

How can cancer affect  
**bone health?**

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with your questions.

**ESMO Patient Guide Series**

based on the ESMO Clinical Practice Guidelines

# **Bone health in cancer**

## **An ESMO guide for patients**

### **Patient information based on ESMO Clinical Practice Guidelines**

This guide has been prepared to help you, as well as your friends, family and caregivers, better understand bone health in cancer. It contains information on the effects of cancer on bone health as well as up-to-date guidance on the types of treatments that may be available and any possible side effects of treatment.

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

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

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

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## Bone health in cancer: A summary of key information

This summary is an overview of the key information provided within the Bone Health in Cancer guide. The following information will be discussed in detail in the main pages of the guide.

### Introduction to bone health

- Bones support and protect the internal organs, work with muscles to move the body, and store minerals, such as calcium. Healthy bones keep their shape and strength by continuously renewing bone tissue via the processes of bone **resorption** and formation.
- Cancer can affect bone health in several ways such as by spreading to the bones (known as bone **metastases** or **secondary bone cancer**) or cancer treatment causing bone loss, which makes the bones more fragile and likely to fracture.

### Bone metastases

- Any type of cancer can spread to the bones, but bone **metastases** are particularly common in patients with breast cancer, prostate cancer, lung cancer and kidney cancer while multiple myeloma almost always affects and weakens the bones.
- Bone **metastases** can cause pain in the affected bones, as well as serious complications such as fractures or **spinal cord compression**.
- Bone **metastases** are typically diagnosed using a series of tests, which may include a **radionuclide bone scan, X-ray, computed tomography (CT) scan, magnetic resonance imaging (MRI) scan** and bone biopsy.
- Treatments for bone **metastases** vary depending on the underlying type of cancer as well as the size and location of the **metastases**. **Radiotherapy**, surgery and **bone-targeted agents** are commonly used in the treatment of bone **metastases**.
- **Bone-targeted agents (denosumab and bisphosphonates)** are drugs that reduce bone **resorption** and help to strengthen bones. They can reduce bone pain and decrease the risk of fractures and complications.
- In some circumstances, **bisphosphonate** treatment can help prevent the development of bone **metastases**, particularly in patients who are at a high risk of their cancer returning after treatment. Currently, **bisphosphonates** are only used for the prevention of bone **metastases** in selected patients with early-stage breast cancer.

### Cancer- and cancer treatment-related bone loss

- In some patients undergoing treatment for cancer, the natural rate of bone loss can be accelerated by the treatments they are receiving, resulting in **osteoporosis**, or bone breakdown and an increased risk for fractures.
- In some patients, for example those with multiple myeloma, bone loss is directly related to **bone marrow** infiltration.

- Patients who are at increased risk for bone loss due to their type of cancer and who are receiving a cancer treatment that is known to increase the risk of bone loss will be evaluated for their risk of bone fracture. Patients will be evaluated based on their age, smoking status, **body mass index**, family history of fractures, use of **steroids**, and **bone mineral density**, which is a measure of the thickness of bones. The fracture risk assessment helps doctors to devise a strategy to reduce the risk of fractures.
- Patients at risk of cancer treatment-induced bone loss may be advised to make lifestyle modifications to reduce the risk of fracture, including stopping smoking, reducing alcohol intake, eating a calcium-rich diet, doing weight-bearing exercises and taking a vitamin D supplement.
- Some patients receiving certain treatments for breast or prostate cancer may be treated with a **bone-targeted agent** to reduce cancer treatment-related bone loss. **Denosumab** and **bisphosphonates** have both been shown to be effective, but **denosumab** is most frequently used.

### Follow up during/after treatment

- Patients who have bone **metastases**, or who are at risk of developing bone **metastases**, or who have cancer- or cancer treatment-related bone loss, will have regular discussions with their oncologist about their bone health during their scheduled cancer follow-up appointments.
- Patients undergoing treatment with **bone-targeted agents** will be asked about any side effects from the medication. Patients receiving a cancer treatment that is known to cause bone loss may have regular scans to monitor their **bone mineral density** known as **DXA** scans.

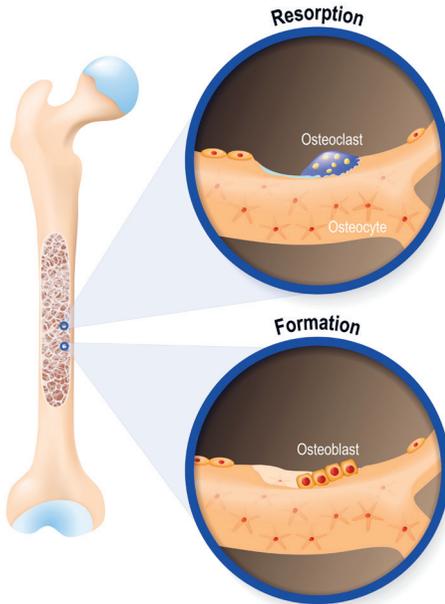
### Emotional support and support groups

- Timely and accurate information about disease and treatment from the oncologist and specialist nurse help patients. Furthermore, specialist counsellors, or psychologists can help patients to deal with the emotional challenges associated with cancer.
- Local, national and international patient support groups are available for specific types of cancer and **osteoporosis**. A list of some useful patient support groups is available in the chapter on support groups. These groups can provide help for patients to better understand their disease, allow them to share their experiences with other patients, and help them to learn how to cope with cancer and **osteoporosis**.

## What bone health problems can occur in cancer?

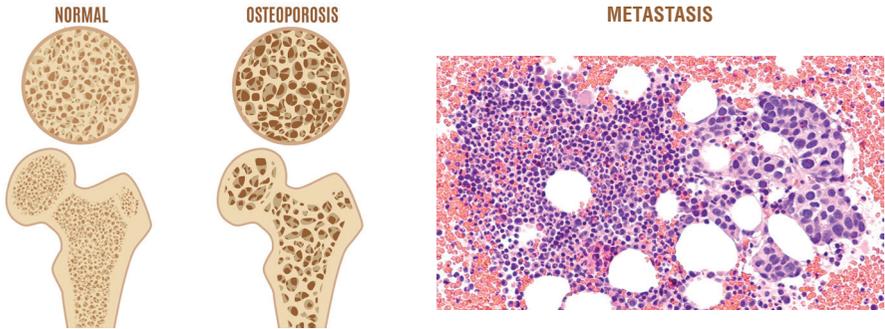
Healthy bones provide support and protection for your internal organs, work with your muscles to move your body, and store minerals such as calcium. Healthy bones keep their shape and strength by continuously renewing the bone tissue (also known as bone turnover). This process involves:

- Bone **resorption**, in which cells called **osteoclasts** break down old bone
- Bone formation, in which cells called **osteoblasts** build new bone



*The process of bone turnover via **resorption** and formation.*

Cancer can affect your bone health. This may be due to the cancer spreading to the bones (known as bone **metastases**) or the cancer treatment causing bone loss (**osteoporosis**), which makes the bones more fragile and likely to fracture.



*Healthy bone, bone loss (**osteoporosis**), and an example of **bone marrow** involvement by breast cancer **metastasis**.*

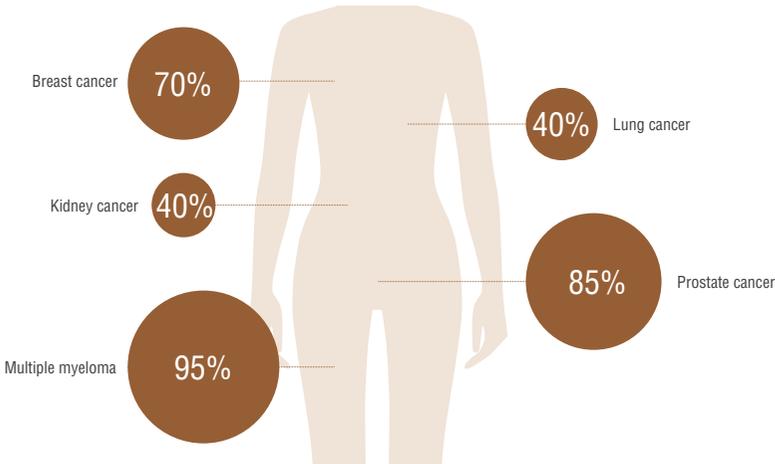
This guide will provide information on the treatment and prevention of bone **metastases** and cancer treatment-related bone loss.

**Bone health can be affected by cancer as well as some types of cancer treatment**

## Bone metastases: How does cancer spread?

**Metastases** develop when a cancer that originated in one part of the body spreads to another area. Cancer cells break away from the original cancer site and move through the bloodstream or **lymphatic system** and form a new cancerous **tumour** in a different part of the body. These new cancerous **tumours** are called **metastases**. **Metastases** contain the same type of cells as the original cancer; for example, if the cancer started in the lungs and has spread to the bones, the **metastases** in the bone will be made up of lung cancer cells.

Bone is a common site for **metastases**. Any kind of cancer can spread to the bones, but some types are particularly associated with a high incidence of bone **metastases**:



*Estimated incidence (measure of the probability of development) of bone **metastases** in different types of **metastatic** cancer (Coleman et al., 2020).*

Bone **metastases** can develop in any bones of the body, but most commonly affect the **axial skeleton** (the skull, spinal bones, pelvis, shoulders and ribs). Patients with bone **metastases** often experience pain in the affected bone. The **metastases** can also result in serious complications such as bone fractures or **spinal cord compression**, in which a **metastasis** or spinal fracture results in pressure on the spinal cord, requiring immediate medical attention. These complications can lead to loss of mobility, reduced quality of life, increased healthcare needs and reduced survival (Coleman et al., 2020).

**Bone metastases can cause bone pain as well as fractures and spinal cord compression**

## How are bone metastases diagnosed?

Bone **metastases** typically occur in multiple sites and cause tenderness and pain in the affected bones. Common symptoms of bone **metastases** include:

- Persistent bone or hip pain
- Backache, which gets worse despite resting
- Bone fractures



More severe complications of bone **metastasis** may be associated with the following symptoms:

- Dehydration, confusion, vomiting, abdominal pain and constipation (due to high levels of calcium in the blood)
- Increased risk of infection, breathlessness, looking pale, bruising and bleeding (due to low levels of healthy blood cells being made in the **bone marrow**)
- Pain and weakness in the legs, numbness, paralysis or loss of sensation and incontinence or inability to hold bowel or bladder function (due to pressure on the spinal cord)

**If you are experiencing bone pain, you should tell your doctor immediately so they can check for metastases**

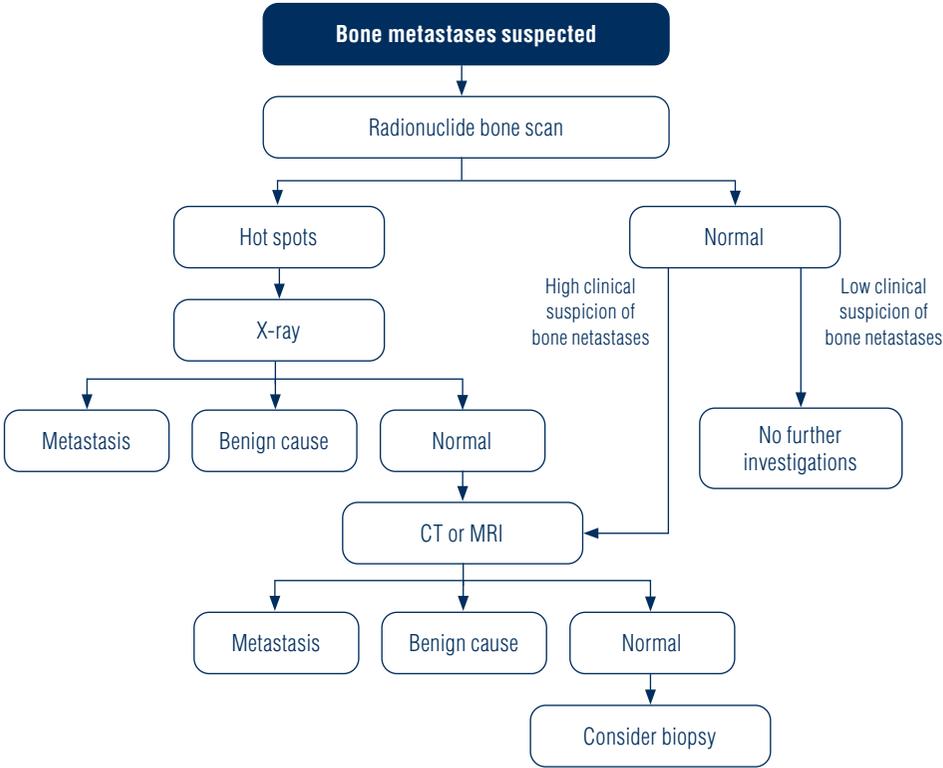
Bone **metastases** can cause many substances to be released into blood and blood tests can be performed to check their amount. Two such substances are calcium and an enzyme called alkaline phosphatase. Their level can also be used to monitor response to treatment. However, higher level of those substances can be caused by some other health problems, not just bone **metastases**.

If your doctor suspects that you have bone **metastases**, you may undergo a **radionuclide bone scan** to look for abnormal changes in your bones. Before the test, a **radioactive** tracer will be injected into a vein. A large **gamma camera** then scans your whole body and detects **radioactivity** from the tracer. The **radioactive** tracer collects in areas of abnormal bone activity, which show up as dark areas on the scan. These dark areas are known as 'hot spots' – they may indicate bone **metastases** but can also occur due to other **benign** (non-cancerous) conditions.

### Imaging tests are used to look for evidence of bone metastases

If hot spots are detected on your **bone scan**, you will usually have an **X-ray** of the abnormal areas to investigate further. **X-rays** can often show whether you have a bone **metastasis** or a **benign** condition affecting the bone. If the **X-ray** does not confirm the cause of your bone symptoms, you may undergo a **computed tomography (CT)** scan or **magnetic resonance imaging (MRI)** scan. **CT** is a type of **X-ray** technique that lets doctors see your internal organs in cross-section. **MRI** uses magnetic fields and radio waves to produce detailed images of the inside of the body.

If the **CT/MRI** scan does not confirm the cause of your bone symptoms, your doctor may recommend that you have a bone **biopsy** to be certain that no bone **metastases** are present in the hot spots detected by the **radionuclide scan**. A bone **biopsy** involves taking a small sample of bone tissue via aspiration to look for cancer cells under a microscope. In some cases, a bone **biopsy** may also be used to confirm a diagnosis of bone **metastases** following diagnosis by **X-ray, CT** or **MRI** (Coleman *et al.*, 2020).



Tests for investigation of suspected bone **metastases** from solid **tumours** (Coleman et al., 2020).

**CT, computed tomography; MRI, magnetic resonance imaging**

It is important to understand that these tests may vary depending on your type of cancer. Your doctor will be able to explain which tests are appropriate for you.

## How will my treatment for bone metastases be decided?

The choice of treatments for bone **metastases** will be discussed with you and your preferences will be taken into account. Your treatment will be discussed by a **multidisciplinary team**, which means that experts in different areas of cancer treatment (e.g. oncologists, radiologists, surgeons and nurses) come together to share their expertise in order to provide the best patient care.

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

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

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

**“What treatment options do I have?”**

**“What are the possible advantages and disadvantages of these treatment options?”**

**“How likely am I to experience benefits or side effects with or without treatment of my bone metastasis?”**

**“Is there a cure for bone metastases?”**

**“Are there any clinical trial options?”**

## What therapies are available to treat bone metastases?

Treatments for bone **metastases** vary depending on the underlying cancer as well as the size and location of the **metastases**. Treatment is usually **palliative** meaning the goals of the treatment are to slow the progression of your cancer, reduce symptoms and improve your quality of life. It is important to understand that treatment of bone **metastases** is rarely **curative**. Your oncologist may recommend one or more of the following approaches for treating bone **metastases**:

### Radiotherapy

**Radiotherapy** uses **ionising radiation** to damage the **DNA** of cancerous cells, causing them to die. **Radiotherapy** uses external beams aimed at the area of a bone **metastasis** and can be very effective in relieving pain. **Radiotherapy** is also used to relieve pressure on the spinal cord in cases of **spinal cord compression**. **Radiotherapy** is often used after surgical treatments, for example after surgery for **spinal cord compression** and after surgery to fix or prevent fractures of the arms or legs (Coleman *et al.*, 2020).



**Radiotherapy is an effective treatment to relieve pain caused by bone metastases**

**Radiotherapy** using **radioisotopes** is also used to treat bone **metastases** in some types of cancer. **Radioisotopes** such as iodine-131 and radium-223 are injected into the blood stream to treat bone **metastases** in thyroid and some cases of prostate cancer respectively.

### Surgery

Surgical treatment for bone **metastases** may be considered if you have **spinal cord compression**, severe pain and/or a bone fracture caused by a bone **metastasis**. You may also receive **radiotherapy** after surgery to help strengthen the bone. Whether or not you undergo surgery will depend on which bone is affected, which part of the bone the cancer is in, what other cancer treatment you are receiving, and your general health.

Some operations for bone **metastases** involve the use of joint replacements, metal plates, rods or a **prosthesis** to help stabilise the surrounding bone. In some cases, small, isolated bone **metastases** can be removed completely; however, this is usually not possible (Coleman et al., 2020).

If you have not experienced a bone fracture but an **X-ray** shows that a **metastasis** has weakened a major bone (for example, the thigh bone), your oncologist might recommend **prophylactic** surgery to strengthen the bone and prevent fracture. **Prophylactic** surgery is associated with better recovery, fewer complications and shorter hospital stays compared with surgery carried out after the bone has already fractured (Coleman et al., 2020).



### Bone-targeted agents

**Bone-targeted agents** are used in the treatment of bone **metastases** arising from all types of cancer. These drugs work by reducing bone **resorption**, thereby helping to strengthen bones. **Bone-targeted agents** can reduce bone pain, reduce the risk of fractures and complications, and reduce calcium levels. It is important to understand that **bone-targeted agents** are not anticancer therapies, but they can maintain or improve quality of life by reducing pain and complications associated with bone **metastases**.

If you have bone **metastases**, your oncologist may recommend that you begin treatment with **bone-targeted agents** even if you are not yet experiencing any bone-related symptoms.

**Bone-targeted agents are commonly used to treat patients with bone metastases, even if no symptoms are present**

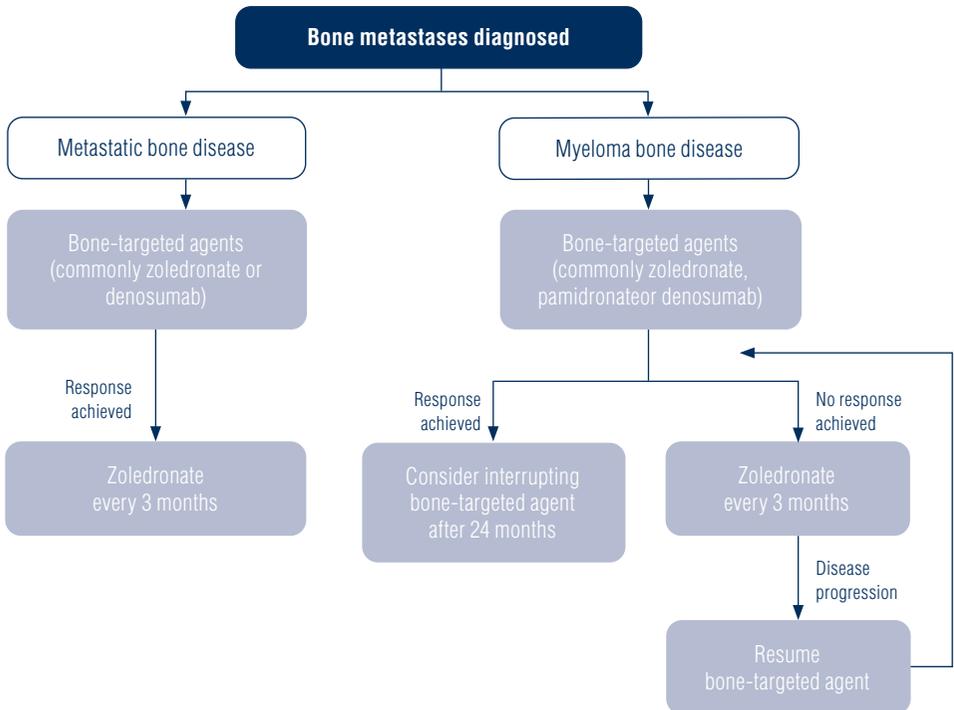
Two types of **bone-targeted agents** are used in the treatment of bone **metastases**:

- **Denosumab** is a **monoclonal antibody** that works by blocking a protein called RANKL, which is found on the surface of **osteoclast** cells. Blocking RANKL reduces bone **resorption**. **Denosumab** is administered by **subcutaneous** injection into the arm or thigh.



- **Bisphosphonates** target areas of high bone turnover. They are absorbed by **osteoclast** cells, which then die, thereby reducing bone resorption. There are several types of **bisphosphonates**, including **zoledronate**, **pamidronate**, **clodronate** and **ibandronate**. These **bisphosphonates** all work in slightly different ways and are suited to different cancer types. You will receive the **bisphosphonate** that works best for your type of cancer. **Bisphosphonates** are administered **intravenously** or orally.

The specific **bone-targeted agent** used and the treatment schedule will depend on the type of cancer present.



Overview of the use of **bone-targeted agents** for bone **metastases** (Coleman et al., 2020).

## Bone health in cancer

The following table provides a summary of the specific **bone-targeted agents** that are used in the treatment of bone **metastases** arising from different types of cancer. Your oncologist will be able to explain the options available to you.

<b>BONE-TARGETED AGENT</b>	<b>CANCER TYPE</b>	<b>ADMINISTRATION</b>
<b>Denosumab</b>	All solid <b>tumours</b> and multiple myeloma	<b>Subcutaneous</b> injection every 4 weeks
<b>Zoledronate</b>	All solid <b>tumours</b> and multiple myeloma	<b>Intravenous</b> injection every 4-12 weeks
<b>Pamidronate</b>	Breast cancer and multiple myeloma	<b>Intravenous</b> injection every 3-4 weeks
<b>Clodronate</b>	<b>Osteolytic lesions</b> from breast cancer	Oral treatment every day
<b>Ibandronate</b>	Breast cancer	Oral treatment every day <u>or</u> <b>intravenous</b> injection every month

*Overview of the use of **bone-targeted agents** for the treatment of bone **metastases** in different cancer types (Coleman et al., 2020).*

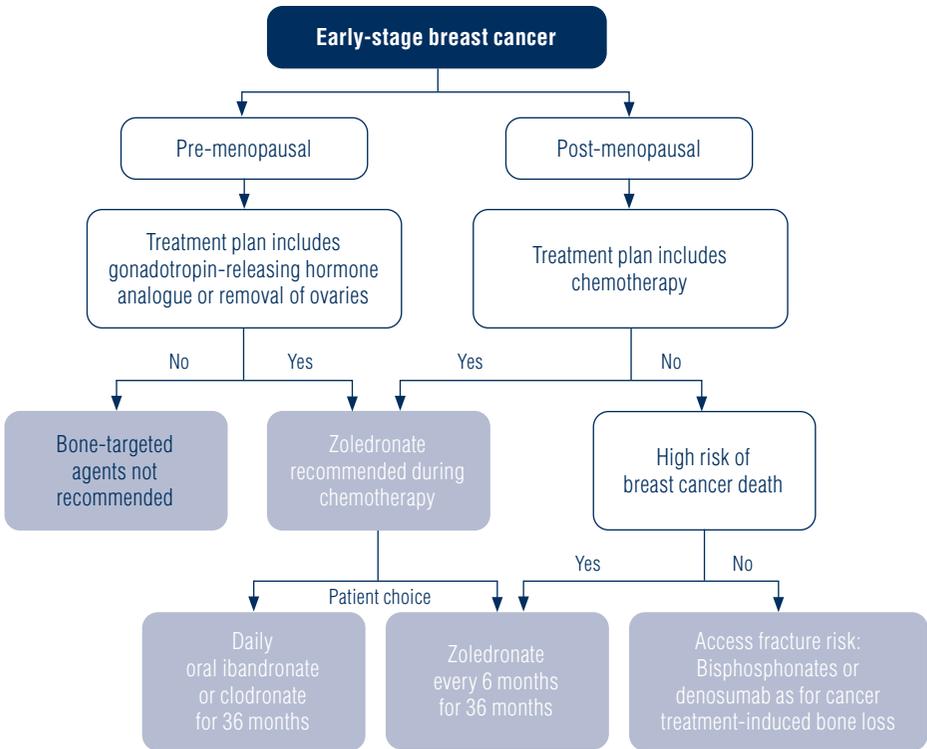
For additional information on breast cancer and multiple myeloma, see ESMO's patient guides on breast cancer (<https://www.esmo.org/for-patients/patient-guides/breast-cancer>) and multiple myeloma (<https://www.esmo.org/for-patients/patient-guides/multiple-myeloma>).

## What treatments are available to prevent bone metastases?

In some circumstances, **bisphosphonate** treatment may be recommended to help prevent the development of bone **metastases**. This may be particularly important for patients who are considered to be at a high risk of their cancer returning after treatment. However, the best evidence for the benefits of this type of preventative treatment has been observed in post-**menopausal** women with early-stage breast cancer (Coleman *et al.*, 2020). Currently, treatment for the prevention of bone **metastases** is not recommended in any other types of cancer apart from breast cancer.

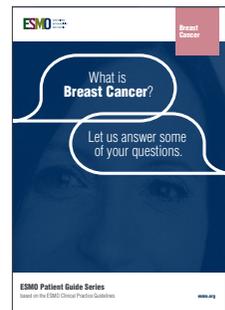
**In patients with breast cancer, bisphosphonates may help to prevent the development of bone metastases**

If you are diagnosed with early-stage breast cancer, are post-**menopausal** (or pre-**menopausal** and receiving a **gonadotropin-releasing hormone analogue**) and are considered to be at high risk of your cancer returning, your oncologist may recommend that you begin treatment with a **bisphosphonate** (usually **zoledronate**, **clodronate** or **ibandronate**). **Bisphosphonate** treatment typically starts at the same time as other **systemic** therapies (such as **chemotherapy**) and continues for 2-5 years (Coleman *et al.*, 2020). The use of **bisphosphonates** in this situation can also lower the risk of treatment-induced bone loss (see section 'What therapies are available to prevent cancer treatment-induced bone loss?' for more information).



Overview of the use of **bone-targeted agents** for the prevention of bone **metastases** in patients with early-stage breast cancer (Coleman et al., 2020).

For additional information on breast cancer, see ESMO’s patient guide on breast cancer (<https://www.esmo.org/for-patients/patient-guides/breast-cancer>).



## What is cancer treatment-related bone loss?

The rate of bone loss naturally increases with advancing age in both men and women. However, in some patients undergoing treatment for cancer, the rate of bone loss may be accelerated by the treatments they are receiving, resulting in **osteoporosis**. These include:

- **Hormone therapy** for breast cancer that works by reducing **oestrogen** levels: long-term treatment with these drugs can cause bone loss and increase the risk of fractures. It is important to understand that not all **hormone therapies** for breast cancer cause bone loss.
- **Hormone therapy** for prostate cancer: bone loss is a side effect of drugs that reduce **testosterone** levels in patients with prostate cancer.
- **Chemotherapy**: some types of **chemotherapy** affect the ovaries or testicles, reducing the levels of **oestrogen** in women and **testosterone** in men, which can lead to bone loss.
- **Steroids**: high-dose or long-term **steroid** treatment can lead to bone loss.
- Surgery: removal of both testicles in men or the ovaries before **menopause** in women reduces **hormone** levels and can lead to bone loss.
- **Radiotherapy**: **radiotherapy** to the ovaries before **menopause** reduces **oestrogen** levels and can lead to bone loss. **Radiotherapy** can also cause changes to the bone in the area being treated, resulting in the bone being unable to cope with normal activity and increasing the risk of fractures. This is most likely when **radiotherapy** is given to the pelvic area.
- It is important to understand that not all cancer treatments increase the rate of bone loss. Your oncologist will be able to explain whether or not your type of treatment puts you at risk of **osteoporosis**.

**Some types of cancer treatment can accelerate bone loss and increase the risk of osteoporosis**

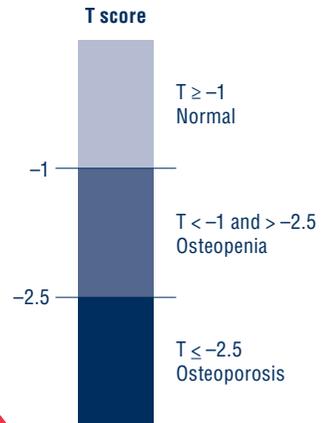
## How is the risk of cancer treatment-related bone loss assessed?

If you are receiving a cancer treatment that is known to increase the risk of bone loss, you will be evaluated for your risk of bone fracture. Factors that are taken into account include your age, whether or not you have ever smoked, your **body mass index**, any family history of hip fractures, long-term treatment with **steroids**, and your **bone mineral density**.

**Bone mineral density** is a measure of the thickness of your bones. People with low **bone mineral density** have a higher risk of bone fracture. **Bone mineral density** is evaluated by a special type of **X-ray** scan called **dual energy X-ray absorptiometry (DXA)**. The **DXA** scan results are given as a number called a **T score**:

- **T score** of  $-1$  or higher: Your **bone mineral density** is normal
- **T score** lower than  $-1$  and above  $-2.5$ : Your **bone mineral density** is below normal (known as **osteopenia**)
- **T score** of  $-2.5$  or lower: Your **bone mineral density** is low and you are at risk of bone fracture (**osteoporosis**)

Your oncologist will use the results of your fracture risk assessment to decide on a management strategy to reduce the risk of fracture. You will undergo regular risk assessments, including **DXA** scans to monitor your **bone mineral density**, during long-term follow up.



**Measuring bone mineral density is an effective way to evaluate bone health and risk of osteoporosis**

## What therapies are available to prevent cancer treatment-related bone loss?

If you are receiving a type of cancer treatment that is known to accelerate bone loss, there are a number of things you can do yourself to reduce your risk of **osteoporosis**. These include:

- Stopping smoking
- Reducing your alcohol intake
- Eating a calcium-rich diet (or taking a calcium supplement)
- Doing weight-bearing exercises
- Taking a vitamin D supplement every day

These steps will improve your bone health and reduce the risk of **osteoporosis**.

If you are a woman receiving an **aromatase inhibitor** or **ovarian function suppression** for breast cancer, or a man receiving **androgen deprivation therapy** for prostate cancer, your oncologist may recommend treatment with a **bone-targeted agent** if you are at risk of **osteoporosis** (Coleman *et al.*, 2020). **Bone-targeted agents** are drugs that reduce bone **resorption**. By reducing bone **resorption**, these drugs help to reduce bone breakdown, thereby strengthening bones and lowering the risk for fracture.

There are two types of **bone-targeted agents** used in the prevention of cancer treatment-related bone loss:

- **Denosumab** is a **monoclonal antibody** that works by blocking a protein called RANKL, which is found on the surface of **osteoclast** cells. Blocking RANKL reduces bone **resorption**. **Denosumab** is administered by **subcutaneous** injection.
- **Bisphosphonates** target areas of high bone turnover. They are absorbed by **osteoclast** cells, which then die, thereby reducing bone **resorption**. There are several types of **bisphosphonates**, including **zoledronate**, **alendronate**, **risedronate** and **ibandronate**. **Bisphosphonates** are administered **intravenously** or orally.

**Denosumab** and **bisphosphonates** have both been shown to reduce cancer treatment-related bone loss, but **denosumab** is the most commonly used treatment:

BONE-TARGETED AGENT	CANCER TYPE	ADMINISTRATION
<b>Denosumab</b>	Breast cancer	<b>Subcutaneous</b> injection every 6 months
	Prostate cancer (treated with <b>ADT</b> )	
<b>Zoledronate</b>	Breast cancer	<b>Intravenous</b> injection every 6 months
	Prostate cancer (treated with <b>ADT</b> )	<b>Intravenous</b> injection every 12 months
<b>Alendronate</b>	Breast cancer	Oral treatment every week
	Prostate cancer (treated with <b>ADT</b> )	
<b>Risedronate</b>	Breast cancer	Oral treatment every week
	Prostate cancer (treated with <b>ADT</b> )	
<b>Ibandronate</b>	Breast cancer	Oral treatment every month
	Prostate cancer (treated with <b>ADT</b> )	

Overview of the use of **bone-targeted agents** for the prevention of cancer treatment-related bone loss in different cancer types (Coleman et al., 2020).

**ADT, androgen deprivation therapy**

For additional information on breast and prostate cancer, see ESMO’s patient guides on breast cancer (<https://www.esmo.org/for-patients/patient-guides/breast-cancer>) and prostate cancer (<https://www.esmo.org/for-patients/patient-guides/prostate-cancer>).



### Special considerations for elderly patients

If you are elderly, you are already at an increased risk of bone fracture and are more likely to need therapy to prevent cancer treatment-induced bone loss. Your oncologist will take a number of factors into account when deciding on the best treatment for you. It is likely that you will receive a **bone-targeted agent**; however, if you have other medical conditions, such as kidney disease, your oncologist will adjust your treatment plan to minimise the risk of additional side effects. Some patients find it difficult to remember to take oral **bone-targeted agents** regularly, so your oncologist may suggest that you have an **intravenous** dose of **zoledronate** every 6 or 12 months, or a **subcutaneous** dose of **denosumab** every 6 months, which are both highly effective.

### Orthopedic aids for patients with bone metastases

Patients with bone **metastases** may need to use orthopedic aids such as orthoses (externally applied devices to support the bones), walkers, and cervical (Schanz) collar.

## Clinical trials

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

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



**Clinical trials** help to improve knowledge about cancer and develop new treatments, and there can be many benefits to taking part. You will have to undergo various tests before entering a trial and be carefully monitored during and after the study. Although the new treatment may offer benefits over existing therapies, it's important to bear in mind that it's not always the case or that new treatments may have side effects that outweigh the benefits (*ClinicalTrials.gov, 2019*).

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

You have the right to accept or refuse participation in a **clinical trial** at any time without any consequences for the quality of your treatment. If your oncologist does not ask you about taking part in a **clinical trial** and you want to find out more about this option, you can ask your oncologist if there is a trial for your type of cancer taking place nearby (*ClinicalTrials.gov, 2019*). If you are still unable to find access to a **clinical trial** it is recommended that you reach out to your local patient organisation for further support.

The European Medical Association has a register of all European **clinical trials**. You can find it here: <https://www.clinicaltrialsregister.eu/> The US National Library of Medicine has a register of clinical trials conducted around the world. You can find it here: <https://clinicaltrials.gov/>

## What are the possible side effects of treatment?

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

Oncologists classify side effects from any cancer therapy by assigning each event a 'grade', on a scale of 1–4, by increasing severity. In general, grade 1 side effects are considered to be mild, grade 2 moderate, grade 3 severe and grade 4 very severe. However, the precise criteria used to assign a grade to a specific side effect varies depending on which side effect is being considered. The aim is always to identify and address any side effect before it becomes severe, so you should always report any worrying symptoms to your oncologist as soon as possible.



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

### Radiotherapy

The side effects of **radiotherapy** for bone **metastases** depend on the area of the body that is treated. Some patients experience nausea and vomiting, but anti-nausea medicines can help with this. When **radiotherapy** first starts, you may experience a temporary increase in your bone pain before it starts to get better; this is a common side effect that can be reduced by treatment with an oral **steroid** before the effect of **radiotherapy** begins (Coleman *et al.*, 2020). **Radiotherapy** may also cause skin to become red and sore (like mild sunburn) in the treatment area. You will be given cream to soothe the skin, and the soreness usually disappears a few weeks after finishing treatment.

**Radiotherapy** with **radioisotopes** can cause diarrhoea and nausea. It can also lead to a decrease in the number of blood cells being made in the **bone marrow**. If this happens, you may feel tired, be more at risk of infection, and bruise or bleed more easily. Most people recover quickly from these side effects.

### Surgery

Following surgery to strengthen a bone or to remove a bone **metastasis**, you will have to stay in hospital for at least a few days, depending on the type of operation you have. It is normal to experience pain for the first week or so after surgery and your doctor or nurse will be able to give you pain medicine to keep you feeling comfortable. A physiotherapist will help you to get moving around as soon as possible after your operation, and they will be able to give you exercises to help with your recovery; however, it is normal to feel tired for several weeks after surgery.

### Bone-targeted agents

Common side effects from **bone-targeted agents** include effects on the **gastrointestinal system** (such as nausea, constipation or diarrhoea) as well as flu-like symptoms and general **fatigue**. Some patients experience a temporary increase in bone pain, which can be treated with pain medicine. **Bone-targeted agents** can also reduce the levels of calcium in the blood, in which case further supplements may be recommended. Consultation with your oncologist is recommended before taking any supplement. If you have kidney disease, you may be treated with **denosumab** rather than **bisphosphonates**, as **bisphosphonates** have been reported to affect kidney function and require additional monitoring in patients with kidney disease.

### Osteonecrosis of the jaw

**Osteonecrosis** of the jaw is a rare but serious side effect of treatment with **bone-targeted agents**, in which the bone tissue in the jaw becomes damaged and dies. Dental problems can increase the risk of **osteonecrosis** of the jaw; therefore, it's very important to look after your oral health and attend regular dental check-ups during treatment with **bone-targeted agents**.

**It is important to ensure that your dentist is aware that you are being treated with bone-targeted agents**

It is important to understand that **osteonecrosis** of the jaw (ONJ) is uncommon and related to the duration and frequency of treatment. Treatment for bone **metastases** or multiple myeloma with **bone-targeted agents** for a year is associated with ONJ in around 1% of patients while for those receiving **bone-targeted agents** to prevent bone loss the risk is considerably less. However, you should contact your oncologist immediately if you experience any oral symptoms such as loose teeth or pain and swelling in the mouth, as early treatment will give you the best chance of a good recovery.

### Atypical femoral fracture

A specific type of fracture of the thigh bone called an **atypical femoral fracture** has been associated with **bone-targeted agents**. However, the risk of **atypical femoral fracture** is very small (around 0.1%) and usually only occurs with long-term treatment. Therefore, the benefit of treatment with **bone-targeted agents** far outweighs the risk of this side effect.

## Rebound osteolysis

After **denosumab** treatment has stopped, some patients can experience rebound **osteolysis**, which is a sudden increase in bone breakdown and a rapid decrease in **bone mineral density** that can result in fractures. The risk of rebound osteolysis can be reduced by short-term treatment with a **bisphosphonate** (Coleman et al., 2020).

## What can I do to improve my well-being?

### Follow-up appointments

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

During cancer treatment, you will have regular appointments to discuss your treatment and progress with your oncologist. If you have bone **metastases**, or if your oncologist thinks you are at risk of developing bone **metastases** or cancer treatment-related bone loss, these appointments will also include a discussion about your bone health.

It is very important that you attend all of your scheduled appointments so that your oncologist can monitor your bone health. If you are experiencing any bone-related symptoms then you should tell your oncologist immediately so that a treatment plan can be discussed. If you are being treated with **bone-targeted agents**, your oncologist will ask you if you are experiencing any side effects from your medication. Your calcium levels and kidney function may also be monitored, and your oncologist will ensure that you are having regular dental check ups. If you are receiving a cancer treatment that is known to cause bone loss, you may have a **DXA** scan every 1–2 years to monitor your **bone mineral density** (Coleman et al., 2020).



The reality of patients with bone **metastases** is the need for care by **multidisciplinary team**. Keeping physically active can bring many benefits to patients with cancer. Patients with bone **metastases** may discuss about precautions on physical activity with oncologist and also with a physiotherapist who will weigh perceived risk from bone complications against potential health benefit and plan carefully an exercise programme.

Talk with a nutritionist about food that may be helpful for bone **metastases**. Nutritionist could recommend changes to your dietary routine in terms of beneficial nutrients and relieve of nausea as some patients experience nausea during treatment.

Sometimes, even if it is not a cure for your disease, reducing pain from bone **metastases** is the only way to improve quality of life. If you are experiencing pain, there are a number of options available to help you. It is important that you tell your oncologist about any persistent or new pain so they can ensure you are receiving appropriate treatment and pain relief medication. For further information and advice on coping with cancer pain, see ESMO's patient guide on cancer pain (<https://www.esmo.org/for-patients/patient-guides/cancer-pain-management>).



## Looking after your health

Consultation with a **multidisciplinary team** is very important since the beginning of treatment including kinesiotherapy specialist, nutritionist, specialist nurses, and psychologist.

During and after treatment for cancer, you may feel very tired and emotional. Give your body time to recover and make sure you get enough rest. Consult with your oncologist if there is limitation to physical activity.

It is important to take good care of yourself and get the support that you need.

- **Take plenty of rest when you need it:** Give your body time to recover. Complementary therapies, such as aromatherapy, may help you relax and cope better with side effects. It is important to find a source of relaxation and wellbeing and your hospital may offer complementary therapy; ask your oncologist for details.
- **Eat well and keep active:** Eating a healthy diet and keeping active can help improve your fitness. It is important to start slowly and build up as you start to feel better.

The following recommendations form a good foundation for a healthy lifestyle for patients with bone **metastases** and cancer- and cancer treatment-related bone loss (*Macmillan Cancer Support*):

- Exercise according provided plan. Weight bearing exercises that work well are walking, jogging, weight training, dancing and stair climbing and can be gradually added in terms of time, distance and weight. However, swimming and bicycling are good aerobically, but they are not weight bearing exercise.
- Eat a healthy diet. Get enough calcium. Dietary calcium is best and food rich in calcium is dairy products, sunflower seeds, broccoli, collard greens, etc. However, the body can absorb only 400-500 mg of calcium at one time. If your oncologist agree that calcium supplementation is right for you, check with your oncologist about amount and formulation.
- Vitamin D supports the body's ability to absorb calcium; vitamin D3 is more effective than vitamin D2.
- Don't drink alcohol.
- Don't smoke.
- Avoid second-hand smoke.

Regular exercise is an important part of a healthy lifestyle, helping you to keep physically fit and avoid weight gain. There is evidence that an exercise programme that includes aerobic, weight-bearing and resistance training can improve **bone mineral density** and reduce the risk of **osteoporosis** in patients who have undergone cancer treatment (Almstedt et al., 2016; Owen et al., 2017). Studies have also shown that regular exercise can improve overall physical function in patients with bone **metastases** (Galvão et al., 2018; Sheill et al., 2018) and improve sleep quality.

**When planning an exercise programme, it is very important that you listen carefully to the recommendations of your oncologist or nurse, and talk to them about any difficulties you have**

You should be aware of 'red flag' symptoms and report them immediately to your oncologist or nurse, in particular bone pain in spine, bone pain on weight bearing especially in thigh bone, worsening and intractable bone pain at any time. Symptoms that indicate **spinal cord compression** are described in the section on how are bone **metastases** diagnosed.

- For healthy lifestyle after cancer (Wolin et al., 2013) besides avoiding smoking and alcohol use, it is also recommended to avoid weight gain, exercise regularly and eat a healthy diet.
- Stay connected with friends, family and other cancer survivors.
- Attend regular check-ups and screening tests.



### Emotional support

It is common to be overwhelmed by your feelings when you have been diagnosed with cancer and when you have been through treatment. If you feel anxious or depressed, talk to your doctor or nurse – they can refer you to a specialist counsellor or psychologist who has experience of dealing with the emotional problems of people coping with cancer. It may also help to join a support group so that you can talk to other people who understand exactly what you are going through.



## Support groups

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



### Breast cancer:

- ABC Global Alliance: [www.abcgloballiance.org](http://www.abcgloballiance.org)
- Advanced BC: <http://advancedbc.org>
- After Breast Cancer Diagnosis: [www.abcdbreastcancersupport.org](http://www.abcdbreastcancersupport.org)
- Breast Cancer Alliance: [www.breastcanceralliance.org](http://www.breastcanceralliance.org)
- Breast Cancer Care: [www.breastcancercare.org.uk](http://www.breastcancercare.org.uk)
- Breast Cancer Network Australia: [www.bcna.org.au](http://www.bcna.org.au)
- EUROPA DONNA: [www.europadonna.org](http://www.europadonna.org)
- Male Breast Cancer Coalition: <http://malebreastcancercoalition.org>
- Metastatic Breast Cancer Network: [www.mbcn.org](http://www.mbcn.org)
- Metavivor: [www.metavivor.org](http://www.metavivor.org)
- National Breast Cancer Coalition: [www.breastcancerdeadline2020.org/homepage.html](http://www.breastcancerdeadline2020.org/homepage.html)
- Susan G. Komen Breast Cancer Foundation: [www.komen.org](http://www.komen.org)
- Unión Latinoamericana Contra al Cáncer de la Mujer: [www.ulaccam.org/index.php](http://www.ulaccam.org/index.php)

### Lung cancer:

- Global Lung Cancer Coalition (GLCC): [www.lungcancercoalition.org](http://www.lungcancercoalition.org)
- Lung Cancer Europe (LuCE): [www.lungcancereurope.eu](http://www.lungcancereurope.eu)
- Women Against Lung Cancer in Europe (WALCE): [www.womenagainstlungcancer.eu/?lang=en](http://www.womenagainstlungcancer.eu/?lang=en)

### Prostate cancer:

- Europa Uomo: <https://www.europa-uomo.org/>

### Multiple myeloma

- Myeloma Patients Europe: <https://www.mpeurope.org/>

### Osteoporosis

- International Osteoporosis Foundation: <https://www.osteoporosis.foundation/>
- Royal Osteoporosis Society: <https://theros.org.uk/>

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## GLOSSARY

### ALENDRONATE

A type of **bisphosphonate** used to treat bone **metastasis** and breakdown

### ANDROGEN DEPRIVATION THERAPY (ADT)

Treatment to suppress or block the production or action of male **hormones**

### AROMATASE INHIBITOR

A type of **hormone therapy** that prevents the formation of **oestrogen**

### ATYPICAL FEMORAL FRACTURE

A stress fracture in the thigh bone that can be a complication of **bisphosphonate** treatment

### AXIAL SKELETON

Part of the body that consists of the skull, spinal bones and ribs

### BENIGN

A **tumour** or lesion that is not cancerous

### BIOPSY

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

### BISPHOSPHONATES

Drugs that help prevent, or slow down, **osteoporosis**, and prevent broken bones and other bone problems caused by bone **metastases**

### BODY MASS INDEX

A measure that relates body weight to height. **Body mass index** can be used to assess whether or not a person is a healthy weight

### BONE MARROW

A spongy tissue found inside bones. It contains stem cells, which are cells that can develop into red blood cells, white blood cells or platelets

### BONE MINERAL DENSITY

A measure of the amount of minerals in a certain volume of bone. **Bone mineral density** measurements are used to diagnose **osteoporosis**

### BONE-TARGETED AGENTS

Drugs that reduce bone **resorption** and help to strengthen bones. **Denosumab** and **bisphosphonates** are examples of **bone-targeted agents**

### CHEMOTHERAPY

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

### CLINICAL TRIAL

A study that investigates new treatments or compares the effects of one treatment with another

### CLODRONATE

A type of **bisphosphonate**

### COMPUTED TOMOGRAPHY (CT)

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

### CURATIVE (TREATMENT)

A treatment that is intended to cure or permanently rid the cancer

### DENOSUMAB

A drug used to treat **osteoporosis** and prevent broken bones and other bone problems caused by bone **metastases**

### DNA

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

### DUAL ENERGY X-RAY ABSORPTIOMETRY (DXA)

An imaging test that measures **bone mineral density** by passing **X-rays** with two different energy levels through the bone. **DXA** scans are used to diagnose **osteoporosis**

### FATIGUE

Overwhelming tiredness

### GAMMA CAMERA

A camera that detects **ionising radiation**, this camera is used to take pictures after injection with a **radioactive** tracer used in a **radionuclide scan**

### GASTROINTESTINAL SYSTEM

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

### GONADOTROPIN-RELEASING HORMONE ANALOGUE

Treatment that stops the ovaries and testicles from making sex **hormones**

### HORMONE

A substance made by glands in the body. **Hormones** circulate in the bloodstream and control the actions of certain cells or organs

### HORMONE THERAPY

Treatments that block the actions of **hormones** such as **oestrogen** or **testosterone**

## GLOSSARY

### IBANDRONATE

A type of **bisphosphonate**

### INTRAVENOUS

A medication or treatment administered into a vein

### IONISING RADIATION

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

### LYMPHATIC SYSTEM

A network of tissues and organs that help rid the body of toxins, waste and other unwanted materials. The primary function of the **lymphatic system** is to transport lymph, a fluid containing infection-fighting white blood cells, throughout the body

### MAGNETIC RESONANCE IMAGING (MRI)

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

### MENOPAUSE

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

### METASTASES/METASTASIS

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

### METASTATIC

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

### MONOCLONAL ANTIBODY

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

### MULTIDISCIPLINARY TEAM

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

### OESTROGEN

**Hormone** that helps to develop and maintain female sex characteristics

### OSTEOBLASTS

Large cells that build up bone

### OSTEOCLASTS

Large cells that mediate the continuous breakdown (or **resorption**) of bone

### OSTEOLYSIS

Degeneration of bone, in which there is an increase in bone turnover and a decrease in **bone mineral density**

### OSTEOLYTIC LESIONS

Areas of bone damage that result from cancerous cells building up in the **bone marrow**. **Osteolytic lesions** are common in multiple myeloma

### OSTEONECROSIS

Loss of blood flow to bones, causing the bone to die

### OSTEOPENIA

A condition in which **bone mineral density** is lower than normal. **Osteopenia** is a less severe form of bone loss than **osteoporosis**

### OSTEOPOROSIS

A decrease in the amount and thickness of bone tissue, which causes the bones to become weak and break more easily

### OVARIAN FUNCTION SUPPRESSION

Treatment that stops or lowers the amount of **oestrogen** made by the ovaries

### PALLIATIVE (TREATMENT)

Treatment and care of patients that does not intend to cure but focuses on providing relief from pain, symptoms and physical and emotional stress.

### PAMIDRONATE

A type of **bisphosphonate**

### PROPHYLACTIC (SURGERY)

Surgery that is carried out to prevent a complication that a patient is at risk of

### PROSTHESIS

An object that replaces a part of the body

### RADIOACTIVE/RADIOACTIVITY

A material that is unstable and spontaneously emits energy (radiation)

### RADIOISOTOPE

An unstable form of a chemical element that releases radiation as it breaks down and becomes more stable

## GLOSSARY

### RADIONUCLIDE SCAN

A procedure in which a small amount of a **radioactive** chemical (radionuclide) is injected into a vein and travels through the blood to different organs. A machine with a **gamma camera** scans the patient and detects the type of radiation given off by the radionuclide. A computer then forms an image of the areas where the radionuclide has collected

### RADIOTHERAPY

Treatment involving the use of high-energy radiation, which is commonly used to treat cancer

### RESORPTION

A process during which bone is broken down and then absorbed by the body

### RISEDRONATE

A type of **bisphosphonate**

### SPINAL CORD COMPRESSION

Pressure on the spinal cord that may be caused by a **tumour**

### STEROID

A type of drug used to relieve swelling and inflammation. Some **steroid** drugs also have anti-**tumour** effects

### SUBCUTANEOUS

A medication or treatment that is administered beneath the skin

### SYSTEMIC

Drugs that spread throughout the body to treat cancer cells wherever they may be. They include **chemotherapy**, **targeted therapy** and immunotherapy

### T SCORE

A measure of **bone mineral density**, compared to the **bone mineral density** of a healthy young adult. A **T score** of 0 indicated that the **bone mineral density** is equal to that of a healthy young adult

### TARGETED THERAPY

A type of cancer treatment that uses drugs or other substances to precisely identify and attack cancer cells, usually while doing little damage to normal cells

### TESTOSTERONE

A **hormone** made mainly in the male reproductive system that is needed to develop and maintain male sex characteristics

### TUMOUR

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

### X-RAY

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

### ZOLEDRONATE

A type of **bisphosphonate**

## Bone health in cancer

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

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

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**We can help you understand how cancer can affect your bone health.**

This guide has been prepared to help you, your family and friends better understand how cancer and its treatment can affect bone health. The medical information described in this document is based on the ESMO Clinical Practice Guideline for bone health in cancer.

For more information, please visit [www.esmo.org](http://www.esmo.org)

