What is prostate cancer?
Let us explain it to you.
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 prostate cancer and appreciate the best treatment choices available according to the subtype of prostate 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 prostate 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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The first version of this guide was published in 2012 and was written by Dr. Ana Ugarte (the Anticancer Fund) and reviewed by Dr. Svetlana Jezdic (ESMO), Prof. Louis Denis (The European Prostate Cancer Coalition and ESMO Cancer Patient Working Group) and Prof. Raphael Catane (ESMO Cancer Patient Working Group).

This is the third update of this guide. Updates reflect changes in the successive versions of the ESMO Clinical Practice Guidelines.

The second update was done by Dr. Ana Ugarte (the Anticancer Fund) and reviewed by Dr. Svetlana Jezdic (ESMO), Prof. Alan Horwich (ESMO), Prof. Raphael Catane (ESMO Cancer Patient Working Group), Prof. Louis Denis (The European Prostate Cancer Coalition and ESMO Cancer Patient Working Group), Anita Waldman (ESMO Cancer Patient Working Group) and Zorana Stokic (ESMO Cancer Patient Working Group).

The third update was done by Dr. Ana Ugarte (the Anticancer Fund) and reviewed by Dr. Svetlana Jezdic (ESMO) and Prof. Alan Horwich (ESMO).
FACTSHEET ABOUT PROSTATE CANCER

Definition of prostate cancer
- Prostate cancer forms in the tissue of the prostate, a gland of the male reproductive system found below the bladder and in front of the rectum*. The prostate gland is made of 2 symmetric lobes.
- It is not to be confused with benign prostatic hyperplasia* which is a non-cancerous enlargement of the prostate gland.

Diagnosis
- Symptoms such as increase in urination frequency, difficulties in starting to urinate, getting up multiple times to urinate at night, urgency or sensation of necessity to urinate immediately may be an indication of prostate cancer.
- A physical examination and the measurement of a protein* produced by the prostate (PSA*) in the blood will guide the diagnosis.
- The diagnosis can only be confirmed by the analysis of pieces of the prostatic tissue (biopsy*) under a microscope.

Treatment according to the extension of the disease (classified into different stages)
- Stage I and stage II prostate cancers are called localised or early stage cancers as the tumour is confined to the prostate:
  o When the cancer is diagnosed at a very early stage and it is considered that the risks of treatment may outweigh the benefits, a “watch and wait” approach can be discussed. It consists of regular check-ups with no intervention unless a check-up indicates the tumour is growing.
  o In all other cases, surgery or radiotherapy* are similarly effective. They however cause different side effects, so risks and benefits of both should be discussed with all patients. In addition, hormone therapy* will be given.
  o Hormone therapy* alone could be proposed to elderly patients and patients unsuitable or unwilling to be treated by radiotherapy* or surgery.
- Stage III prostate cancers are called locally advanced cancers as the tumour has spread through the outside layer of tissue surrounding the prostate called the capsule:
  o Radiotherapy* and additional hormone therapy* is the standard of care.
  o In selected cases, surgery could also be an option.
- Stage IV prostate cancers are called advanced or metastatic cancers as the tumour has spread further:
  o Hormone therapy* is the preferred initial treatment option. In men fit enough for chemotherapy, hormone therapy can be combined with docetaxel.
  o Surgery and radiotherapy* can also help to relieve symptoms related to cancer.
  o In case of resistance of the cancer to hormone therapy (castration-resistant disease) further therapies to continue hormone suppression are recommended, considering previous therapies that the patient might have taken.
Follow-up

- To detect if the cancer has come back, PSA* is measured regularly. An increase of the PSA* level is not sufficient to confirm that the cancer has come back and therefore results have to be combined with other findings such as positive biopsy* or abnormal CT-scan* results.
- The follow-up* also aims to evaluate adverse effects of the treatment and to provide psychological support and information to enhance return to normal life.
DEFINITION OF PROSTATE CANCER

Prostate cancer is a cancer that forms in tissues of the prostate (a gland in the male reproductive system found below the bladder and in front of the rectum*). Prostate cancer usually occurs in older men. It is not to be confused with benign prostatic hyperplasia* which is the enlargement of the prostate gland due to an increase in the number of cells but that does not spread to other parts of the body, and for which symptoms are associated with the compression of adjacent structures, i.e. the urethra*.

Anatomy of the male reproductive and urinary systems, showing the prostate, testicles, bladder, and other organs.
IS PROSTATE CANCER FREQUENT?

Prostate cancer is the most common cancer amongst men. In Europe, about one out of 10 men will develop prostate cancer at some point in his life. This probability is lower in some Nordic countries and in Mediterranean Europe.

In Europe, in 2008 it was estimated that 382 000 in total or 65 men out of 100 000 were diagnosed with prostate cancer, ranging from 18 in Greece to 126 in Ireland. However, this difference depends on the difference of frequency of the use of prostate cancer screening between countries.

In its initial phases, prostate cancer may not cause symptoms and in otherwise healthy men aged between 55 and 69 years it is commonly detected by a blood screening test called prostate specific antigen* (PSA*). It has been suggested that screening with PSA* test reduces death rate due to prostate cancer by 21%. Nevertheless, prostate cancer develops relatively slowly and symptoms at diagnosis indicate an advanced stage. The utility of PSA* test as screening method has been widely studied and it is believed that although it certainly decreases slightly the rate of deaths due to prostate cancer, many patients could be being over treated, reducing their quality of life unnecessarily, so that systematic screening with PSA* test is not recommended. Men that are older than 70 and who do not have symptoms should not be tested for PSA levels.
WHAT CAUSES PROSTATE CANCER?

Today, it is not clear why prostate cancer occurs. Some risk factors* have been identified. A risk factor* increases the risk of cancer occurring, but is neither necessary nor sufficient to cause cancer. A risk factor* is not a cause in itself.

Some men with these risk factors* will never develop prostate cancer and some without any of these risk factors* will nonetheless develop prostate cancer.

The main risk factors* of prostate cancer are:

- **Aging**: The risk of prostate cancer is largely influenced by age. After 50 years of age the risk increases exponentially every year. The exact mechanism is unclear, but aging of the cells and the consecutive changes in their DNA* have been pointed out.

- **Ethnicity**: In developed countries, black men are at higher risk of developing prostate cancer than white and Asian men. The reasons are unclear.

- **Genes**: Recent research has shown that there are several inherited genes related to higher risk of developing prostate cancer, but apparently they account for a small amount of cases. Currently, studies are being developed to see if tests looking for those genes are useful to predict prostate cancer risk.

- **Family history of prostate cancer**: It has been shown that there is a familial predisposition to have prostate cancer, especially in men whose fathers or brothers are or were affected.

- **Diet**: It is unclear whether diet and lifestyle play a role in the development of prostate cancer. Some studies suggest that a diet high in red meat or dairy products slightly increases the risk of developing prostate cancer. On the other hand, some studies suggest that a diet rich in lycopene from tomatoes, and selenium (a mineral* mainly found in red meat, fish and seafood, eggs and cereals) both slightly decrease the risk of prostate cancer. However, more evidence is necessary. Obesity also increases the risk of having prostate cancer.

- **Lifestyle**: Smoking may slightly increase the risk of having prostate cancer whereas being more physically active seems to slightly lower the risk.

- **Hormones**: High blood levels of testosterone* have an increased risk of prostate cancer. Also some hormones related to growth have been associated with cancer, but further studies have to be done to confirm this.

Other factors have been suspected to be associated with an increased risk of prostate cancer, but the evidence is inconsistent. Unfortunately, the factors that have the highest influence on the risk of prostate cancer like age, ethnicity, genes and familial history of prostate cancer cannot be changed.
**HOW IS PROSTATE CANCER DIAGNOSED?**

Prostate cancer develops slowly and symptoms mainly appear only when the illness is advanced. Some common symptoms in that case could be urinary symptoms like increase in urination frequency, difficulties in starting to urinate, getting up multiple times to urinate during the night, urgency or sensation of necessity to urinate immediately. Other less common symptoms are blood in the urine and semen, bone pain and loss of bladder control. These symptoms are in fact less specific than the previous ones. Consequently, men with the previously mentioned symptoms, or risk factors* like age or family history of prostate cancer should be screened.

Cancer suspicion relies on PSA* level in the blood and digital rectal examination (DRE) for patients with symptoms, or those patients who request to be screened during a regular check-up. The PSA* and DRE results need to be confirmed with a biopsy* and histopathological examination.

1. **Digital Rectal Examination (DRE)**

DRE is a clinical test to check the size, consistency, sensitivity and limits of the prostate. Because the prostate is situated in front of the rectum* the doctor can feel it by inserting a gloved, lubricated finger into the rectum*. DRE by itself could miss around half of the cases of prostate cancer. Therefore, it should be done in combination with PSA* test in an appropriately counselled patient in whom there is clinical suspicion of prostate cancer or in patients who wish to be screened for prostate cancer.

2. **PSA* test**

PSA* stands for *prostate-specific antigen*. It is a protein* produced exclusively by the prostate. The PSA* test measures the level of PSA* in the blood. Normally it is present in the blood, but an increase can suggest prostate cancer. In non-symptomatic patients PSA* level is monitored over time to evaluate any changes. In patients with suspicion of cancer a biopsy* is recommended. However, a single elevated PSA level should not prompt a prostate biopsy; and should be verified by a second value. It must be considered that prostate cancer is not the only reason why the PSA* level increases. Non-malignant conditions such as an inflammation (prostatitis), urinary tract infection and benign prostatic hyperplasia* can cause PSA* levels to rise. Administration of certain drugs, having a prostate biopsy* performed previously or a DRE, riding a bike and having sex are some common reasons of having an elevated PSA* level. These situations should be avoided before measuring PSA*.

3. **Biopsy**

The diagnosis can only be confirmed with the laboratory examination of a sample of the tumour cells (biopsy*). In this procedure, samples of prostatic tissue are taken from the prostate in order to analyse the cells. The samples can be obtained by inserting a needle through either the rectum*, the perineum* or the urethra*.
• Rectal route: When the biopsy* is performed through the rectum*, the application of an enema* to clean the rectum* is needed beforehand. Antibiotics* can minimize the risk of infection. It can be done under local or general anaesthesia*. Transrectal ultrasound* (TRUS) is generally used to guide the needle to the correct biopsy* location; although sometimes a needle guide is attached to the doctor’s finger, he or she has to insert a finger into the rectum*. The needle is then slid along the guide through the wall of the rectum* and into the prostate; the needle is turned to collect tissue samples and then pulled out. A transrectal biopsy* takes around 30 minutes. This is the most commonly used route to perform a prostate biopsy*.

• Perineal route: When the biopsy* is done through the perineum* local or general anaesthesia* can be used; the doctor will insert a finger into the patient’s rectum* to hold the prostate while the samples are taken. A small cut (incision) is made in the patient’s perineum*, then the needle is inserted through it and into the prostate. To collect a sample of tissue the needle is gently turned and pulled out. Pressure is applied to stop the bleeding and a small bandage is placed over the cut. This kind of biopsy* usually takes about 15 to 30 minutes.

• Urethral route: When the biopsy* is performed through the urethra*, general, spinal or local anaesthesia* may be used. A lighted scope (cystoscope) is inserted into your urethra*. It allows the doctor to look directly at the prostate gland. A cutting loop is passed through the cystoscope to remove small pieces of prostate tissue. A transurethral biopsy* usually takes about 30 to 45 minutes.

Typically several biopsy* samples will be taken from different parts of the prostate at the same time. This allows the doctor to determine where the cancer cells are located as well as the growth of the cancer.

Antibiotics* prior to the procedure should be prescribed to prevent infection. A second histopathological examination of the tumour and the lymph nodes* removed by surgery will be performed later.

The decision on whether or not a biopsy* is necessary should be made in the light of DRE findings, prostate size, ethnicity, age, other diseases, history of cancer in the family, patient values, history of a previous biopsy* and PSA* level. Before repeating a biopsy, multi-parametric magnetic resonance imaging (MRI) is recommended with a view to MRI-guided or MRI-transrectal ultrasound (TRUS) fusion biopsy. A multi-parametric MRI is an imaging technique that not only give information on the structure of the prostate but also the function.
WHAT IS IMPORTANT TO GET AN 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

- Personal medical history
- History of cancer in relatives, especially prostate cancer
- Results from the clinical examination* by the doctor
- General well-being
- Results from blood tests performed to assess the white blood cells*, the red blood cells* and the platelets* and to identify any problem in the liver and renal function as well as any bone problems.
- Patient’s age and expected lifespan
- Patient’s other illnesses such as heart and pulmonary* problems or diabetes.
- Patient’s personal preferences about the treatment options with regard to the possible risks and side effects and to the chances of success (risks and benefits).

Relevant information about the cancer

- Results of the biopsy*

The diagnosis of prostate cancer can only be confirmed after a biopsy*. In this procedure, samples of prostatic tissue are taken from the prostate to analyse the cells. As previously explained, the samples are obtained by inserting a needle through the rectum*, the perineum* or the urethra*.

Once the samples have been analysed, the pathologist assigns a grade* to the cancer cells, mostly according to the Gleason system. The Gleason system uses a 1 to 5 scale, depending on how much the cancer cells look like normal prostate cells.

1 means that the cancer cells look a lot like normal prostate cells.
5 means that the cancer cells seem to be spread in an unorganized way and subsequently the tissue does not resemble prostate tissue anymore.
2, 3 and 4 are between the two extremes.

1 and 2 grades, however, are no longer used.

The Gleason score is determined by adding the grade assigned to the majority of the cancer cells to the highest grade observed.

A Gleason score <6 is well differentiated* or low-grade. On average, prognosis* is better.
A Gleason score 7 is moderately differentiated* or intermediate-grade. On average, prognosis* is intermediate.
A Gleason 8-10 is poorly differentiated* or high-grade. On average, prognosis* is lower.

Sometimes the biopsy* results are inconclusive and the procedure should be repeated.
**Staging**

Doctors use staging to assess the extent 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 in the body (M), will classify the cancer into one of the following stages.

The stage is fundamental in order to make the right decision about the treatment. The more advanced the stage, the worse the prognosis*. Staging may be performed twice: after clinical* and radiological examination and again after surgery. If surgery is performed, staging may be changed by the laboratory examination of the removed tumour.

The table below presents the different stages prostate cancer.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>The tumour involves just one of the two lobes of the prostate. It can be found incidentally through a biopsy* done after observing a high level of PSA. The cancer has not spread to the lymph nodes* or elsewhere in the body.</td>
</tr>
<tr>
<td>Stage II</td>
<td>The tumour has spread to the other lobe and can involve the whole prostate without breaking out of the capsule surrounding it. The cancer has not spread to the lymph nodes* or elsewhere in the body.</td>
</tr>
<tr>
<td>Stage III</td>
<td>The tumour has spread outside of the prostate to the seminal vesicles*, which are a pair of glands above the prostate that secrete an important proportion of the fluid that contains the semen. The cancer has not spread to the lymph nodes* or elsewhere in the body apart from the seminal vesicles*.</td>
</tr>
<tr>
<td>Stage IV</td>
<td>The tumour has invaded adjacent structures other than the seminal vesicles*, for instance the rectum*, the muscles or pelvic wall; or, regardless of the invasion of adjacent structures, it has spread to other parts of the body including lymph nodes* and bones.</td>
</tr>
</tbody>
</table>

**Risk categories**

To estimate their aggressiveness, localised prostate cancers are categorized as low-, intermediate- or high-risk according to the tumour size, Gleason score and PSA* level. Low-risk prostate cancer has a tumour limited to one lobe of the prostate (which has two lobes) and a Gleason score <7 and a PSA* level <10 ng/ml (nanograms per millilitre). The intermediate-risk prostate cancer has a tumour that has invaded the other lobe of the prostate, partially or completely and a Gleason score =7 or a PSA* level between 11 and 19 ng/ml. The high-risk prostate cancer has a tumour that has invaded structures adjacent to the prostate with a Gleason score >7 or a PSA* level >20 ng/ml.

When the risk is low no bone scintigraphy is routinely recommended. The goal of a bone scintigraphy is to look for a possible dissemination of the cancer to the bones. When the risk is intermediate there are two options: if it is planned that the patient is treated with radiotherapy* he should have ideally pelvic magnetic resonance imaging (MRI)*, if, on the contrary, it is planned that he will have a surgery the risk/benefit of lymph node* removal based on prognosis should be discussed. When the risk is high bone scintigraphy* should be carried out and MRI* of the pelvis should be considered. Under the suspicion of bone metastasis*, bone scintigraphy* is only performed if the Gleason score is at least 7 and the PSA* higher than 10 ng/ml.
WHAT ARE THE TREATMENT OPTIONS?

The planning of the treatment involves an inter-disciplinary team of medical professionals. This usually implies a meeting of different specialists, called multidisciplinary opinion* or tumour board review. In this meeting, the planning of the treatment will be discussed according to the relevant information mentioned above.

The extent of the treatment will depend on the stage of the cancer, on the characteristics of the tumour and on the risks involved.

There are a lot of treatment options, but there is no consensus as to what constitutes optimum management. The different kinds of treatment listed below have their benefits, their risks and their contraindications. It is advisable to ask oncologists about the expected benefits and risks of every treatment in order to be informed of the consequences of the treatment. For some kinds of treatment, several possibilities are available. After weighing up the benefits and risks of a particular kind of treatment, the right choice can be made.

Treatment plan by stage of prostate cancer

Treatment plan for localised prostate cancer (Stages I and II)

In stages I and II prostate cancer, the tumour involves just one lobe of the two lobes of the prostate, or both lobes, without invading other tissues outside the prostate. The cancer has not spread to the lymph nodes* or elsewhere in the body. In low-risk patients watchful waiting* (“watch and wait”) is an option to be discussed, in patients with intermediate-risk surgery or radiotherapy* plus hormone therapy* are part of the treatment. Hormone therapy* alone could be proposed to elderly patients and patients unsuitable for or unwilling to have other treatments.

There is no consensus regarding optimum management of localised disease. The different treatment options possible have side effects that patients should be aware of, that is why patients should consult with both an urologist and a radiation oncologist. Low- and intermediate-risk cancer patients belong to this group. In low-risk prostate cancer patients watchful waiting* (“watch and wait”) is an option that should be discussed with doctors, since so far no advantage in life prolongation has been shown from initiating early treatment in this group of patients. In patients with intermediate-risk treatment options include full removal of prostate by surgery or external radiotherapy* plus hormone therapy* (lowering the level of testosterone* in blood) or brachytherapy*.

Too elderly patients who do not have symptoms or patients who have other serious health problems or those unwilling to have treatment, close follow-up* of their condition and, in the event of progression of symptoms, hormone therapy* could be proposed. Hormone therapy alone, however, is not recommended as initial treatment of non-metastatic disease.

Hormone therapy* is aimed at lowering the level of the hormone called testosterone*, which is linked to the growth of the cancer cells in the prostate. It is recommended to be administered upon the appearance of signs of disease progression when a patient is under watchful waiting* (“watch and wait”) strategy.
The treatment options meant to remove or shrink the tumour are:

- **Prostatectomy**, which is the removal of the prostate by a surgical intervention. Laparoscopic* prostatectomy is a modality of prostatectomy that apparently has similar results to open surgery, although recovery of bladder control may be slightly delayed. The nerve-sparing approach by laparoscopic* technique increases the chance of recovery of sexual activity. Laparoscopic* robotic-assisted radical prostatectomy apparently has advantages over open approach in terms of pain, blood loss and recovery time. This procedure is expected to be more precise than regular laparoscopic surgery, but the time taken for surgeons to become fully proficient with the robotic techniques is a factor to be taken into account. Also, since this is a new technique, long-term outcomes have yet to be evaluated.

- **Radiotherapy**, which is the use of radiation* to kill cancer cells, is also a treatment option. Cancer cells are less capable of recovery from radiation* damage than normal cells, allowing radiotherapy* to be used as a treatment. External radiotherapy* and brachytherapy* are the two modalities of radiotherapy* in use. In external radiotherapy* the radiation* is produced by an external source and then directed at the tumour. Conformal techniques that allow the beam of radiation* to be more accurate should be used in order to prevent side effects. Conformal techniques are Intensity-modulated radiotherapy* (IMRT) and stereotactic radiotherapy*, to name just a few. In brachytherapy* the source of radiation* is placed inside the prostate as small radioactive pellets.

  Before treatment with radiotherapy*, initial treatment (neoadjuvant) of 4-6 months with hormone therapy* should be considered in men with intermediate risk prostate cancer.

- The effectiveness of radiotherapy* and prostatectomy are equivalent. In order to make a choice between them, the side effects of both need to be considered and evaluated. This should be done with the support of an oncology surgeon and a radiation* oncologist.

**Treatment plan for locally advanced prostate cancer (Stage III)**

*In stage III prostate cancer, the tumour has spread outside of the prostate to the seminal vesicles*. The cancer has not spread to the lymph nodes* or elsewhere in the body apart from the seminal vesicles*. Radiotherapy* and additional hormone therapy* is the standard of treatment. In selected cases surgery could also be an option.

High-risk patients are part of this group. The standard treatment is radiotherapy* and neoadjuvant hormone therapy followed by additional hormone therapy* for two to three years. It was shown that this combination might have a benefit regarding life prolongation compared to radiotherapy* alone. Hormone therapy* alone is not recommended. In certain cases surgery including important removal of lymph nodes* is another option. For men with no symptoms who are not suitable or are unwilling to have the above mentioned treatments, watchful waiting* (“watch and wait”) could be chosen. If afterwards there is evidence that the cancer has grown hormone therapy* could be started.
In order to secure treatment efficacy, different therapies are combined as part of the same protocol. Neoadjuvant therapy is a therapy administered to the patient before the main therapy. Adjuvant therapy is the administration of a therapy in parallel to and/or following the main therapy. For men with high-risk prostate cancer who are treated by radiotherapy*, neoadjuvant hormone therapy with LHRH* agonist for four to six months before starting radiotherapy* is recommended. In addition, adjuvant hormone therapy* is recommended for two to three years.

Adjuvant hormone therapy* can be based on bicalutamide* 150 mg daily rather than LHRH* agonist in men who place a high value in retaining sexual function during the treatment, but they should understand that the data concerning outcome of bicalutamide are still limited.

After full prostate removal, immediate postoperative radiotherapy* could be considered, although it is not routinely recommended. Patients likely to have residual disease after surgery, tumour positive margins* or disease extended beyond the prostate to surrounding tissues, should be appropriately informed on the benefits and disadvantages of the administration of adjuvant radiotherapy*. Adjuvant hormone therapy* after full prostate removal is not recommended.

**Treatment plan for advanced prostate cancer (Stage IV)**

*The tumour has invaded adjacent structures other than the seminal vesicles*, for instance the rectum*, the muscles or pelvic wall; or, regardless of the invasion of adjacent structures, it has spread to other parts of the body including lymph nodes* and bones. Hormone therapy* is the standard of care. Surgery and radiotherapy* can also help to relieve symptoms caused by tumour mass.

The initial preferred treatment is hormone therapy in patients with metastatic disease who have not received hormone therapy before. Docetaxel (chemotherapy) together with hormone therapy is an option in men that have not received hormone therapy previously and who are fit enough for chemotherapy. Other treatment options are external radiotherapy* plus hormone therapy* and surgery to relieve symptoms such as bleeding or urinary obstruction. When castration-resistant disease develops (resistance to hormone therapy), other options to manipulate hormone levels are available, such as antiandrogens*, corticosteroids*, oestrogens* and CYP17 inhibitors*. Also, if besides being hormone resistant the patient has never before received chemotherapy, abiraterone and enzalutamide are drugs that could be options.

**Hormone therapy**

The goal of the hormone therapy* is to decrease the level of androgens* in the blood, in this case testosterone*. Testosterone* stimulates the growth of the cells. Hormone therapy* can be achieved surgically (removal of both testicles also called bilateral orchiectomy*) or non-surgically (administration of drugs called LHRH agonists). When done surgically, the organs that produce testosterone*, the testicles, are removed, this is known as surgical castration. Non-surgically, the administration of LHRH agonists prevents the release of one hormone in the brain called LH (luteinizing hormone), which is responsible for the production of testosterone* in the testicles, this is called chemical castration. Consequently, the hormone therapy* will decrease the level of testosterone* in the blood.
Considering its benefit and associated cost the first choice for hormone management of metastatic prostate cancer should be based on surgical or chemical castration that results ultimately in androgen* levels decrease in blood. A recent large-scale trial showed that addition of docetaxel, a chemotherapy drug, to hormone therapy improved survival and delayed the progression of the disease. The addition of docetaxel requires that the patient is in good general shape so that he could tolerate the side effects of chemotherapy.

One particular effect of the hormone therapy deserves a detailed explanation:

- **Flare:** one effect from treatment with the LHRH agonists* is the initial “flare” phenomenon, in which the testosterone* level in the blood increases due to the initial stimulation of the androgen* receptors. This can cause a short-term increase in cancer growth; and if the patient has bone metastases* they become painful. In case of spinal metastases*, even a small increase in the volume can produce spinal cord compression and paralysis. To prevent this flare phenomenon, antiandrogens* can be administered for a few weeks. LHRH antagonists* were developed recently and appear to offer equivalent testosterone* reduction without the need of an antiandrogen* to control the transient testosterone* surge.

**Castration-resistant disease**

During hormone therapy* castration-refractory disease can develop. In this condition the cancer being treated with hormone therapies* starts to become resistant to this kind of treatment. Patients who develop resistance to castration treatments (hormone therapies*) should continue androgen* suppression as part of their hormone therapy* and they are candidates for further hormone therapies including antiandrogens*, corticosteroids*, oestrogens* and CYP17 inhibitors* (blockers of pivotal enzyme in androgen synthesis), such as abiraterone.

Corticosteroids decrease production of androgens and lead to decrease of PSA levels and general improvement of the patient’s health. Dexamethasone appears to be more active than prednisolone. However, the value of corticosteroids and other hormonal manipulations, which do not have a proven overall survival benefit, is not supported by randomised trials, the arguments in favour of their use are the price and that some of them have low toxicity.

Abiraterone or enzalutamide are recommended for asymptomatic/mildly symptomatic men with chemotherapy-naive metastatic castration-resistant disease.

Chemotherapy* might be preferable in patients with poor initial response to hormones or who experience severe symptoms. Docetaxel* has been shown to extend survival. In patients whose disease continues to progress after the use of docetaxel* and that the disease has not yet spread to other organs, hormone therapy* with abiraterone* or enzalutamide* with prednisone* should be discussed if they were not used previously. Cabazitaxel* is another drug considered in patients whose treatment with docetaxel* seems unsuccessful.
Radium-223 is another recommended option for castration-resistant disease. This strategy is a type of radioisotope therapy, in which a bone-targeted radiation emitter is administered (by intravenous injection), so that it would reach the target (bones) and release radiation. This therapy also showed that it could improve survival.

Sipuleucel-T*, an immunotherapy that uses dendritic cells, also showed to improve survival. This is an option in asymptomatic/mildly symptomatic chemotherapy-naive patients with castration-resistant prostate cancer. However, the lack of any impact on disease response or progression, together with logistic considerations and cost, has limited its use.

In patients with castration-resistant disease on systemic treatment, regular imaging studies should be done to monitor disease response/progression.

**Bone metastasis**

With aging, men are prone to osteoporosis and consequently to fractures. The risk increases with androgen* deprivation. The bone mineral density* is an indicator of the risk of fracture. When this density is low, the risk of fracture is increased. Bone mineral density* should be monitored annually. If the density decreases, zoledronic acid* is a treatment option. Metastases* by themselves can cause fractures. Spinal cord compression due to a spine fracture is a severe complication that can be diagnosed early by imaging and can be successfully treated.

A single administration of external radiotherapy* should be offered to patients with moderate number of painful bone metastases* from castration-refractory disease (resistant to androgen* deprivation).

Radioisotope therapy/bone targeted therapy with strontium-89*, radium-223* or samarium-153* should be considered for patients with painful bone metastases* from castration-refractory disease. This technique is based on the intravenous* injection of molecules that are radioactive and have an affinity for the bones. After injection, the molecules reach the bones and emit radiations* locally.

Zoledronic acid* or denosumab* should be considered for patients with bone pain resistant to palliative radiotherapy* and conventional analgesics.

Denosumab* has shown to delay events associated to bones damage due to metastases* better than zoledronic acid*, however some of its side effects could be more frequent compared to zoledronic acid*. Neither showed improvement in how long the patients may live (survival).

Spinal cord compression is a devastating complication of prostate cancer with vertebral metastases* and its early detection is critical for successful management. MRI* of the spine should be considered in men with vertebral metastasis* and back pain to detect cord compression.
WHAT ARE THE POSSIBLE SIDE EFFECTS OF THE TREATMENT?

Surgery

Prostate removal by surgery can result in some side effects like urinary incontinence, impotence and sterility, due to damage to the structures and nerves controlling the ability to have an erection.

Radiotherapy

It may cause side effects such as urinary incontinence, impotence, bladder and bowel problems, tiredness, narrowing of the urethra*, lymphatic obstruction* and consequently fluid retention* and swelling of the tissues.

As it implies the placement of a radioactive source, brachytherapy* makes the patient radioactive. Because some radiation* may reach the body surface, there is a period of time in which the patient has to avoid contact with pregnant women and children.

Radioisotope therapy/Bone targeted therapy

Blood and urine will be radioactive for some time. Your doctor and nurses will give you advice concerning the safety measures to be taken.

Hormone therapy

Some of the side effects related to hormone therapy* are loss of libido, impotence, hot flashes, mood changes, osteoporosis, muscle weakness, abnormal development of the breasts (gynaecomastia), insulin resistance* and an increase in body fat. Patients should be monitored if such side effects occur.

- Abiraterone*: Some specific side effects of this drug are high blood pressure, fluid retention* and tissue swelling (oedema*), fatigue, urinary infections, cardiac arrhythmias* and liver damage.
- Enzalutamide*: It is associated, amongst others, to headache, hot flushes, high blood pressure, back pain, respiratory infections, anxiety, diarrhoea, fatigue, seizures, blood in urine and tissue swelling (oedema*).

Chemotherapy*

- Docetaxel: Some side effects related to the use of docetaxel are neutropenia*, fatigue, hair loss, diarrhoea, neuropathy*, peripheral oedema* and nail dystrophy*.
- Mitoxantrone*: It is associated to fatigue, hair loss, nausea, vomiting, diarrhoea, lymphopenia* and thrombocytopenia*.
- Cabazitaxel*: Some side effects related to its use are fatigue, diarrhoea, haematuria (blood in the urine), anaemia, neutropenia*, hair loss and peripheral oedema* (tissue swelling due to fluid retention*).
Zoledronic acid

Side effects due to the use of zoledronic acid include anaemia, fever, oedema* (fluid retention*), fatigue, myalgia (muscle pain) and also jaw necrosis. To reduce the risk of jaw necrosis (but unfortunately, not to eliminate it), good oral hygiene along with regular dental care is recommended. In selected cases of patients receiving intravenous* zoledronic acid*, the use of an antibiotic* such as clindamycin can be indicated, combined with the use of an antimicrobial mouthwash with chlorhexidine 4 times daily.

Denosumab*

The most common side effects associated with denosumab* are back pain, skin rash sometimes with blisters, bloody urine and difficult urination, muscle and bone pain.

Sipuleucel-T*

This therapeutic vaccine is associated with fever, signs of inflammation and sometimes infection around the site where the cells to elaborate the vaccine were taken and the site where the vaccine was administered. Its side effects also include nausea, headache, back pain and pain in different parts of the body.
WHAT HAPPENS AFTER THE TREATMENT?

There is no treatment that does not have any side effects, although new techniques are intended to reduce them.

The side effects of the treatment, like impotence, incontinence and infertility have to be openly discussed with the patient.

The main kinds of treatment have consequences afterwards. For example: sexual activity is mostly affected by surgery and the urinary and intestinal functions are affected by external radiotherapy and brachytherapy.

Follow-up* with doctors

After the treatment has been completed, doctors will propose a follow-up* program aiming to:

- Detect possible recurrence* as soon as possible.
- Evaluate adverse effects of the treatment and treat them.
  For instance:
  - Chronic bowel symptoms after radiotherapy should be investigated by a gastroenterologist.
  - Men on long-term hormone therapy should be monitored for osteoporosis and metabolic syndrome*.
- Provide psychological support and information to enhance the return to normal life.

Follow-up* visits with the oncologist should include:

- History-taking (reviewing a patient’s medical history), eliciting symptoms and physical examination.
- The PSA* level should be measured on a regular basis after complete tumour eradication.

After surgery, due to the removal of prostatic cancer cells, undetectable levels of PSA* in the blood are to be expected, but sometimes some PSA* is still circulating in the blood. In this case doctors may recommend waiting some weeks to perform this test again.

After radiotherapy* the PSA* levels are not expected to drop dramatically. This process happens gradually, reaching the lowest level of PSA* after 2 years. In many cases, if not the majority, a patient receiving radiotherapy* nowadays also undergoes hormone therapy* which is initiated before radiotherapy*. In this case his PSA* is likely to be undetectable or very low even before radiation* commences. Since in this case, the PSA* remains low after radiotherapy*, another protein* produced only by the prostate, called prostatic acid phosphatase (PAP)*, can be measured during the follow-up*.

The PSA* values fluctuate slightly over time. A small increase does not mean cancer recurrence* (or that the cancer has not been cured). However, it may be an indication, so it has to be monitored.
Routine digital rectal examination (DRE) after local treatment is not recommended while the PSA* remains at baseline levels. Biopsy* of the prostatic bed* should not be performed in men with prostate cancer who have had a radical prostatectomy. Biopsy* of the prostate after radiotherapy* should only be performed in men with prostate cancer who are being considered for a salvage therapy (e.g. HIFU, cryotherapy*, salvage surgery).

Additional treatment may be recommended if PSA* levels show an increasing trend over a period of time (biochemical relapse), as follows:

- For men who have been under active surveillance; if their PSA* level has doubled in less than 3 years or if they have a PSA* velocity (change in PSA* level over time) of greater than 0.75 ng/ml per year, or if they have a prostate biopsy* showing evidence of worsening cancer.

- For men who have had a radical prostatectomy (removal of the prostate gland); if their PSA* level does not fall below the limits of detection after surgery or if they have a detectable PSA* level (> 0.3 ng/ml) that increases on two or more subsequent measurements after having no detectable PSA*.

- For men who have had other initial therapy*, such as radiotherapy* with or without hormone therapy*; if their PSA* level has risen by 2 ng/ml or more after having no detectable PSA* or a very low PSA* level.

These findings have to be combined with others, such as positive prostate biopsy*, or abnormal CT scan*. Patients who present with symptoms after radiotherapy such as anorexia*, diarrhoea, nausea, vomiting and weight loss should be evaluated to exclude potential inflammatory bowel disease*, colorectal cancer, or radiation enteropathy*.

**Return to normal life**

It can be hard to live with the idea that the cancer can come back. Based on what is known today, no specific way of decreasing the risk of recurrence* after completion of the treatment can be recommended, apart from avoiding weight gain and doing regular physical activity. As a consequence of the cancer itself and of the treatment, return to normal life may not be easy for some people.

It is mostly elderly men who are affected by prostate cancer and they may have impotence, bowel and urinary problems before treatment. In general they make a full mental and physical recovery, but sometimes it can take up to 2 years after the treatment to get back to normal. Back to normal means back to how they were before the treatment. It will unfortunately include any impotence, bowel or urinary problem that was already present before treatment.

**What if the cancer comes back?**

If the cancer comes back it is called recurrence* and the treatment depends on the extent of the recurrence*.
Locally, prostate cancer can recur in tissues next to the prostate (muscles that help to control urination, the rectum*, the wall of the pelvis) or in the seminal vesicles*. The lymph nodes* surrounding the prostate region or lymph nodes* outside the area can also be affected by the cancer.

Prostate cancer can also reappear in other parts of the body. This is called metastases*.

To determine the recurrence* of the tumour and to start a new kind of treatment, tumour size, lymph node* involvement, Gleason score and stage, have to be taken into account.

The abnormal increase of PSA* levels, also known as PSA* failure or sometimes biochemical failure, suggests that the cancer has come back. In this case other tests like imaging may have to be done.

Sometimes the disease progresses without a significant rise in PSA*. In this case, neuroendocrine change* should be investigated using biopsy* or blood analyses looking for neuron-specific enolase and/or chromogranin A, since this indicates a low chance of response to hormone therapies. Patients with evidence of neuroendocrine change in their prostate cancer should be selected for chemotherapy* rather than hormone therapy*.

The treatment options for cancer recurrence* depend on the treatment that the patient has had already.

Following full prostate removal PSA* levels in the blood should be monitored. Early salvage radiotherapy to the area where the prostate was located is recommended in case of PSA* failure.

Immediate hormone therapy* is not usually recommended for men who have a PSA* failure, except for patients with symptomatic local disease progression, proven metastases* or if their PSA* level has doubled in less than 3 months.

Intermittent hormone therapy* consists of an initial active androgen* suppression period, usually between 6 and 9 months, followed by a corresponding length of time where no active therapy* is undertaken. Patients are then followed and when criteria for reactivation of disease are met, active hormone therapy* is reinitiated. Although this intermittent approach is still under study early results have shown it is not inferior to the continuous regimen and has quality-of-life benefits.

If the patient becomes resistant to the initial hormone therapy* a second hormone therapy* option is antiandrogens*, corticosteroids*, oestrogens* and CYP17 inhibitors*.

In patients with poor response to hormone therapy* or experiencing severe symptoms following chemotherapy* drugs should be considered:

Docetaxel (used together with prednisone* or prednisolone*) has demonstrated a gain in life prolongation as treatment for castration refractory disease.

Cabazitaxel* is an anticancer drug used with prednisone* to treat hormone-resistant prostate cancer that has spread and that had been treated with docetaxel.

Mitoxantrone* (together with prednisone* or prednisolone*) can be used if docetaxel is contraindicated or if expected side effects from cabazitaxel* might not be tolerated. It is an active drug against prostate cancer but does not prolong life.
DEFINITIONS OF DIFFICULT WORDS

**Abiraterone**
A drug used with prednisone* to treat prostate cancer that has spread to other parts of the body and has not gotten better with other hormone therapy*. It is also being studied in the treatment of other types of cancer. Abiraterone acetate lowers the amount of androgens* (male hormones), such as testosterone*, made by the body. This may stop the growth of cancer cells that need androgens* to grow. Abiraterone acetate is a type of antiandrogen*.

**Anaemia**
Condition characterised by the shortage of red blood cells or haemoglobin; the haemoglobin contains iron that carries oxygen from the lungs to the whole body, this process is diminished in this condition.

**Anaesthesia**
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.

**Androgen**
A type of hormone that promotes the development and maintenance of male sex characteristics.

**Anorexia**
Condition in which the patient loses his appetite whatever the cause.

**Antiandrogen**
A substance that keeps androgens* (male hormones) from binding to their receptors, which can be found in prostate cells and cells of some other tissues. Treatment with antiandrogens may stop prostate cancer cells from growing. Examples of antiandrogens used to treat prostate cancer are flutamide, bicalutamide*, enzalutamide*, and nilutamide.

**Antibiotic**
A drug used to treat infections caused by bacteria and other micro-organisms.

**Benign**
Not dangerous to health. 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
A benign (not cancer) 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 and BPH.

Bicalutamide
A drug used with another drug to treat prostate cancer that has spread to other parts of the body. Bicalutamide binds to proteins* called androgen* receptors, which are found in some prostate cancer cells. These proteins* bind to androgens* (male hormones) and may cause cancer cells to grow. Bicalutamide blocks these proteins* and may keep cancer cells from growing. It is a type of antiandrogen*.

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.

Blood platelets
Small cell fragments that play a fundamental role in the formation of blood clots. Patients with a low platelet count are at risk of severe bleeding. Patients with a high count are at risk of thrombosis, the formation of blood clots that can block blood vessels and result in stroke or other severe conditions, and can also be at risk of severe bleeding because of platelet dysfunction.
Bone mineral density
A measure of the amount of minerals* (mostly calcium and phosphorous) contained in a certain volume of bone. Bone mineral density measurements are used to diagnose osteoporosis (a condition marked by decreased bone mass), to see how well osteoporosis treatments are working, and to predict how likely the bones are to break. Low bone mineral density can occur in patients treated for cancer. Also called BMD, bone density, and bone mass.

Brachytherapy
A type of radiation* therapy in which radioactive material sealed in needles, seeds, wires, or catheters is placed directly into or near a tumour. Also called implant radiation* therapy, internal radiation* therapy, and radiation* brachytherapy.

Cabazitaxel
A drug used with prednisone* to treat hormone-resistant prostate cancer that has spread and that had been treated with docetaxel. It is also being studied in the treatment of other types of cancer. Cabazitaxel blocks cell growth by stopping cell division and may kill cancer cells.

Cardiac arrhythmias
A problem with the rate or rhythm of the heartbeat. The heart can beat too fast, too slow, or with an irregular rhythm.

Chemotherapy
A type of cancer treatment using drugs that 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 to the limb or by infusion to the liver, according to cancer location.

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

Clinical trial
A type of research study that tests how well new medical approaches work in people. These studies test new methods of screening, prevention, diagnosis, or treatment of a disease. Also called a clinical study.

Corticosteroid
Any steroid hormone made in the outer part of the adrenal gland. They are also made in the laboratory. Corticosteroids have many different effects in the body, and are used to treat many different conditions. They may be used as hormone replacement, to suppress the immune system, and to treat some side effects of cancer and its treatment. Corticosteroids are also used to treat certain lymphomas and lymphoid leukaemia’s.

Cryosurgery
A minimally invasive treatment that uses extreme cold to freeze and destroy diseased tissue, including cancer cells.
CT-scan
A form of radiography in which body organs are scanned with X-rays and the results are synthesized by a computer to generate images of parts of the body.

CYP17 inhibitors
Type of medication that inhibits an enzyme called CYP17, which is pivotal for androgen synthesis. Therefore, it inhibits androgen* synthesis. Abiraterone is a type of CYP17 inhibitor.

Denosumab
A drug used to prevent or treat certain bone problems. It is used to prevent broken bones and other bone problems caused by solid tumours that have spread to bone. It is also used in certain patients to treat giant cell tumour of the bone that cannot be removed by surgery. It is also used to treat osteoporosis (a decrease in bone mass and density*) in postmenopausal women who have a high risk of breaking bones. Denosumab is also being studied in the treatment of other conditions and types of cancer. It binds to a protein* called RANKL, which keeps RANKL from binding to another protein* called RANK on the surface of certain bone cells, including bone cancer cells. This may help keep bone from breaking down and cancer cells from growing.

Differentiation/differentiated
The biological process in which a less specialized cell becomes a more specialized cell type. Differentiation is a common process and can change the cell’s shape, size, activity and potential. Differentiated tumour cells look like normal cells and usually grow at a slower rate than undifferentiated or poorly differentiated tumour cells, which look very different from normal cells and grow rapidly.

DNA
Abbreviation for deoxyribonucleic acid. DNA serves as the carrier of genetic information.

Docetaxel
Docetaxel belongs to the group of anticancer medicines known as the taxanes*. Docetaxel blocks the ability of cells to destroy the internal ‘skeleton’ that allows them to divide and multiply. With the skeleton still in place, the cells cannot divide and they eventually die. Docetaxel also affects non-cancer cells such as blood cells, which can cause side effects.

Enema
The injection of a liquid through the anus into the large bowel.

Enzalutamide
A drug used to treat prostate cancer that has spread to other parts of the body and did not get better with other treatment, including docetaxel. Enzalutamide binds to proteins called androgen* receptors, which are found in some prostate cancer cells. These proteins* bind to androgens* (male hormones) and may cause cancer cells to grow. Blocking these proteins* may keep cancer cells from growing. Enzalutamide is a type of antiandrogen*.

Fluid retention
A medical condition in which the body is unable to release fluid and abnormal quantities of it accumulate within the body or in a localised area. Also known as oedema*.
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.

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.

Hormone therapy
The use of hormones as medical treatment.

Inflammatory bowel disease
A general term that refers to the inflammation of the colon and rectum*. Inflammatory bowel disease includes ulcerative colitis and Crohn disease.

Intensity-Modulated Radiotherapy (IMRT)
A type of 3-dimensional radiation* therapy that uses computer-generated images to show the size and shape of the tumour. Thin beams of radiation* of different intensities are aimed at the tumour from many angles. This type of radiation* therapy reduces the damage to healthy tissue near the tumour.

Intravenous
Into or within a vein. Intravenous usually refers to a way of giving a drug or other substance through a needle or tube inserted into a vein. Also called IV.

Laparoscopy/Laparoscopic
An operation where surgical instruments are introduced in the abdomen or in the pelvis through small incisions and with the help of a camera.

Luteinizing-hormone-releasing hormone agonist or LHRH agonist
Any substance that stimulates the Luteinizing hormone-releasing hormone (LHRH) which is a hormone that controls sex hormones in men and women.

Luteinizing-hormone-releasing hormone antagonist or LHRH antagonist
Any substance that inhibits the luteinizing hormone-releasing hormone (LHRH) which is a hormone that controls sex hormones in men and women.

Lymphatic obstruction
Blockage of the lymph vessels that normally drain fluid from tissues throughout the body and allow immune cells to travel where they are required.

Lymph node
A rounded mass of lymphatic tissue that is surrounded by a capsule of connective tissue. Lymph nodes filter lymph and they store lymphocytes. They are located along lymphatic vessels. Also called lymph gland.
**Lymphopenia**
A condition in which there is a lower-than-normal number of lymphocytes, a type of white blood cell*.

**Magnetic Resonance Imaging (MRI)**
An imaging technique that is used in medicine. It uses magnetic resonance. Sometimes, a fluid that enhances the contrast between different tissues to make structures more clearly visible is injected.

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

**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.

**Mineral**
A mineral is a naturally occurring solid chemical substance that is found in the earth's crust. Minerals play a crucial role in the human body, for the creation of enzymes, the regulation of heart rhythm, the formation of bones and other processes. They are obtained by diet or manufactured by the body.

**Mitoxantrone**
A drug used to treat advanced prostate cancer that does not respond to hormones, adult acute non-lymphocytic leukaemia, and advanced or chronic multiple sclerosis. It is also being studied in the treatment of other cancers. It belongs to the family of drugs called antitumour antibiotics*.

**Multidisciplinary opinion**
A treatment planning approach in which a number of doctors who are experts in different specialties (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.

**Nail dystrophy**
Condition in which the nails are severely damaged, appearing partially destroyed.

**Neuroendocrine change/Neuroendocrine differentiation**
Normal prostate has some cells called neuroendocrine cells; these cells secrete some hormones and products involved in normal growth, differentiation and some functions of the prostatic gland. In prostate cancer these cells might increase and since they do not have hormone receptors they are resistant to hormone therapy.
Neuropathy
Refers to any disease of the nervous system. This includes the brain, the spinal cords and the nerves.

Neutropenia
A condition in which there is a lower-than-normal number of neutrophils, a type of white blood cell*. It may be seen with viral infections and after radiation* and chemotherapy*. It lowers the immunologic barrier to bacterial and fungal infections.

Oedema
An abnormal collection of fluid beneath the skin or in a body cavity.

Oestrogen
A type of hormone made by the body that helps develop and maintain female sex characteristics and the growth of long bones. Oestrogens can also be made in the laboratory. They may be used as a type of birth control and to treat symptoms of menopause, menstrual disorders, osteoporosis and other conditions.

Orchiectomy
Surgical procedure to remove one or both testes.

Perineum
The area of the body between the anus and the vulva in females, and between the anus and the scrotum in males.

Prednisolone
Drug that belongs to the class of drugs called steroids. It prevents the release of substances that cause inflammation in the body, and is used to reduce the level of testosterone* in the body.

Prednisone
A drug that lessens inflammation and suppresses immune responses. It is used with other drugs to treat leukaemia and lymphoma and other types of cancer. Prednisone is also used to treat many conditions, including arthritis, certain skin diseases, allergies, low levels of some adrenal hormones, loss of appetite and anaemia. It is a therapeutic glucocorticoid.

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

Protein
An essential nutrient that is made up of amino acids. Proteins* are essential for the working of many organisms, including the human body. They are responsible for transport and communication between cells, for chemical changes and they maintain the structure of cells.

Prostate-specific antigen (PSA)
Prostate-specific antigen is a protein* produced by the prostate. PSA* is elevated in case of prostate cancer and a number of other prostate conditions. A blood test measuring the PSA*-level can detect prostate cancer.
**Prostatic acid phosphatase (PAP)**
An enzyme produced by the prostate. It may be found in increased amounts in men who have prostate cancer. Also called PAP.

**Prostatic bed**
It is the slightly depressed place below the bladder where the prostate is located. It is a common place of dissemination of prostate cancer.

**Pulmonary**
Having to do with the lungs.

**Radiation**
Radiation can be defined as energy travelling through space. Examples of radiation include UV (ultraviolet) and x-rays, which are commonly used in medicine.

**Radiotherapy**
A therapy in which radiation* is used in the treatment of cancer that is always oriented to the specific location of the cancer.

**Radium-223**
A drug used to treat prostate cancer that has spread to the bone and has not gotten better with other treatment. It is also being studied in the treatment of other types of cancer. Radium-223 dichloride contains a radioactive substance called radium-223. Radium-223 accumulates in bone and gives off radiation that may kill cancer cells. Radium-223 dichloride is a type of radiopharmaceutical.

**Rectum**
The last several inches of the large intestine closest to the anus.

**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.

**Red blood cell**
The most common type of blood cell. It is the substance that makes the blood appear red. The main function is the transport of oxygen.

**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.
Samarium-153
A radioactive substance used in the treatment of bone cancer and bone metastases* (cancers that have spread from the original tumour to the bone). Samarium-153 is a radioactive form of the element samarium. It collects in bone, where it releases radiation* that may kill cancer cells. It is a type of radioisotope.

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 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 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.

Sipuleucel-T
A drug used to treat prostate cancer that has spread. It is made from immune system cells collected from a patient with prostate cancer. The cells are treated with a protein* that is made by combining a protein* found on prostate cancer cells with a growth factor. When the cells are injected back into the patient, they may stimulate T cells to kill prostate cancer cells. Sipuleucel-T is a type of vaccine and a type of cellular adoptive immunotherapy.

Stereotactic radiotherapy
A type of external radiation* therapy that uses special equipment to position the patient and precisely give a single large dose of radiation* to a tumour. It is used to treat brain tumours and other brain disorders that cannot be treated by regular surgery. It is also being studied in the treatment of other types of cancer. Also called radiation* surgery, radiosurgery, and stereotaxic radiosurgery.

Strontium-89
A radioactive form of the metal strontium that is taken up by a part of growing bone. It is being studied in the treatment of bone pain caused by some types of cancer.

Testosterone
A hormone produced mainly in the testes (part of the male reproductive system). It is needed to develop and maintain male sex characteristics, such as facial hair, deep voice, and muscle growth. Testosterone can also be produced in the laboratory and is used to treat certain medical conditions.

Thrombocytopenia
The presence of abnormally few blood platelets* in the blood.
Ultrasound
A procedure in which high-energy sound waves are bounced off internal tissues or organs and make echoes. The echo patterns are shown on the screen of an ultrasound machine, forming a picture of body tissues called a sonogram. Also called ultrasonography.

Urethra
The tube that connects the bladder with the outside of the body. In males, the urethra carries urine as well as semen.

Watchful waiting
Closely watching a patient’s condition but not giving treatment unless symptoms appear or change. Watchful waiting is sometimes used in conditions that progress slowly. It is also used when the risks of treatment are greater than the possible benefits. During watchful waiting, patients may be given certain tests and exams. Watchful waiting is sometimes used in prostate cancer. It is a type of expectant management.

White blood cell
Cells of the immune system that are involved in the body's defence against infections.

Zoledronic acid
A drug used to treat patients with hypercalcemia (high blood levels of calcium) caused by cancer. It is also used together with other drugs to treat multiple myeloma and to prevent bone fractures and reduce bone pain in people who have cancer that has spread to the bone. Zoledronic acid belongs to a group of drugs called bisphosphonates.
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](http://www.esmo.org) and [www.anticancerfund.org](http://www.anticancerfund.org)