)	Abdominal pain Alopecia Anaemia Constipation Decreased appetite Decreased magnesium Hyponatraemia Diarrhoea Dry eye Dry mouth Dry skin Dysgeusia Fatigue Hand-foot syndrome Increased liver enzymes Musculoskeletal pain Nail problems Nausea Stomatitis	Your blood cell counts will be monitored frequently throughout your treatment in order to detect any anaemia — your doctor may adjust your treatment according to test results Effects on the gastrointestinal system (e.g. dry mouth, diarrhoea, stomatitis, dysgeusia, nausea, constipation, abdominal pain) may result in loss of appetite and fatigue. Your doctor or nurse will be able to help you to prevent or manage these side effects Your liver function, blood cell counts and blood electrolyte levels will be monitored before and during treatment — your doctor may adjust your treatment according to test results To prevent and treat hand-foot syndrome, you can try keeping hands and feet cool by exposing them to cool water (soaks, baths or swimming), avoiding excessive heat/hot water and keeping them unrestricted (no socks, gloves or shoes that are tight fitting). Your treatment schedule may need to be adjusted if you experience severe hand-foot syndrome but in most cases, symptoms will be mild and treatable with creams and ointments and will subside once you have finished treatment Let your doctor or nurse know if you experience any pain, hair loss, skin/nail reactions or eye irritation, so that they can decide how to manage these

Important side effects associated with targeted therapies in the treatment of bladder cancer. The most recent Summary of Product Characteristics (SPCs) for any individual drug can be located at: http://www.ema.europa.eu/ema/.

Long-term side effects

After completing treatment for bladder cancer, you may experience some long-term physical and psychological side effects, so it is important that you tell your doctor or nurse about any persistent or new symptoms that are affecting you. Your doctor or nurse will also work with you to develop a personalised survivorship care plan.

Urination

Surgery for bladder cancer can result in significant changes to your body. After a radical **cystectomy** you will have to pass urine in a different way, depending on the type of surgery you have had (see section 'What are the possible side effects of treatment?' for more information). If you have a **urostomy**, you will have to learn how to care for your **stoma** and change your **urostomy** bags. If you have a **neobladder**, you will learn how to use your abdominal muscles to empty the new bladder. These changes can be distressing, and it is important to allow yourself time to adjust. Some patients may feel nervous about coping with these changes when going about their normal life, but you will get used to your new urination method. If you tell your family and friends how you feel, they can support you.

It can take time to get used to the physical changes after surgery

Occasionally, **radiotherapy** can cause the bladder to shrink slightly, which may make you feel like you have to pass urine very often. There may also be long-term damage to the bowel, which can result in diarrhoea, urgency of bowel movements and incontinence. These side effects are rare, but it's important to tell your doctor or nurse if you experience any problems as they may be able to help reduce the symptoms.

Relationships and sex

You may find that your sex life changes after having surgery for bladder cancer. Having a **stoma** can affect the way you feel about yourself and having sex, and your partner might need a bit of time to get used to what your **stoma** looks like. It's important for you and your partner to be open about what's worrying you.

In men, the prostate gland is removed during radical **cystectomy**, meaning you will not be able to ejaculate. If any nerves are damaged during surgery or



radiotherapy, you may not be able to get an erection. Your doctor or nurse will be able to help you by prescribing drugs or explaining other options that can help you to get an erection (e.g. penile pumps or implants).

In women, surgery and **radiotherapy** for bladder cancer can narrow or shorten the vagina, making sex painful. Your doctor or nurse will be able to help; for example, dilators can be used to gently and gradually stretch the vagina to make sex more comfortable. If your ovaries have been removed you will experience early **menopause** – your doctor or nurse may suggest **hormone replacement therapy** to help you cope with this.

Bladder cancer treatment can affect your sex life, but help is available

Emotional support

Your cancer diagnosis, as well as the treatment and side effects, can affect you emotionally for a long time after your treatment has finished, but there are things you can do to minimise the effects on your mental health. You may find it helpful to educate yourself about all aspects of your cancer and treatment so you can fully understand the long-term changes that you are experiencing. Don't be afraid to ask your doctor to explain things several times to ensure you are fully informed. Having a frank conversation with your surgeon before undergoing surgery can help to prepare you for the long-term physical changes.

Talking to other people about your feelings and experiences can help you to process the changes — some people choose to talk to family and friends, while others prefer to talk to a trained professional such as a cancer nurse or therapist. Some patients find it helpful to talk to people who have been through a similar experience — your doctor or nurse will be able to tell you if there is a support group in your area. If there is no support group in your region, you can consider setting up your own network (see section 'Support aroups' for more information).



For further information and advice regarding how to regain your life as far as possible after treatment for cancer, see ESMO's patient guide on survivorship (https://www.esmo.org/for-patients/patient-guides/survivorship).



What happens next?

Follow-up appointments

You will be able to discuss any concerns you have at your follow-up appointments

After treatment for bladder cancer, your doctor will arrange follow-up appointments to ensure that any **recurrences** are diagnosed and treated quickly, and long-term side effects are managed effectively.

Your doctor will let you know how often you need to return for further follow-up appointments; the schedule will vary between regions. During these appointments, you may have a **cystoscopy** and/or **CT** scan.



What if I need more treatment?

Despite the best possible treatment at diagnosis, there is a chance that your cancer may return. Cancer that comes back is called a **recurrence**. The treatment that you will be offered depends on the extent of the **recurrence**, your previous treatment and your overall health. Usually, **recurrences** of bladder cancer are treated in the same way as **metastatic** bladder cancer, but your doctor will discuss all of the treatment options with you.

Looking after your health

After you have had treatment for bladder cancer, you may feel very tired and emotional. Give your body time to recover and make sure you get enough rest, but there is no reason to limit activities if you are feeling well. It is important to take good care of yourself and get the support that you need.

The following eight recommendations can form a good foundation for a healthy lifestyle after cancer (Wolin et al., 2013):

- Don't smoke
- Avoid second-hand smoke
- Exercise regularly
- Avoid weight gain
- Eat a healthy diet as far as possible
- Don't drink alcohol
- Stay connected with friends, family and other cancer survivors
- Attend regular check-ups



A healthy, active lifestyle will help you to recover physically and mentally

A healthy diet and regular exercise are essential parts of a healthy lifestyle, helping you to keep physically fit and avoid weight gain. It is very important that you listen carefully to the recommendations of your doctor or nurse, and talk to them about any difficulties you have with exercise. It is also important that you do not change your diet or start a new exercise programme without talking to your doctor or nurse first.

Support groups

In Europe, there are patient advocacy groups, which help patients, caregivers and their families to navigate the bladder cancer landscape. They can be local, national or international, and they work to ensure patients and caregivers receive appropriate and timely care and education. These groups can provide you with the tools you may need to help you better understand your disease, and to learn how to cope with it, living the best quality of life that you can.



The World Bladder Cancer Patient Coalition is a global community of patient organisations dedicated

to improving the lives of people affected by bladder cancer. For further information about The World Bladder Cancer Patient Coalition, and to find support groups in your country, visit: https://worldbladdercancer.org/

It is important that patients don't feel alone; therefore, if there isn't a support group in your region, you can consider setting up your own network by reaching out to other patients with bladder cancer. The World Bladder Cancer Patient Coalition can provide advice on how to do this.

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ADENOCARCINOMA

Cancer that begins in glandular (secretory) cells

ALOPECIA

Hair loss

ANAEMIA

A condition in which there is a shortage of haemoglobin (a protein in red blood cells that carries oxygen throughout the body)

ANTI-HYPERTENSIVE (TREATMENT)

A type of drug used to treat high blood pressure

AROMATIC AMINES

Chemicals found in industrial and manufacturing plants, tobacco smoke, commercial hair dyes and diesel exhaust

ARTHRALGIA

Joint pain

ATEZOLIZUMAB

A type of **immunotherapy** that blocks a protein called **PD-L1** on the surface of certain immune cells called T-cells; this activates the T-cells to find and kill cancer cells. It is administered through a drip into a vein in your arm or chest

AUTOIMMUNITY

A condition in which the body's immune system mistakes its own healthy tissues as foreign and attacks them. Most autoimmune diseases cause inflammation that can affect many parts of the body

AVELUMAB

A type of immunotherapy that blocks a protein called PD-L1 on the surface of certain immune cells called T-cells; this activates the T-cells to find and kill cancer cells. It is administered through a drip into a vein in your arm or chest

BACILLUS CALMETTE-GUERIN (BCG)

A weakened form of the bacterium *Mycobacterium bovis* that does not cause disease. **BCG** is used to stimulate the immune system in the treatment of bladder cancer

BIOPSY

A medical procedure in which a small sample of cells or tissue is taken for examination under a microscope

BONE MARROW

A spongy tissue found inside some bones (e.g. hip and thigh bones). It contains stem cells, which are cells that can develop into red blood cells, white blood cells or platelets

CARBOPLATIN

A type of **chemotherapy** that is administered through a drip into a vein in your arm or chest

CHEMOTHERAPY

A type of cancer treatment using medicine that kills the cancer cells by damaging them, so that they cannot reproduce and spread

CISPLATIN

A type of **chemotherapy** that is administered through a drip into a vein in your arm or chest

CLINICAL TRIAL

A study that compares the effects of one treatment with another

COMPUTED TOMOGRAPHY (CT)

A scan using **X-rays** and a computer to create detailed images of the inside of the body

CONNECTIVE TISSUE

Tissue that supports, protects and gives structure to other tissues and organs in the body. Types of **connective tissue** include bone, cartilage, fat, blood and lymphatic tissue

CYSTECTOMY

Surgery to remove all or part of the bladder

CYSTOSCOPY

Examination of the bladder and **urethra** using a thin, tube-like instrument with a light and a lens, inserted into the **urethra**

DIETICIAN

A qualified health professional who is an expert on diet and nutrition

DNA

The chemical that carries genetic information in the cells of your body

DYSGEUSIA

A change in the sense of taste

DYSPHONIA

Difficulty speaking, including hoarseness and changes in the pitch or quality of the voice

DYSPNOEA

Shortness of breath

ELECTROLYTE

A substance that breaks up into ions (particles with electrical charges) when it is dissolved in water or body fluids. Some examples of ions are sodium, potassium, calcium, chloride and phosphate

ENFORTUMAB-VEDOTIN (EV)

A type of targeted therapy used to treat bladder cancer. It consists of a monoclonal antibody, which binds to a protein found on cancer cells, as well as a chemotherapy drug. It is administered through a drip into a vein in the arm or chest

ENZYMES

Proteins that speed up chemical reactions in the body

ERDAFITINIB

A type of **targeted therapy** used to treat bladder cancer that has certain **FGFR** mutations. It targets **FGFR** and prevents the cancer cells from growing, thus helping to slow down **tumour** growth. It is administered orally

FATIGUE

Overwhelming tiredness

FIBROBLAST GROWTH FACTOR RECEPTOR (FGFR)

A protein that is involved in cell division, cell maturation, formation of new blood vessels, wound healing and bone growth and development. A mutation in an FGFR gene may cause an FGFR protein to become overactive in certain cancers

FIRST-LINE (TREATMENT)

The initial treatment(s) given to a patient

GASTROINTESTINAL SYSTEM

The system of organs responsible for getting food into and out of the body and for making use of food to keep the body healthy – includes the oesophagus, stomach and intestines

GEMCITABINE

A type of **chemotherapy** that is administered through a drip into a vein in your arm or chest

GENE

A piece of **DNA** responsible for making a substance that the body needs to function

GENERAL ANAESTHETIC

A medication that causes a reversible loss of consciousness

HAIR FOLLICLE

A small sac in the skin which hair grows from

HAND-FOOT SYNDROME

A condition marked by pain, swelling, numbness, tingling or redness of the hands or feet. It sometimes occurs as a side effect of certain anti-cancer drugs

HORMONE REPLACEMENT THERAPY

Treatment with hormones to replace natural hormones when the body does not make enough. For example, hormone replacement therapy may be given to women after menopause to replace oestrogen and progesterone

HYPERGLYCAEMIA

An increase in the level of glucose (sugar) in the blood

HYPERTENSION

Abnormally high blood pressure

HYPONATRAEMIA

An abnormally low level of sodium in the blood

IMMUNOTHERAPY

A type of cancer treatment that stimulates the body's immune system to fight the cancer

INTRAVENOUS

Administered into a veir

INTRAVESICAL

Administered into the bladder

IONISING RADIATION

Any type of particle or electromagnetic wave that carries enough energy to ionise or remove electrons from an atom (e.g. **X-rays**)

LAMINA PROPRIA

A thin layer of **connective tissue** that surrounds the **urothelium**

LEUKOPENIA

A decrease in the number of leukocytes (a type of white blood cell) in the blood, which places individuals at increased risk of infection

LOCAL ANAESTHETIC

A medication that causes reversible absence of pain sensation around the site of administration

LYMPH NODES

Small structures throughout the lymphatic system that work as filters for harmful substances, such as cancer calls or hosteria.

MACROSCOPIC

Visible to the naked eye

MAGNETIC RESONANCE IMAGING (MRI)

A type of scan that uses strong magnetic fields and radio waves to produce detailed images of the inside of the body

MAINTENANCE (TREATMENT)

Treatment given after the initial cycles of **chemotherapy** with the aim of keeping the cancer under control

MARGIN

The edge or border of the tissue removed in cancer surgery. The **margin** is described as negative or clean when no cancer cells are found at the edge of the tissue, suggesting that all of the cancer has been removed. The **margin** is described as positive or involved when cancer cells are found at the edge of the tissue, suggesting that all of the cancer has not been removed.

MENOPAUSE

When a woman stops having periods and is no longer able to get pregnant naturally

METASTASES/METASTASIS

Cancerous tumours that have originated from a primary tumour/growth in another part of the body

METASTATIC (CANCER)

A cancer that has spread from its site of origin to different parts of the body

MICROSCOPIC

Too small to be seen without a microscope

MITOMYCIN C

A type of **chemotherapy** that is administered directly into the bladder in the treatment of bladder cancer

MONOCLONAL ANTIBODY

A type of targeted therapy. Monoclonal antibodies recognise and attach to specific proteins produced by cells. Each monoclonal antibody recognises one particular protein. They work in different ways depending on the protein they are targeting

MULTIDISCIPLINARY TEAM

A group of healthcare workers who are members of different disciplines (e.g. oncologist, nurse specialist, physiotherapist, radiologist) and provide specific services to the patient. The activities of the team are brought together using a care plan

MUSCLE-INVASIVE BLADDER CANCER (MIBC)

Bladder cancer that has spread into or through the muscle layer of the bladder

MUSCULARIS PROPRIA

The thick, outer muscle layer of the bladder

MUSCULOSKELETAL

Relating to muscles, bones, tendons, ligaments, joints and cartilage

MUTATION

A permanent alteration in the **DNA** sequence that makes up a **gene**, such that the sequence differs from what is found in most people and alters the function of the related protein

NEOADJUVANT (TREATMENT)

Treatment given as a first step to shrink a tumour before the main treatment (usually surgery) is given. Examples of neoadjuvant therapy include chemotherapy and radiotherapy

NEOBLADDER

A replacement bladder created from a section of the bowel and attached to the ureters and urethra

NEPHROTOXICITY

Toxicity in the kidneys

NEUTROPENIA

An abnormally low level of **neutrophils** in the blood which increases the risk of infection

NEUTROPHIL

A type of white blood cell that plays an important role in fighting off infection

NON-MUSCLE-INVASIVE BLADDER CANCER (NMIBC)

Early-stage bladder cancer in which the cancer cells are only in the inner lining of the bladder and have not grown into the deeper muscle layer.

OBESITY

Abnormal or excessive fat accumulation that may impair health

OEDEMA

A build-up of fluid in the body which causes the affected tissue to become swollen

PALLIATIVE (CARE)

The care of patients with advanced, progressive illness. It focuses on providing relief from pain, symptoms and physical and emotional stress, without dealing with the cause of the condition

PAPILLARY CARCINOMA

A **tumour** that appears as long, thin growths and develops in tissue that lines the inside of an organ. **Papillary tumours** can be benign (not cancer) or malignant (cancer)

PEMBROLIZUMAB

A type of immunotherapy that blocks a protein called

PERIPHERAL NEUROPATHY

PERIVESICAL TISSUE

PROGNOSIS

PROGRAMMED DEATH-LIGAND 1 (PD-L1)

tumour to evade detection by the body's immune system

PRURITUS

RADIOTHERAPY

RECURRENCE

REGIMEN

RISK FACTOR

SECOND-LINE (TREATMENT)

SEMINAL VESICLES

SPERM BANKING

SQUAMOUS CELL CARCINOMA

STOMA

A surgically-created opening from an area inside the

STOMATITIS

STROMA

is mostly made up of connective tissue, blood vessels.

SUBEPITHELIAL

Beneath an epithelial layer (e.g. the lamina propria beneath the urothelium)

SYSTEMIC BCG INFECTION

An infection caused by **BCG** getting into the blood stream

SYSTEMIC SCLEROSIS

skin, connective tissue and blood vessels

TARGETED THERAPY

usually while doing little damage to normal cells

THROMBOCYTOPENIA

TINNITUS

The hearing of a sound (such as ringing, whining or

TRANSURETHRAL RESECTION OF THE BLADDER TUMOUR (TURBT)

TUMOUR

A lump or growth of abnormal cells. **Tumours** may be benign (not cancerous) or malignant (cancerous). In this guide, the term '**tumour**' refers to a cancerous growth, unless otherwise stated

URETER

The tube that carries urine from the kidney to the bladder

URFTHRA

The tube through which urine leaves the body

URINARY TRACT

The organs of the body that produce and discharge urine, including the kidneys, **ureters**, bladder and **urethra**

UROSTOMY

Surgery to create an opening from inside the body to the outside, creating a new way to pass urine

UROTHELIAL CARCINOMA

Cancer that begins in the urothelial cells that line the urinary tract

UROTHELIUM

The lining of the urinary tract

X-RAY

An imaging test, using a type of radiation that can pass through the body, which allows your doctor to see images of inside your body

This guide has been prepared to help you, your friends and your family better understand the nature of bladder cancer and the treatments that are available. The medical information described in this document is based on the clinical practice guidelines of the European Society for Medical Oncology (ESMO) for the management of bladder cancer. We recommend that you ask your doctor about the tests and types of treatments available in your country for your type and stage of bladder cancer.

This guide has been written by Kstorfin Medical Communications Ltd on behalf of ESMO.

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We can help you understand bladder cancer and the available treatment options.

The ESMO Guides for Patients are designed to assist patients, their relatives and caregivers to understand the nature of different types of cancer and evaluate the best available treatment choices. The medical information described in the Guides for Patients is based on the ESMO Clinical Practice Guidelines, which are designed to guide medical oncologists in the diagnosis, follow-up and treatment in different cancer types.

For more information, please visit www.esmo.org

