Bladder Cancer

What is bladder cancer?

Let us explain it to you.

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ESMO/ACF Patient Guide Series
based on the ESMO Clinical Practice Guidelines
BLADDER CANCER: A GUIDE FOR PATIENTS

PATIENT INFORMATION BASED ON ESMO CLINICAL PRACTICE GUIDELINES

This guide for patients has been prepared by the Anticancer Fund as a service to patients, to help patients and their relatives better understand the nature of bladder cancer and appreciate the best treatment choices available according to the subtype of bladder cancer. We recommend that patients ask their doctors about what tests or types of treatments are needed for their type and stage of disease. 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. This guide for patients has been produced in collaboration with ESMO and is disseminated with the permission of ESMO. It has been written by a medical doctor and reviewed by two oncologists from ESMO including the lead author of the clinical practice guidelines for professionals. It has also been reviewed by patient representatives from ESMO’s Cancer Patient Working Group.

More information about the Anticancer Fund: www.anticancerfund.org

More information about the European Society for Medical Oncology: www.esmo.org

*For words marked with an asterisk, a definition is provided at the end of the document.*
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This is the first update of this guide. Updates reflect changes in the successive version of the ESMO Clinical Practice Guidelines. This first update was done by Dr. Ana Ugarte (ACF) and was reviewed by Dr. Svetlana Jezdic (ESMO) and Vanessa Marchesi, PhD (ESMO).
FACT SHEET ABOUT BLADDER CANCER

Definition of bladder cancer
Cancer that starts in bladder cells. This guide focuses on cancer that emerges in the inner lining of the bladder, called transitional cell carcinoma. Other types of bladder cancer also exist but are not discussed here.

Diagnosis
- Common symptoms of bladder cancer are urinary problems, blood in the urine, pain and urine blockage. However, these symptoms are not specific to bladder cancer and can also occur in many other conditions that are not related to cancer. To confirm the presence of bladder cancer, an examination called a cystoscopy is performed to inspect the interior of the bladder and the urethra for the presence of tumours.
- There are specific tests that help with the diagnosis and evaluation of the dissemination of the disease. The diagnosis can only be confirmed through a histopathological examination in which samples of tissue from the tumour are examined in a laboratory. This reveals specific characteristics of the tumour and is used to determine the type of bladder cancer.

Treatment according to the extension of the disease (classified into stages)
- Non-muscle invasive disease (stage 0a, stage 0is, stage I) involves a tumour confined to the mucosa (superficial layer of tissue in the lining of the bladder).
  - After cystoscopy all patients have the tumour removed by transurethral resection of bladder tumour (TURBT)*. This could eventually be curative if the complete tumour can be removed.
  - Sometimes adjuvant* therapy can be administered, such as chemotherapy or immunotherapy* instilled directly into the bladder, to avoid recurrence of the disease.
  - If these treatments fail, removal of the bladder (cystectomy) is an option.
- Muscle invasive bladder cancer (stage II, stage III) involves a tumour that has invaded the muscle layer of the bladder or has extended through the bladder reaching the surrounding tissues.
  - The recommended treatment is radical removal of the bladder, including complete or partial removal of some surrounding organs. This process can be slightly modified to preserve organs as much as possible.
  - Chemotherapy or radiotherapy are recommended before surgery in order to improve the outcome. If a patient refuses surgery or if he/she is not fit enough to have it, radiotherapy alone, aggressive TURBT* or TURBT* combined with radiotherapy and/or chemotherapy are possibilities.
- Advanced and metastatic disease (stage IV) involves a tumour that has grown through the bladder into the wall of the pelvis or the abdomen, or has spread to distant organs.
  - Chemotherapy is preferred as surgery, for this stage of disease, is unlikely to be curative. Surgery and radiotherapy after chemotherapy could be beneficial for selected patients.
  - Radiotherapy could also be useful to alleviate pain or bleeding.
- Treatment of relapse:
  - Chemotherapy with the drug vinflunine plus best supportive care are indicated.
  - In case of failure, taxane- or platinum-based chemotherapy are proposed.
  - Patients are also encouraged to participate in clinical trials.
Follow-up
Different tests may be performed during scheduled visits, depending on the staging and risk of recurrence. In non-muscle invasive cancer, these visits should take place every 3-6 months in the first 2 years and every 6 to 12 months thereafter (or as indicated by your medical team).
DEFINITION OF BLADDER CANCER

This definition is adapted from and is used with the permission of the National Cancer Institute (NCI) of the United States of America.

Bladder cancer is a cancer that forms in tissues of the bladder. The bladder is the organ that stores urine. The most frequent type of bladder cancer (90%) is transitional cell carcinoma*. This type of cancer begins in cells that normally form the inner lining of the bladder, also called the transitional epithelium* or urothelium*. Other types of bladder cancer include squamous cell carcinoma*, which begins in the thin, flat cells in the lining of the bladder, and adenocarcinoma*, a cancer that begins in cells in the lining of the bladder that release mucus. Some other rare forms of bladder cancer also exist. This guide relates to transitional cell carcinoma.

Anatomy of the male (left) and female (right) urinary system showing the kidneys, ureters*, bladder, and urethra*. Urine is made in the renal tubules* and collects in the renal pelvis*. The urine flows from the kidneys through the ureters to the bladder. The urine is stored in the bladder until it leaves the body through the urethra*.
IS BLADDER CANCER FREQUENT?

In 2012, it was estimated that approximately 151,297 patients were diagnosed with bladder cancer in Europe. Bladder cancer is the 5th most common cancer in Europe.

Bladder cancer is approximately five times more frequent in men than in women. It is estimated that 17.7 out of 100,000 men and 3.5 out of 100,000 women developed bladder cancer in 2012. Of all cancers, bladder cancer is the 4th most common cancer in men, and the 13th most common cancer in women.

In the European Union, the likelihood for a man to develop bladder cancer at some point in his life lies between 1.5 and 2.5%. For men living in Flanders (Belgium), Malta, Spain and Italy this is somewhat higher: between 3.1 and 4.2%. For a woman in the European Union, the chances of developing bladder cancer at some point in her life are less than 1%.

The risk of developing bladder cancer increases with age: overall, 70% of patients who develop bladder cancer present symptoms after the age of 65.
WHAT CAUSES BLADDER CANCER?

Currently, it is not entirely clear what causes bladder cancer. A number of risk factors* have been identified, but in many cases none of these seem to be present. A risk factor increases the risk that a cancer may occur, but is neither necessary nor sufficient to cause cancer. A risk factor is not a cause in itself.

Some people with these risk factors will never develop bladder cancer and some people without any of these risk factors may nonetheless develop bladder cancer.

The main risk factors for bladder cancer are:

- Aging: bladder cancer occurs most frequently in elderly people. Overall, 70% of patients developing bladder cancer are diagnosed after the age of 65.
- Previous history of bladder cancer.
- Cigarette smoking: cigarette smoking is the most important risk factor for bladder cancer. Stopping cigarette smoking for more than 4 years can lower the risk.
- A number of chemicals have been identified that may cause bladder cancer:
  o Aniline dyes: chemicals that may be present in coloured fabrics.
  o Cyclophosphamide: a chemotherapeutic* drug used for cancer treatment.
  o Aromatic amines: exposure to these chemicals can occur in various occupations such as those in the painting, leather, car, metal, paper and rubber industry, but also amongst truck drivers, dry cleaners, dental technicians and hairdressers. In these circumstances, bladder cancer does not occur until 30 to 50 years after exposure.
  o Arsenic: in a Taiwanese region where water contained high arsenic levels, an increased risk of bladder cancer has been found.
  o Aristolochia fangchi: this is a Chinese herb used in some dietary supplements and herbal remedies. An increased risk of bladder cancer was found in people that had used a dietary supplement in which this herb had been mistakenly added.
- Irradiation: exposure to ionizing irradiation* in the region of the bladder, for example during radiotherapy for prostate* cancer, is thought to increase the risk of bladder cancer.
- Some risk factors are particularly important for a specific type of bladder cancer, namely squamous cell carcinoma*. This tumour is caused by chronic irritation or inflammation of the bladder. In Western countries, the main risk factors for squamous cell carcinoma include a badly-functioning bladder, prolonged presence of a catheter* in the bladder, bladder stones and chronic bladder infection. In Africa and the Middle East, an important risk factor for squamous cell carcinoma is infection with Schistosoma hematobium, a microbe that is common in these regions. It can infect the bladder and lead to chronic inflammation.
- Diabetes*: individuals with type-2 diabetes have an increased risk of developing bladder cancer.
Other factors have been suspected to be associated with an increased risk of bladder cancer, but the evidence is inconsistent:

- Coffee, artificial sweeteners and alcohol: there is no clear evidence that consumption of these substances produces a risk for developing bladder cancer.
- Tap water with high levels of trihalomethanes: these chemicals are the broken down products of the disinfectant chlorine. Some studies show that prolonged ingestion of this kind of tap water may increase the risk for bladder cancer, but the evidence is inconsistent.
- Genes: overall, having a family member with bladder cancer conveys a slightly increased risk of developing the disease. Bladder cancer as a result of an inheritable faulty gene* is very rare.
- Body weight: one study has shown that being overweight is associated with a higher risk of bladder cancer, but other studies do not confirm this.

Some factors have been proposed to protect against the development of bladder cancer, but clear evidence for this is not available.

- Fluid intake: it has been proposed that high fluid intake may reduce the risk of developing bladder cancer in men, but inconsistencies exist between studies.
- Fruit and vegetables: consumption of fruit and vegetables is said to have a protective effect against bladder cancer.
HOW IS BLADDER CANCER DIAGNOSED?

Bladder cancer may be diagnosed during a routine physical check-up, or can be suspected on the basis of specific symptoms.

The main symptoms are:

- Blood in the urine (called hematuria): this is usually painless and is experienced by 85% of bladder cancer patients.
- Urinary problems: the need to urinate more frequently than usual (called frequency), the need to pass urine urgently (called urgency) or pain when passing urine (called dysuria).

However, these symptoms are not specific to bladder cancer and can also occur in many conditions that are not related to cancer, such as urinary infection, kidney stones or benign* prostatic hyperplasia*.

Bladder cancer may block the flow of urine from the kidney. Accumulation of urine within the kidney may lead to distension of the kidney (called hydronephrosis) and pain.

Besides asking about the symptoms mentioned above, the doctor will also perform a general physical examination and ask for laboratory blood tests to measure blood cell counts and kidney function.

The diagnosis of bladder cancer is based on the following examinations:

1. **Clinical examination***

   A physical examination provides information about signs of bladder cancer and other health problems. The doctor might examine the rectum and, in women, the vagina to determine the size of a bladder tumour and to see if and how far it has spread.

2. **Cystoscopy***

   A cystoscopy is a technical examination of the bladder: the doctor inserts a lighted tube with a camera at the end into the urethra* to inspect the interior of the bladder and the urethra for the presence of tumours. Cystoscopy can be performed in the doctor’s office; with the use of a local anaesthetic* gel, this procedure is usually well tolerated. However, cystoscopy may also be performed under general anaesthesia* together with the clinical bimanual examination of the bladder.

   The doctor can insert a fine surgical instrument into the cystoscope tube to remove – under direct vision - tissue samples from the tumour or from any other suspicious area. This specimen is called a biopsy*. For certain bladder cancers, the doctor may immediately resect the entire tumour: this is called transurethral resection of the bladder tumour (TURBT)*. In this case, the cystoscopy also constitutes the first step in the treatment.
In specific circumstances, the doctor will also inspect the ureters, a procedure called ureteroscopy*. In other circumstances, cystoscopy also includes biopsy sampling from the urethra*.

3. **Urine cytology**

This is a laboratory test performed to detect the presence of tumour cells in urine.

4. **Histopathological examination**

This is the laboratory investigation of the tumour cells. It is performed on tissue removed from the tumour during cystoscopy*. The histopathological* information will confirm the diagnosis of bladder cancer and will reveal the specific characteristics of the tumour, allowing the doctor to determine the type of bladder cancer.

If surgery is indicated after the cystoscopy (usually a TURBT*), a second histopathological examination will be performed on the tumour tissue obtained during surgery. This is very important to confirm the results of the first biopsy* and to provide more accurate information on the cancer and the stage of the cancer.

5. **Radiological examination**

If the histopathological examination* shows that the tumour has grown into the deeper layers (the muscle layers) of the bladder, then radiological investigation is needed to determine if the tumour has also grown into the tissues and lymph nodes* outside the bladder.

The radiological investigation is part of a diagnostic process called staging* and can be performed using computed tomography (CT)* or magnetic resonance imaging (MRI)* of the abdomen and pelvis. Since a synchronous upper tract urothelial tumour may exist in 2.5% of patients, upper urinary tract imaging with either CT urograms, or intravenous or retrograde pyelograms (special X-ray examination of the kidneys, bladder and ureters) should be undertaken. In patients with a high risk of metastases, additional tests may be performed, such as a CT* of the chest, and also a bone scintigraphy* if there are symptoms of tumour spread in the bones.
WHAT IS IMPORTANT TO KNOW TO DEFINE THE OPTIMAL TREATMENT?

Doctors will need to consider many aspects of both the patient and the cancer in order to decide on the best treatment.

Relevant information about the patient

- Gender
- Personal medical history, previous illnesses and treatments
- History of bladder cancer in relatives
- General well-being and specific physical complaints
- Results from the clinical examination*
- Results from laboratory tests on blood counts, kidney and liver function

Relevant information about the cancer

- Staging*

Doctors use staging to assess the extension of the cancer and the prognosis of the patient. The TNM staging system is commonly used. The combination of size of the tumour and invasion* of nearby tissue (T), involvement of lymph nodes* (N), and metastasis* or spread of the cancer to other organs of the body (M) will classify the cancer as being at one of the stages described below.

The stage* is fundamental in order to make the right decision about the treatment. The less advanced the stage, the better the prognosis. Staging is performed when the clinical and radiological investigations* and the histopathological examination* of the biopsy* are completed. If surgery is indicated, a second staging will be performed on the basis of the laboratory examination of the surgical specimen.

The table below presents the different stages of bladder cancer. Since the definitions are somewhat technical, it is recommended to ask your doctor for a more detailed explanation.
<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition (see figure of the bladder wall below)</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0a</td>
<td><em>Non-invasive papillary carcinoma</em>: the tumour is confined to the innermost cell layers of the bladder lining (the epithelium*)</td>
<td>Non-muscle invasive bladder cancer</td>
</tr>
<tr>
<td>Stage 0is</td>
<td><em>Carcinoma in situ</em>, also referred to as <em>flat tumour</em>: a high-grade tumour that is confined to the innermost cell layers of the bladder lining (the epithelium*)</td>
<td>Non-muscle invasive bladder cancer</td>
</tr>
<tr>
<td>Stage I</td>
<td>The tumour invades the deeper connective tissues of the bladder lining (the lamina propria*)</td>
<td>Non-muscle invasive bladder cancer</td>
</tr>
<tr>
<td>Stage II</td>
<td>The tumour invades the muscle of the bladder. Stage II is divided into 2 stages: T2a: the tumour invades the inner half of the muscle of the bladder. T2b: the tumour invades the outer half of the muscle of the bladder</td>
<td>Muscle-invasive bladder cancer</td>
</tr>
<tr>
<td>Stage III</td>
<td>The tumour invades the tissues surrounding the bladder. Stage III is divided into 3 stages: T3a: microscopic invasion*. T3b: macroscopic invasion*. T4a: invasion of organs surrounding the bladder: the prostate* in men, the uterus and/or vagina in women.</td>
<td>Muscle-invasive bladder cancer</td>
</tr>
<tr>
<td>Stage IV</td>
<td>The tumour invades the pelvic wall and/or abdominal wall or the tumour is accompanied by metastasis* in lymph node(s) or in an organ at a distance from the bladder</td>
<td>Advanced and metastatic disease</td>
</tr>
</tbody>
</table>

Layers of the bladder wall showing the mucosa* (the bladder lining consisting of the epithelium* and lamina propria*) and the muscle layers.
**Results of the biopsy**

Tissue from the tumour biopsy is examined in a laboratory by a pathologist*. This examination is called histopathology*. If surgery is performed after cystoscopy*, histopathological examination involves the examination of the tumour and the lymph nodes* removed during surgery. This is very important to confirm the results of the initial findings and to provide more information on the stage of the cancer. The results of the examination of the biopsy include:

- **Histological type**
  
  The histological type refers to the type of cells that compose the tumour. About 90% of bladder cancers are transitional cell carcinomas*. This guide relates to transitional cell carcinoma, also called urothelial carcinoma, which is a tumour that arises from the transitional epithelium*. The transitional epithelium consists of multiple layers of cells that can change shape as the bladder stretches and that line the innermost wall of the bladder.

  The remaining 10% are predominantly squamous cell carcinomas* and adenocarcinomas*. Other histological types are very rare.

- **Grade**

  The grade is determined on the basis of how different the tumour cells look from the cells normally found in a healthy bladder lining. The abnormal features indicate the rate at which the cells multiply and the degree to which they are invasive. There are four different grades of bladder cancer:

  - Papilloma: a tumour composed of non-malignant cells.
  - Papillary urothelial neoplasm of low malignant potential (PUNLMP): a tumour composed of non-malignant cells typically covered with a thickened layer of transitional epithelium*.
  - Urothelial carcinoma low grade: a malignant tumour that grows slowly and is unlikely to spread.
  - Urothelial carcinoma high grade: a malignant tumour that grows faster and that is more likely to spread.
WHAT ARE THE TREATMENT OPTIONS?

Treatment planning involves a team of professionals from different medical disciplines. It usually involves a meeting of the different specialists, called a multidisciplinary meeting* or tumour board review*. In this meeting, the treatment planning will be discussed according to the relevant information mentioned above.

The treatment will usually combine therapies that:
- Act on the cancer locally, such as surgery, radiotherapy*, local chemotherapy* and local immunotherapy*
- Act on the cancer cells all over the body using systemic chemotherapy

The exact treatment will depend on the stage of the cancer, on the characteristics of the tumour and on the risks for the patient.

The treatments listed below have their benefits, their risks and their contraindications*. It is recommended that patients ask their doctors about the expected benefits and risks of every treatment in order to be informed about the consequences of the treatment. For some treatments, several possibilities are available. The choice should be discussed according to the balance between benefits and risks.

Treatment plan for non-muscle invasive disease (stage 0a, stage 0is, stage I)

At these stages, the tumour is confined to the superficial layer of the bladder wall (mucosa*) and does not invade the muscle of the bladder. The main goal of the treatment is to remove the local tumour by surgery during a TURBT*. However, additional treatment delivered locally in the bladder (called adjuvant* intravesical* treatment) is recommended since it lowers the risk of the tumour recurring or progressing.

The type of adjuvant therapy* used depends on the risk of progression* and recurrence*: for each patient with a stage 0a or stage I tumour, this is calculated using a scoring system based on several tumour-specific characteristics.

Cystoscopy* and transurethral resection of the bladder tumour (TURBT)*

After an initial cystoscopy, all patients undergo a TURBT*. Often, the complete tumour is resected, and, in this case, the TURBT* is the definitive treatment. However, sometimes it is recommended to give additional treatment (called adjuvant treatment*) with drugs that are applied directly into the bladder (called intravesical* treatment). The type of additional treatment used depends on the individual risk of recurrence and progression*, but also on the patient’s capability to tolerate the potential side effects* associated with the treatment.

In selected patients with high risk tumours, a second TURBT* is recommended either before or after intravesical therapy to detect any residual disease and to provide a more accurate staging.
Intravesical* chemotherapy* or immunotherapy*

In order to reduce the risk of recurrence and progression*, all patients that have had a TURBT* are given one single intravesical instillation* with a chemotherapeutic* agent immediately after surgery. In most cases the drug used is Mitomycin C*, but epirubicin* or doxorubicin* may also be used.

For patients with a tumour at low risk of recurrence and progression, one single instillation completes the treatment. For patients who are considered to have an intermediate or high risk of tumour recurrence or progression, the first instillation should be followed by further intravesical chemotherapy, or by intravesical immunotherapy* with bacillus Calmette Guérin (BCG)* (see below). Whether chemotherapy or immunotherapy* is chosen depends on the individual risk profile. Chemotherapy is usually given for up to one year. Immunotherapy* is given for a minimum of one year.

Intravesical* immunotherapy* with bacillus Calmette-Guérin (BCG)*

For patients with certain risk profiles, it is recommended to give intravesical treatment with bacillus Calmette-Guérin (BCG), a vaccine used to protect against tuberculosis*. The working mechanism of intravesical BCG therapy is not exactly understood. It is thought that BCG induces an immune reaction that kills cancer cells. Treatment with BCG is therefore considered as immunotherapy*. Usually, an initial 6-week treatment regimen is given (called induction therapy), and this is followed by so-called maintenance therapy for a minimum of one year. Some maintenance regimens last two years.

Cystectomy*

Cystectomy is recommended for patients with stage 0is and stage I tumours that do not respond to adjuvant* intravesical* treatment.

Treatment plan for muscle invasive bladder cancer (stage II, stage III)

At these stages, the tumour has invaded the muscle layer of the bladder or has extended through the bladder wall into the tissues surrounding the bladder. The treatment aims to surgically remove the entire bladder as well as the lymph nodes* in the pelvis and the neighboring organs. Prior to surgery, chemotherapy* is administered, with the aims of reducing tumour size, attacking tumour cells in metastases* that are too small to be detected, and reducing the risk that tumour cells will spread to other parts of the body during surgery.

Radical cystectomy*

The standard treatment for muscle invasive bladder cancer includes radical cystectomy. For male patients this involves the complete removal of the bladder, all visible tumour tissue, but also the urethra*, prostate*, seminal vesicles*, the lower parts of the ureters* and the lymph nodes* in the pelvis. For female patients, radical cystectomy involves removal of the bladder, all visible and resectable tumours, the entire urethra, the lower part of the ureters, the adjacent vagina*, the uterus* and the lymph nodes in the pelvis.

In certain patients, this procedure may be slightly modified in order to preserve certain structures. Whether or not this is possible depends on the extent to which the tumour has spread and needs to be carefully evaluated in each individual patient.

Radical cystectomy* leads to the loss of bladder function, that is, the storage of urine. The surgeon will therefore connect the ureters* to a new outlet to allow evacuation of urine (called a
urinary diversion*). This new outlet may be either the urethra*, the skin of the abdomen, or the very last part of the large bowel (called a rectosigmoid diversion). The choice of approach depends on many factors such as the tumour stage, the structures that can be preserved after radical cystectomy, the patient’s general medical condition and the patient’s preference. The different options are explained further in the text (see Side effects* of therapies).

In addition, radical cystectomy may involve the removal of certain reproductive organs*. This may lead to sexual dysfunction* and/or the loss of reproductive function* (see Side effects of Therapies).

Chemotherapy*

It is recommended to give neo-adjuvant* combination chemotherapy to patients with stage T2 or T3 disease. This means that a combination of chemotherapeutic* drugs is given prior to cystectomy* or definitive radiotherapy*. The recommended combinations are gemcitabine* and cisplatin* (abbreviated GC), or methotrexate*, vinblastine*, doxorubicin* and cisplatin (abbreviated MVAC). The purpose of neo-adjuvant therapy* is to eradicate micrometastases*, reduce tumour size and reduce the risk of tumour cells spreading during the surgical procedure.

Radiotherapy*

Radiotherapy alone may be indicated for patients who are medically not fit enough to undergo the extensive surgery of radical cystectomy*. Radiotherapy may be given as part of a combination treatment in selected cases where the treatment aims to preserve the bladder* (see: organ preservation therapy*).

Organ preservation therapy*

Organ preservation therapy refers to a treatment where the bladder is preserved. This is proposed to patients who do not wish to undergo radical cystectomy*, or who are not medically fit enough to tolerate this kind of surgery. This treatment can be: aggressive TURBT*, TURBT* in combination with radiotherapy* or chemotherapy*, or TURBT* in combination with radiotherapy and chemotherapy. The latter is called trimodality combination treatment and it is the preferred approach.

Organ preservation therapy may also be considered in selected patients with early stage bladder cancer, provided they meet a number of other stringent medical criteria.

Organ preservation therapy requires a stringent lifelong follow-up* with cystoscopy* and urine cytology* to evaluate the response to treatment and to detect disease recurrence. If persistent or recurrent disease is observed, an immediate cystectomy is recommended, if possible.

Treatment plan for advanced and metastatic* disease (stage IV)

At this stage, the tumour has grown through the bladder wall into the wall of the pelvis or the abdomen, or beyond the abdomen to distant organs. Since it is difficult or not medically indicated to remove the complete tumour by surgery, the primary goal of the treatment is to target tumour cells using chemotherapy that is given through a vein and that therefore acts systemically.
Chemotherapy*

The standard combination regimen consists of the drugs cisplatin* with gemcitabine* (abbreviated as GC) or methotrexate*, vinblastine*, doxorubicin* and cisplatin (abbreviated as MVAC). The MVAC regimen causes more toxic side effects* than GC. Patients with limited advanced disease (lymph node* involvement and no visceral* metastasis* in organs*) and those who are medically fit may be able to receive high-dose MVAC in combination with granulocyte-colony stimulating factor* (G-CSF), a growth factor that can increase tolerability of the chemotherapy.

Approximately half of patients are medically not fit enough to tolerate cisplatin due to poor general health, poor kidney function or the presence of other diseases. These patients are treated with carboplatin* and gemcitabine* (abbreviated CarboGem), with methotrexate*, carboplatin and vinblastine (abbreviated M-CAVI) or with taxane* or gemcitabine only. CarboGem is the reference treatment in this case. M-CAVI causes slightly more toxic effects than CarboGem.

The doctor evaluates the tolerability after each cycle of chemotherapy and evaluation of response to treatment is done after 2 to 3 cycles of chemotherapy by the same radiographic methods used to detect tumour lesions.

Surgery and radiotherapy* after systemic chemotherapy*

Systemic chemotherapy followed by cystectomy and lymphadenectomy* or radiotherapy may be considered for selected patients with locally advanced disease.

Radiotherapy*

Radiotherapy can be useful to alleviate pain or bleeding.

Treatment of relapse

So far, vinflunine* plus best supportive care is recommended when the disease reappears after treatment with platinum-based chemotherapy for metastatic disease. Vinflunine as second-line chemotherapy is proposed when progression occurs less than 12 months after first-line treatment. In this case, taxane*-based chemotherapy or participation in a clinical trial may also be proposed. If progression occurs later than 12 months after first-line treatment, platinum-based chemotherapy rechallenge may be considered.

Treatment of complications caused by disease

Blockade of urinary flow

Bladder cancer may block the flow of urine and cause urine to accumulate in the kidney. This may cause pain and disturbance of kidney function. If cystectomy* is not possible because of advanced disease or because the patient is medically not fit enough to undergo this procedure, it may be necessary to divert urine flow away from the bladder to the exterior. This can be done by surgically connecting the kidney or the ureter* to the skin of the abdomen. This is called nephrostomy and ureterostomy, respectively. The urine is collected in a plastic bag attached to the skin.
WHAT ARE THE POSSIBLE SIDE EFFECTS OF THE TREATMENTS?

Surgery

**General risks and side effects**

Some risks are common for every surgical intervention performed under general anesthesia*. These complications are unusual and include formation of a blood clot in the veins, heart or breathing problems, bleeding, infection, or reactions to the anesthesia*. These are largely prevented by thorough medical evaluation before surgery.

The bladder is located in the pelvis together with the local lymph nodes*, parts of the bowel, major blood vessels, and the female reproductive organs*. Depending on the extent of surgical resections needed to obtain the best results, some of these structures may become damaged. Accurate preoperative staging* and imaging* will help to minimize this risk.

When lymph nodes* in the pelvis and the abdomen are removed, it can damage or block the lymph system* resulting in lymphedema*, a condition where lymph fluid* accumulates in the legs and makes them swell. This may occur soon after the intervention, but also later.

**Loss of bladder function after cystectomy**

The consequence of cystectomy is that the function of the bladder is lost. Several surgical options exist to divert and collect the urine, either within or at the exterior of the body. The best choice needs to be carefully evaluated and will depend on the tumour stage, the surgical treatment given, the patient’s general condition, and the patient’s preference. The different possibilities are discussed briefly below. It is recommended to ask your doctor for more information.

**Orthotopic neobladder.** A new bladder organ (called a neobladder) is constructed: tissue from the bowel is used to form a pouch that is placed between the ureters* and the urethra*. Orthotopic means that the new bladder is in the same place as the original bladder. This pouch will store urine, and urine will be passed through the urethra.

**Abdominal diversion.** The surgeon connects the ureters* to an artificial opening in the abdominal wall, called a stoma*. This may be a direct connection or the surgeon may use tissue from the small intestine to guide the urine to the stoma. The urine is collected in a small plastic bag attached to the skin. The surgeon may also form a pouch on the inner side of the abdomen and a stoma that does not allow spontaneous passage of urine to the exterior: in this case the pouch can be emptied from the exterior using a catheter*. This is called a continent urinary diversion*.

**Rectosigmoid diversion.** The surgeon connects the ureters* to the very last part of the large bowel, called the rectosigmoid. The rectosigmoid normally holds the stool and will now have the same function for urine. The surgeon may place a segment of intestine between the ureters and the rectosigmoid.

The nature and frequency of the side effects* of these diversion* procedures will depend on the type of procedure. The most frequent problems are narrowing of the ureter at the stoma* and infection of the kidneys.
Sexual dysfunction and/or loss of reproductive function*

Radical cystectomy* in men includes the resection of the urethra*, seminal vesicles* and prostate*. In women it includes the resection of the uterus* and part of the vagina*. The loss of these reproductive organs* may lead to sexual dysfunction*, the loss of the ability to conceive children, and in women it will lead to the loss of the ability to bear children. The doctor will refer such patients to specialized support providers.

Radiotherapy*

Side effects* of radiotherapy may occur in organs that are directly targeted, but also in healthy organs that lie close to the bladder and that cannot be avoided by the X-rays*. For bladder cancer, modern radiation techniques are very safe and major complications occur in less than 5% of patients. Effects on the urinary system include pain while passing urine, an urgent need to urinate, blood in the urine, blockage of urinary flow, and ulceration of the inner lining of the bladder. Effects of radiation on the lower intestines include discomfort, diarrhea, mucus and blood discharge, and, rarely, perforation of the intestines.

In women, vaginal narrowing is a possible late effect of radiotherapy in the pelvic region. The oncologist will advise on strategies to maximally prevent and relieve these reactions.

Intravesical instillation* therapy

The main side effect* of intravesical BCG* instillation is inflammation of the bladder, called cystitis*. The most severe side effect is a generalized infection, which may result when the bacilli are taken up through the bladder wall into the blood. Therefore, this therapy is not indicated in patients with reduced function of the immune system*. In general, side-effects of intravesical BCG therapy can be managed.

Intravesical instillation of chemotherapy such as Mitomycin C* may have several side effects, such as cystitis*, allergy and skin reactions.

Chemotherapy*

Side effects* of chemotherapy are frequent but nowadays can be well controlled using adequate supportive measures. Side effects will depend on the drug(s) administered, on the dose and on factors specific to individual patients. If a patient has suffered from other medical problems in the past, some precautions should be taken and/or changes of the treatment should be made. Side effects are more severe when chemotherapy is given systemically (usually through a vein), than when it is given locally, directly into the bladder (see: intravesical* drug therapy).

Listed below are the side effects that are known to occur with one or several of the chemotherapy drugs currently used for bladder cancer. The nature, frequency and severity of the side-effects vary for every combination used.

The most frequent side effects are:

- Hair loss or hair thinning
- Decreased blood cell counts, which may lead to anemia*, bleeding and bruising, and infections
- Tiredness
- Feeling sick or being sick
Other side effects that may occur frequently with one or more of the chemotherapy drugs used for bladder cancer include:

- Mouth sores or ulcers
- Taste changes
- Diarrhea
- Gritty or watery eyes
- Sensitivity to sunlight
- Kidney damage
- Hearing loss
- Damage to the fetus in the womb of a cancer patient receiving chemotherapy
- Loss of fertility
- Interruption of periods in women (amenorrhea), which may be temporary

Occasional side effects include:

- Changes in liver function
- Damage to the heart muscle
- Numbness or tingling in fingers and toes (peripheral neuropathy)
- Constipation
- Blurred vision
- Skin rash or reddening of skin
- Cough or shortness of breath
- Liver changes
- Changes in color of skin and/or nails
- Allergic reaction
- Inflammation around the drip/injection site
- Fever and chills

Rare side effects are:

- Depression
- Sore eyes
- Headaches
- Increased heart rate
- Dizziness
- High blood pressure

Finally, it should be noted that some chemotherapy drugs can enter breast milk and may be harmful if passed to the baby.
WHAT HAPPENS AFTER THE TREATMENT?

It is not unusual for cancer patients to experience treatment-related symptoms after the treatment has been completed.

- Patients may experience anxiety, difficulty sleeping or depression, and may need psychological support.
- During and after treatment, nutrition may become problematic due to reduced appetite, nausea and general malaise.
- Difficulties in concentration and memory problems are not uncommon side effects* of systemic chemotherapy, i.e. when administered in a vein or orally.

Follow-up* with doctors

After completion of treatment the doctor will propose a follow-up aiming to:

- Detect and prevent adverse effects of the treatment.
- Detect possible recurrence* as soon as possible and direct appropriate treatment.
- Provide medical information, psychological support and referral to specialized support providers to optimize the return to normal daily life.

The follow-up protocol will include regularly timed office visits and investigations. The protocol depends on the grade* and staging* of the bladder tumour that was treated, and on the type of treatment given. In general, follow-up visits may include a combination of the following investigations:

- History of general physical health and bladder cancer-related symptoms since the last visit
- Cystoscopy* to detect recurrence* and to perform a biopsy* of new lesions
- Imaging of the upper urinary system
- Urinary cytology*: laboratory examination of the urine for the presence of tumour cells that are shed by a potentially recurring bladder tumour.
- Laboratory investigations: blood chemistry and kidney function
- Repeated radiological investigations* in case initial examinations showed abnormal findings

There are no generally accepted follow-up protocols. The following are recommended possible regimens:

In non-muscle invasive bladder cancer, regular cystoscopy and urine cytology every 3–6 months during the first 2 years, based on the risk of recurrence, and every 6–12 months thereafter.

After definitive treatment of muscle invasive bladder cancer with radical cystectomy, urine cytology, liver function and renal function tests should be carried out every 3–6 months for 2 years, and subsequently as clinically indicated. Imaging of the chest, upper urinary tract, abdomen and pelvis should also be undertaken every 3–6 months for 2 years based on the risk of recurrence, and subsequently as clinically indicated.
For muscle invasive bladder cancer patients in whom an organ preservation strategy has been adopted, there is a need to evaluate response to treatment after induction chemoradiation. After completion, the same follow-up regimen as for patients with radical cystectomy is recommended. However, cystoscopy and urine cytology plus random biopsies every 3–6 months for 2 years are needed. During follow-up, monitoring of long-term treatment toxicities and potential recurrences of secondary tumours should be performed.

Returning to normal life

Returning to normal daily life may be difficult knowing that the cancer may come back. It is advised to eliminate any of the known risk factors* for bladder cancer.

Follow-up* visits with the doctor provide an opportunity for the patient to obtain medical information, psychological support and referral to specialized support providers. Additional expert psychological advice may be valuable, and some patients may find support in patient groups or patient-targeted information media. Dieticians may provide advice on adequate nutrition. Social workers may help in finding resources to ensure successful rehabilitation.

What if the cancer comes back?

If the cancer returns, it is called recurrence*. The extent of the recurrence will direct the treatment decision, and this should be carefully determined for each individual patient.

In patients treated with organ preservation therapy*, residual tumour can be detected in 20% of cases during restaging. An additional 20-30% of patients with initial complete responses will develop new or recurrent disease in the preserved bladder. Up to 70% of patients are free of tumours after the first cystoscopy* control. A quarter of them develop a new lesion at a later time that requires additional treatment (cystectomy when possible).

For patients with metastatic* disease who experience progression* after completing a first-line platinum-containing regimen, a second-line chemotherapy regimen with vinflunine* is recommended.
**DEFINITIONS OF DIFFICULT WORDS**

**Adenocarcinoma**
Cancer that begins in cells that line certain internal organs and that have gland-like (secretory) properties.

**Adjuvant (treatment)**
Adjuvant treatment in cancer is a therapy that helps another therapy to reach its ultimate goal and reinforces its effect. For example, radiotherapy and/or chemotherapy* help a surgery to accomplish its goal of eliminating a cancerous tumour. In a non-oncological context, it can also be an agent added to vaccines to stimulate the immune system's response to an antigen.

**Anesthetic (gel)/ anesthesia**
Reversible state of loss of awareness in which the patient feels no pain, has no normal reflexes, and responds less to stress, induced artificially by the employment of certain substances known as anaesthetics. It can be complete or partial and allows patients to undergo surgery.

**Bacillus Calmette Guérin (BCG)**
A weakened form of the bacterium *Mycobacterium bovis* (bacillus Calmette-Guérin) that does not cause disease. Bacillus Calmette-Guérin is used in a solution to stimulate the immune system in the treatment of bladder cancer and as a vaccine to prevent tuberculosis*.

**Benign**
For a tumour, benign means not cancerous. Benign tumours may grow larger, but do not spread to other parts of the body. Also called non-malignant.

**Benign prostatic hyperplasia (BPH)**
A benign (non-cancerous) condition in which an overgrowth of prostate tissue pushes against the urethra* and the bladder, blocking the flow of urine. Also called benign prostatic hypertrophy.

**Biopsy**
The removal of cells or tissues for examination by a pathologist*. The pathologist may study the tissue under a microscope or perform other tests on the cells or tissue. There are many different types of biopsy procedures. The most common types include: (1) incisional biopsy, in which only a sample of tissue is removed; (2) excisional biopsy, in which an entire lump or suspicious area is removed; and (3) needle biopsy, in which a sample of tissue or fluid is removed with a needle. When a wide needle is used, the procedure is called a core biopsy. When a thin needle is used, the procedure is called a fine-needle aspiration biopsy.

**Carboplatin**
A drug that is used to treat advanced ovarian cancer that has never been treated or symptoms of ovarian cancer that have come back after treatment with other anticancer drugs. It is also used with other drugs to treat advanced, metastatic*, or recurrent* non-small cell lung cancer and is being studied in the treatment of other types of cancer. Carboplatin* is a form of the anticancer drug cisplatin* and causes fewer side effects* in patients. It attaches to DNA in cells and may kill cancer cells. It is a type of platinum compound. Also called Paraplatin.
Catheter
A tube that can be inserted into the body. It has many uses including draining or administering fluids or gases.

Chemotherapeutic/Chemotherapy
A type of cancer treatment that uses drugs to kill cancer cells and/or limit their growth. These drugs are usually administered to the patient by slow infusion into a vein but can also be administered orally, by direct infusion into a limb or by infusion into the liver, according to the location of the cancer.

Cisplatin
A drug used to treat many types of cancer. Cisplatin contains the metal platinum. It kills cancer cells by damaging their DNA and stopping them from dividing. Cisplatin is a type of alkylating agent. Also called Platinol.

Clinical examination
The examination of the body to search for signs of disease.

Contraindication
A condition or symptom that prevents the administration of a given treatment or procedure to the patient. Contraindications are either absolute, meaning the treatment should never be given to patients with this condition or symptom, or relative, meaning that the risk can be outweighed by the benefits in some patients with this condition or symptom.

Computed tomography/ CT-scan
A form of radiography in which body organs are scanned with X-rays* and the results are put together by a computer to generate detailed images of parts of the body.

Cystitis
Inflammation of the bladder.

Cystoscopy
Examination of the bladder and urethra* using a cystoscope inserted into the urethra. A cystoscope is a thin, tube-like instrument with a light and a lens for viewing. It may also have a tool to remove tissue to be checked under a microscope for signs of disease.

Diabetes
Any of several diseases in which the kidneys make a large amount of urine. Diabetes usually refers to diabetes mellitus in which there is also a high level of glucose (a type of sugar) in the blood because the body does not make enough insulin (a hormone needed for cells to absorb and use glucose) or use it the way it should.

Doxorubicin
A drug that is used to treat many types of cancer and is being studied in the treatment of other types of cancer. Doxorubicin comes from the bacterium Streptomyces peucetius. It damages DNA and may kill cancer cells. It is a type of anthracycline antitumour antibiotic. Also called Adriamycin PFS, Adriamycin RDF, doxorubicin hydrochloride, hydroxydaunorubicin, and Rubex.
**Epirubicin**
A drug used together with other drugs to treat early breast cancer that has spread to lymph nodes*. It is also being studied in the treatment of other types of cancer. Epirubicin is a type of anthracycline antibiotic. Also called Ellence and epirubicin hydrochloride.

**Epithelium**
The term epithelium refers to cells that line hollow organs and glands and those that make up the outer surface of the body. Epithelial cells help to protect or enclose organs. Most produce mucus or other secretions.

**Follow-up**
Monitoring a person’s health over time after treatment. This includes keeping track of the health of people who participate in a clinical study or clinical trial for a period of time, both during the study and after the study ends.

**Granulocyte-Colony Stimulating Factor (G-CSF)**
A growth factor that stimulates the production of neutrophils (a type of white blood cell). It is a cytokine that is a type of hematopoietic (blood-forming) agent. Also called filgrastim and G-CSF.

**Gemcitabine**
The active ingredient in a drug that is used to treat pancreatic cancer that is advanced or has spread. It is also used with other drugs to treat breast cancer that has spread, advanced ovarian cancer, and non-small cell lung cancer that is advanced or has spread. It is also being studied in the treatment of other types of cancer. Gemcitabine blocks cells from making DNA and may kill cancer cells. It is a type of antimetabolite.

**General anesthesia**
A temporary loss of feeling and a complete loss of awareness that feels like a very deep sleep. It is caused by special drugs or other substances called anesthetics*. General anesthesia keeps patients from feeling pain during surgery or other procedures.

**Grade**
A description of a tumour based on how abnormal the cancer cells look under a microscope and how quickly the tumour is likely to grow and spread. Grading systems are different for each type of cancer.

**Histopathology (histopathological examination, histological type)**
The study of diseased cells and tissues using a microscope.

**Inheritable faulty gene**
Abnormal or mutated gene that is passed from parents to their offspring.

**Intravesical instillation**
Pouring a liquid into the bladder, slowly or drop by drop.

**Intravesical (treatment)**
An intravesical therapy is administered directly into the bladder.
Ionizing irradiation
A type of radiation made (or given off) by X-ray* procedures, radioactive substances, rays that enter the Earth’s atmosphere from outer space, and other sources. At high doses, ionizing radiation increases chemical activity inside cells and can lead to health risks, including cancer.

Immunotherapy
Treatment to boost or restore the ability of the immune system to fight cancer, infections, and other diseases. Also used to lessen certain side effects* that may be caused by some cancer treatments. Agents used in immunotherapy include monoclonal antibodies, growth factors, and vaccines. These agents may also have a direct antitumour effect. Also called biological response modifier therapy, biological therapy, biotherapy, and BRM therapy.

Lamina propria
The lamina propria is a thin layer of loose connective tissue which lies beneath the epithelium* and together with the epithelium constitutes the mucosa*. The term mucosa (or mucous membrane) always refers to the combination of the epithelium plus the lamina propria.

Lymph node
A rounded mass of lymphatic tissue that is surrounded by a capsule of connective tissue. Lymph nodes filter lymph (lymphatic fluid) and they store lymphocytes (a type of white blood cell). They are located along lymphatic vessels. Also called lymph gland.

Lymphedema
A condition in which extra lymph fluid builds up in tissues and causes swelling. It may occur in an arm or leg if lymph vessels are blocked, damaged, or removed by surgery.

Macroscopic invasion
Extension of cancer to the adjacent tissues which is visible to the naked eye.

Magnetic Resonance Imaging (MRI)
An imaging technique used in medicine that uses magnetic resonance (magnetism and radio waves) to create a picture of organs and tissues inside the body. Sometimes, a fluid is injected that enhances the contrast between different tissues to make structures more clearly visible.

Metastasis
The spread of cancer from one part of the body to another. A tumour formed by cells that have spread is called a metastatic tumour or a metastasis. The metastatic tumour contains cells that are like those in the original tumour.

Micrometastasis
Small numbers of cancer cells that have spread from the primary tumour to other parts of the body and are too few to be picked up in a screening or diagnostic test.

Microscopic invasion
Extension of the cancer cells to adjacent tissues that can only be seen under a microscope.
Methotrexate
A drug used to treat some types of cancer, rheumatoid arthritis, and severe skin conditions, such as psoriasis. Methotrexate stops cells from making DNA and may kill cancer cells. It is a type of antimetabolite. Also called amethopterin, MTX, and Rheumatrex.

Mitomycin C
An anticancer drug that belongs to the family of drugs called antitumour antibiotics.

Mucosa
The moist, inner lining of some organs and body cavities. Glands in the mucosa make mucus. Also called mucous membrane.

Multidisciplinary opinion / tumour board review
A treatment planning approach in which a number of doctors who are experts in different areas of specialization (disciplines) review and discuss the medical condition and treatment options of a patient. In cancer treatment, a multidisciplinary opinion may include that of a medical oncologist (who provides cancer treatment with drugs), a surgical oncologist (who provides cancer treatment with surgery), and a radiation oncologist (who provides cancer treatment with radiation). Also called tumour board review.

Organ preservation therapy/surgery
Surgery in which a given organ is spared at its maximum, to keep its functionality and structure. It is offered to patients who cannot or do not wish to undergo radical surgery in which the organ might be removed completely.

Pathologist
A doctor specialized in histopathology*, which is the study of diseased cells and tissues using a microscope.

Prognosis
The likely outcome or course of a disease; the chance of recovery or recurrence*.

Progression
In medicine, the course of a disease, such as cancer, as it becomes worse or spreads in the body.

Prostate
A gland in the male reproductive system*. The prostate surrounds the part of the urethra* (the tube that empties the bladder) just below the bladder, and produces a fluid that forms part of the semen.

Radiological investigation/examination
Test that uses imaging technology (such as radiography, ultrasound*, computed tomography* or nuclear medicine) to visualize organs, structures and tissues within the body to both diagnose and treat diseases.

Radiotherapy
A therapy in which radiation is used in the treatment of cancer. It is always oriented to the specific location of the cancer.
Recurrence
Cancer or disease (usually auto-immune) that has come back, usually after a period of time during which the cancer or disease was not present or could not be detected. This may happen in the same location as the original (primary) tumour or in another location in the body. Also called recurrent cancer or disease.

Reproductive organs/system
The organs involved in producing offspring. In women, this includes the ovaries, the fallopian tubes, the uterus, the cervix, and the vagina. In men, it includes the prostate*, the testes, and the penis.

Renal pelvis
The area at the center of the kidney. Urine collects here and is funneled into the ureter*, the tube that connects the kidney to the bladder.

Renal tubules
Small canals within the tissue of the kidneys that contain a filtrate that eventually becomes urine. They are part of the nephrons, which are the basic functional unit of the kidneys.

Risk factor
Something that increases the chance of developing a disease. Some examples of risk factors for cancer are age, a family history of certain cancers, use of tobacco products, being exposed to radiation or certain chemicals, infection with certain viruses or bacteria, and certain genetic changes.

(Bone) Scintigraphy
A procedure that produces pictures (scans) of structures inside the body, including areas where there are cancer cells. Scintigraphy is used to diagnose, stage, and monitor disease. A small amount of a radioactive chemical (radionuclide) is injected into a vein or swallowed. Different radionuclides travel through the blood to different organs. A machine with a special camera moves over the person as they are lying on a table and detects the type of radiation given off by the radionuclides. A computer forms an image of the areas where the radionuclide builds up. These areas may contain cancer cells. Also called radionuclide scanning.

Seminal vesicles
A pair of tubular glands of about 5 cm in length that are each curled up inside an ampullary structure. They are located above the prostate*. Each of them has a duct that connects with the prostate. They produce most of the fluid contained in the semen.

Sexual dysfunction
Inability to fully enjoy sexual intercourse. It includes a wide variety of problems that affect the sexual act at any stage: desire, arousal, orgasm, and resolution.

Side effect
A problem that occurs when treatment affects healthy tissues or organs. Some common side effects of cancer treatment are fatigue, pain, nausea, vomiting, decreased blood cell counts, hair loss, and mouth sores.
Squamous cell carcinoma
Cancer that begins in squamous cells, which are thin, flat cells that look like fish scales. Squamous cells are found in the tissue that forms the surface of the skin, the lining of the hollow organs of the body, and the passages of the respiratory and digestive tracts. Also called epidermoid carcinoma.

Stoma
A surgically created opening from an area inside the body to the outside.

Taxane
A type of drug that blocks cell growth by stopping mitosis (cell division). Taxanes interfere with microtubules (cellular structures that help move chromosomes during mitosis). They are used to treat cancer. A taxane is a type of mitotic inhibitor and a type of antimicrotubule agent.

Transurethral resection of bladder tumour (TURBT)
Surgery performed with a special instrument, called a cystoscope*, inserted through the urethra*. It is used to diagnose bladder cancer and to remove unusual growths on the inside surface of the bladder when these growths are shallow (non-invasive). The tissue removed in the procedure will be sent to a laboratory for testing.

Tuberculosis
A disease caused by a specific type of bacteria that spreads from one person to another through the air. Tuberculosis can affect many parts of the body, but most often affects the lungs. A person may not have symptoms of tuberculosis for years, but they may appear when the patient becomes ill with a serious condition like diabetes*, AIDS, or cancer. Tuberculosis can usually be treated and cured with antibiotics. Also called TB.

Transitional cell carcinoma
Cancer that forms in transitional cells in the lining of the bladder, ureter*, or renal pelvis* (the part of the kidney that collects, holds, and drains urine). Transitional cells are cells that can change shape and stretch without breaking apart.

Transitional epithelium*
Type of tissue consisting of multiple layers of cells. These cells can contract and expand so that the shape of the surface cells changes depending on the degree of stretch of the tissue.

Ureteroscopy
Examination of the inside of the kidney and ureter*, using a ureteroscope. A ureteroscope is a thin, tube-like instrument with a light and a lens for viewing. It may also have a tool to remove tissue to be checked under a microscope for signs of disease. The ureteroscope is passed through the urethra* into the bladder, ureter, and renal pelvis* (part of the kidney that collects, holds, and drains urine).

Ureters
The tubes that carry urine from the kidneys to the bladder.

Urethra
The tube that connects the bladder with the outside of the body. In males, the urethra* carries urine as well as semen.
Urinary diversion
A surgical procedure to make a new way for urine to leave the body. It may involve redirecting urine into the colon, using catheters* to drain the bladder, or making an opening in the abdomen and collecting urine in a bag outside the body.

Urine cytology
Tests performed on cells in urine to detect disease.

Urothelium
The lining of the urinary tract, including the renal pelvis*, the area at the center of the kidney, ureters*, bladder, and urethra*.

Vinblastine
The active ingredient in a drug used together with other drugs to treat several types of cancer, including advanced Hodgkin lymphoma and advanced testicular germinal-cell cancers. It is also being studied in the treatment of other types of cancer. Vinblastine comes from the periwinkle plant Vinca rosea Linn. It blocks cell growth by stopping cell division and may kill cancer cells. It is a type of vinca alkaloid and a type of antimitotic agent.

Vinflunine
An anticancer medicine for second-line treatment of bladder cancer. It belongs to the group of anticancer medicines known as the vinca alkaloids. It attaches to a protein in cells called tubulin, which is important in the formation of the internal ‘skeleton’ that cells need to assemble when they divide. By attaching to tubulin in cancer cells, vinflunine stops the formation of the skeleton, preventing the division and spread of the cancer cells.

Visceral
Relating to the viscera, which are the soft internal organs of the body, including the lungs, the heart, and the organs of the digestive, excretory, reproductive*, and circulatory systems.

X-rays
X-rays are a form of radiation used to take images of the inside of objects. In medicine, X-rays are commonly used to take images of the inside of the body.
The ESMO / Anticancer Fund 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. These guides are produced by the Anticancer Fund in close collaboration with the ESMO Guidelines Working Group and the ESMO Cancer Patient Working Group.

For more information please visit www.esmo.org and www.anticancerfund.org