What is multiple myeloma?
Let us explain it to you.
MULTIPLE MYELOMA: A GUIDE FOR PATIENTS

PATIENT INFORMATION BASED ON ESMO CLINICAL PRACTICE GUIDELINES

This guide for patients has been prepared by the Anticancer Fund as a service to patients, to help patients and their relatives better understand the nature of multiple myeloma and appreciate the best treatment choices available according to the subtype of disease. 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 multiple myeloma. 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 leading author of the clinical practice guidelines for professionals. It has also been reviewed by representatives from the European Oncology Nursing Society (EONS) and the patient representative from ESMO’s Patient Advocates Working Group.

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

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

For words marked with an asterisk, a definition is provided at the end of the document.
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This text was written by Dr Alberto Mussetti (for the Anticancer Fund) and reviewed by Dr Ana Ugarte (Anticancer Fund), Dr Svetlana Jezdic (ESMO), Prof. Philippe Moreau (ESMO), Prof. Christian Buske (ESMO), Vanessa Marchesi, PhD (ESMO), Claire Bramley (ESMO), Prof. Jean-Yves Douillard (ESMO), Anita Margulies BSN RN (EONS), Patricia Bosman, MSc (EONS), Ananda Plate (ESMO Patient Advocates Working Group; Myeloma Patients Europe), Alfonso Aguarón (Myeloma Patients Europe) and Ana Vallejo (Myeloma Patients Europe).
FACTSHEET ABOUT MULTIPLE MYELOMA

Definition:
- Multiple myeloma is a cancer that develops from plasma cells*. Plasma cells are a type of white blood cell made in the bone marrow. These cells are part of the immune system and their function is to produce antibodies* which protect us from infections.

Diagnosis:
- Specific symptoms* such as fatigue, more frequent infections, bone pain or spontaneous fractures can be present at diagnosis.
- The tests that are necessary to make a diagnosis are:
  o Detection of monoclonal protein* (an antibody* produced by plasma cells* in patients with multiple myeloma) in the blood or 24-hour urine samples;
  o Bone marrow aspirate* or biopsy* to measure the percentage of myeloma cells in the bone marrow;
  o Evaluation of bone lesions* may be performed by your doctor. This can be done by either a magnetic resonance imaging (MRI), a whole body low dose radiation computed tomography (CT) scan* or positron emission tomography (PET)*.
  o Blood tests to assess kidney function and levels of calcium and haemoglobin*.

Treatment:
- Treatment is only required in case of symptomatic* disease (in the presence of hypercalcemia*, kidney problems, anaemia* or bone lesions*) or high risk asymptomatic disease*.
- First line treatment is divided into two groups:
  o Patients in good physical condition who are suitable for autologous transplant*: 4-6 cycles of bortezomib*-based chemotherapy* followed by high dose melphalan* and autologous transplant* as part of disease reduction after consolidation*.
  o Patients with significant comorbidities* or who are not physically fit enough to undergo autologous transplant*: oral combinations of melphalan* and prednisone* plus newer drugs are the standard treatments in this setting. In this case there is no need for further therapy after the end of the planned cycles of treatment.
- Relapsed* and refractory* disease treatment:
  The choice of treatment depends on several parameters regarding the patient (age and health status) and previous therapies. Autologous transplant* can still be an option. Allogeneic transplant* should be carried out only in the context of clinical trials.
  - Enrolment in clinical trials is strongly recommended for both first line and subsequent treatments since there are several newer active drugs currently being tested.

Follow-up:
- Since multiple myeloma is characterised by recurrent symptoms*, a long term follow-up is necessary to detect disease relapse* as quickly as possible to avoid organ damage.
- Blood and urine tests should be carried out every 2-3 months. Radiological exams* and bone marrow examination* should be done with individual evaluation.
- If the multiple myeloma comes back, the goal is to obtain a further response by choosing between different available therapies.
DEFINITION OF MULTIPLE MYELOMA

Multiple myeloma is a cancer of plasma cells*. These are a type of white blood cell which originate in the bone marrow. The function of plasma cells* is to produce antibodies*. Antibodies* occur naturally in our immune system and help protect us from infections caused by agents such as bacteria or viruses. When plasma cells* grow in an uncontrolled way it suppresses the growth of other bone marrow cells. This can lead to conditions such as anaemia*, bleeding disorders, infections and bone lesions*.

In most cases there is also an abnormal production of non-functional antibodies* called monoclonal protein*. In multiple myeloma a large amount of a single type of abnormal antibody* is produced which has no useful role in the body.

In most cases, treatments can induce long intervals without any symptoms* of the disease allowing patients to have a good quality of life. Therefore, multiple myeloma can be considered as a chronic condition.

Illustration of bone marrow where plasma cells* are made: normal plasma cells* and abnormal plasma cells* of multiple myeloma are shown.
Multiple myeloma is not as common as breast, colon, lung or prostate cancer but it is considered to be the second most common blood cancer after Non-Hodgkin lymphomas*. Its incidence* increases with age, thus it is considered a disease of the elderly. The probability that a person in Europe will develop multiple myeloma during his or her lifetime is 0.31%. This means for example, in Europe, 4 to 6 cases will be diagnosed among 100 000 people every year. The incidence* is lower for women. Median age at diagnosis is 72 years. Incidence rates are higher in people of Afro-American origin and lower in Asians.
WHAT CAUSES MULTIPLE MYELOMA?

Today the causes of multiple myeloma are not clear. Some risk factors* have been identified. A risk factor* increases the chance of cancer occurring, but is neither necessary nor sufficient to cause cancer. A risk factor* is not a cause in itself.

Some people with these risk factors* will never develop multiple myeloma and some people without any of these risk factors* may develop multiple myeloma.

The main risk factors* of multiple myeloma are:

- Monoclonal Gammapathy of Uncertain Significance (MGUS): most multiple myelomas arise from a benign* condition known as MGUS. People affected by this condition have a little abnormal production of monoclonal protein* without any symptoms*. The majority of people with this condition will never develop symptomatic* multiple myeloma. In most cases MGUS is discovered by accident during routine blood tests.

- Older age: the chance of developing multiple myeloma increases with age.

- Genetic predisposition: the incidence* of multiple myeloma is slightly different between ethnicities. In addition, female sex is a modest protective factor in multiple myeloma.

- Environmental factors: radiation exposure, benzene and insecticides have been associated with multiple myeloma. These associations have a minor role in the development of multiple myeloma.

Besides the presence of MGUS and age, the evidence for all the other risk factors* has not been proven.
HOW IS MULTIPLE MYELOMA DIAGNOSED?

Multiple myeloma often arises from MGUS. If MGUS is present, patients are monitored by a doctor. If MGUS progresses and develops into multiple myeloma prompt treatment can prevent the development of disease symptoms*.

**Symptoms* characterising multiple myeloma**

**Symptoms* caused by bone marrow infiltration:**
- Fatigue: this is the physical feeling of being tired even after rest. It is related to anaemia* (low level of haemoglobin*) and to the abnormal presence of multiple myeloma in the body.
- Bone pain and fractures: sometimes progressively intense bone pain is present which rarely responds to common painkillers. This pain is often felt in the spine, ribs or hip bones and could be a result of bone fractures.
- Infections: infections may occur more frequently and these infections may take longer to heal than in the past in the same person. This is related to both a decreased white cell count and the abnormal function of plasma cells*.
- Bleeding: rarely, abnormal bleeding may occur (for example, when brushing your teeth) or you may notice that bruising or haematomas* occur more easily. This is related to low platelet* count and to abnormalities in mechanisms responsible for stopping the bleeding because of monoclonal protein* in the blood.

**Symptoms* or signs related to excessive monoclonal protein* production:**
- Mild to severe kidney problems: this condition is caused by direct damage from monoclonal protein* filtered by the kidneys. Usually this condition does not cause symptoms* until the damage is severe.
- Amyloidosis*: this is caused by abnormal accumulation of monoclonal protein* in specific sites of the body (heart, kidney etc.). The abnormal stores of the protein can cause chronic inflammation and organ damage.
- Peripheral neuropathy: this is a result of nerve damage caused by monoclonal protein*. Sensory disturbances (tingling, altered heat perception in hands and feet etc.) are the most common symptoms*.

The **diagnosis of multiple myeloma** is based on the following examinations:

Detection of monoclonal protein* in the blood or 24-hour urine samples: this is obtained by a test called protein electrophoresis*. Other tests are then performed, such as immunofixation* (to identify the types of monoclonal protein* present), and tests to measure the levels of serum free light chain*.

The percentage of myeloma cells in the bone marrow is analysed using a bone marrow aspirate* and/or biopsy*. Both procedures are minimally invasive, and last for about 10-15 minutes. Local anaesthesia* is used before the procedure and a mild burning sensation should be expected. The samples obtained are necessary to quantify the percentage of plasma cells* present in the bone marrow and to perform genetic tests, such as Fluorescence In situ Hybridization (FISH)*. These tests are helpful as they provide additional information on the prognosis* of the disease which is important since it could influence the choice of treatment.
Evaluation of bone lesions*: a complete radiological skeletal bone scan is necessary to identify possible fractures or areas of disease infiltration. Magnetic resonance imaging (MRI)* of the spine and pelvis is more sensitive than X-ray* in detecting bone lesions*. This is helpful to identify lesions when they are not yet causing symptoms*. A whole body low dose CT scan* or a PET scan* may also be needed to evaluate bone lesions*.

Blood tests: complete blood cell count*, calcium, creatinine*, albumin* and beta-2-microglobulin* levels are all necessary to examine if the disease is symptomatic* and for prognostic* reasons.

These tests allow differentiation between three conditions:

**Monoclonal Gammopathy of Uncertain Significance (MGUS)**: a benign* condition which rarely develops into multiple myeloma and is characterised by serum monoclonal protein* <3g/dl; tumoural bone marrow plasma cells* <10%; normal calcium levels, normal kidney function*, normal haemoglobin* levels and no bone lesions*.

**Asymptomatic* (smoldering) multiple myeloma**: a pathologic condition which progresses to multiple myeloma at a rate of 10% per year over the first 5 years following diagnosis. It is characterised by serum monoclonal protein* >3g/dL or urinary monoclonal protein* >500mg/24 hour and/or tumoural bone marrow plasma cells* 10-60% without any multiple myeloma defining events (listed in the table below) or amyloidosis*.

**Multiple myeloma**: the symptomatic* condition which requires treatment. It has the same features of asymptomatic* (smoldering) multiple myeloma plus multiple myeloma defining events (listed in the table below).

<table>
<thead>
<tr>
<th>Multiple myeloma defining events</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypercalcemia*</td>
<td>Serum calcium &gt;1mg/dL higher than the upper limit of normal or &gt;11mg/dL</td>
</tr>
<tr>
<td>Kidney problems</td>
<td>Creatinine clearance* &lt;40mL per min or serum creatinine* &gt;2mg/dL</td>
</tr>
<tr>
<td>Anaemia*</td>
<td>Haemoglobin* value of &gt;2g/dL below the lower limit of normal or &lt;10g/dL</td>
</tr>
<tr>
<td>Bone lesions*</td>
<td>One or more bone lesions* on skeletal radiography, CT*, PET-CT* or MRI*</td>
</tr>
<tr>
<td>Bone marrow plasma cells* excess</td>
<td>Tumoural bone marrow plasma cell* percentage &gt;60%</td>
</tr>
<tr>
<td>Very high serum free light chain ratio*</td>
<td>Involved: uninvolved serum free light chain ratio* &gt;100</td>
</tr>
</tbody>
</table>

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WHAT IS IT IMPORTANT TO KNOW TO GET THE OPTIMAL TREATMENT?

To choose the best treatment, the doctor needs to consider many aspects, taking into account both the patient and the multiple myeloma.

Relevant information about the patient

- General health status: this has to be evaluated with specific scores related to your daily activities. There are other physical factors that also have to be evaluated before starting treatment:
  1. heart function (electrocardiogram* and echocardiography*)
  2. respiratory function (pulmonary function tests)
  3. liver and kidney function (blood tests)
- Personal medical history: knowing relevant past or current health issues, such as previous surgical procedures or chronic diseases (diabetes, atrial fibrillation, viral infections etc.), is necessary to choose the correct treatment.
- Age: even if age itself should not be considered as the only criterion to judge the general status of a patient, there are standard age limits which are used to decide if a patient could be eligible for a more intensive therapy. Usually, being younger than 65 years allows patients to receive intensive therapy, while being older than 70 years excludes them from this option. For people between 65 and 70, this decision depends upon their general health status.

Relevant information about the multiple myeloma

Treatment for multiple myeloma is not necessary when there are no symptoms*.

Disease staging* and cytogenetics* are not necessary for asymptomatic* (smoldering) multiple myeloma.

Staging*

Information about the stage of the disease is necessary when multiple myeloma is symptomatic* and treatment has to be started.

The information about stage is important to select the right treatment. The lower the stage, the better the prognosis*. The International Staging System (ISS) is a very helpful score used for this disease. It relies only on the serum levels of albumin* and beta-2-microglobulin*.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>Serum beta-2-microglobulin* &lt;3.5 mg/dl and serum albumin* &gt; 3.5 g/dl</td>
</tr>
<tr>
<td>Stage II</td>
<td>Not stage I or III</td>
</tr>
<tr>
<td>Stage III</td>
<td>Serum beta-2-microglobulin* &gt; 5.5 mg/l</td>
</tr>
</tbody>
</table>

Cytogenetics* gives additional important information regarding prognosis* as it is known that some genetic abnormalities are associated with a poorer outcome.
### How to measure response to therapy

Therapy efficacy is measured by reduction of monoclonal protein*, measured in blood serum or urine. Further tests, e.g. bone marrow evaluation*, may be done on an individual basis if your doctor thinks they are necessary or if you are undergoing treatment as part of a clinical trial.

<table>
<thead>
<tr>
<th>Type of response</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stringent complete</strong></td>
<td>Disappearance of monoclonal protein* in serum or urine (immunofixation* negative, normal free light chain ratio*, absence of tumour plasma cells* in the bone marrow)</td>
</tr>
<tr>
<td><strong>Complete response</strong></td>
<td>Disappearance of monoclonal protein* in serum and/or urine (immunofixation* negative, abnormal free light chain ratio*, &lt;5% plasma cells* in bone marrow)</td>
</tr>
<tr>
<td><strong>Very good partial</strong></td>
<td>90% or greater reduction in serum protein plus urine protein &lt;100mg per 24 h or serum and/or urine protein detectable by immunofixation* but not with electrophoresis*</td>
</tr>
<tr>
<td><strong>Partial response</strong></td>
<td>≥50% reduction of serum protein and reduction in 24 h urinary protein by ≥90% or to &lt;200mg per 24 h</td>
</tr>
<tr>
<td></td>
<td>In patients without measurable serum and urine monoclonal protein* levels, the difference between involved and uninvolved free light chain levels * can be used</td>
</tr>
<tr>
<td></td>
<td>In patients without measurable serum and urine monoclonal protein* levels and without measurable involved free light chain levels*, bone marrow plasma-cell* percentage can be used</td>
</tr>
<tr>
<td></td>
<td>Appearance of a new bone lesion(s)* or increase of existing lesion(s) if this is the only measure of disease</td>
</tr>
<tr>
<td><strong>Minimal response</strong></td>
<td>As for partial remission* but serum or urine protein reduction comprised between ≥25% but &lt;49%</td>
</tr>
<tr>
<td><strong>Stable disease</strong></td>
<td>Response criteria not fulfilling definition of complete response, very good partial response, partial response, minor response</td>
</tr>
<tr>
<td><strong>Progressive disease</strong></td>
<td>Any one or more of the following criteria: Increase of 25% from lowest confirmed response value in one or more of the following criteria: Serum monoclonal protein* or urine monoclonal protein*. In patients without measurable serum and urine monoclonal protein* levels, the difference between involved and uninvolved free light chain levels * can be used In patients without measurable serum and urine monoclonal protein* levels and without measurable involved free light chain levels*, bone marrow plasma-cell* percentage can be used Appearance of a new bone lesion(s)* or increase of existing lesion(s) if this is the only measure of disease Increase in circulating plasma cells* if this is the only measure of disease</td>
</tr>
</tbody>
</table>
WHAT ARE THE TREATMENT OPTIONS?

There are three questions to consider when selecting a treatment for multiple myeloma:
1) Is the disease localised in only one place without general involvement of the bones?
2) Is the disease symptomatic*?
3) Is autologous stem cell transplantation* an option?

Answering these questions will help to decide which treatment to choose and when it should be started.

1) **Is the disease localised in only one site without general involvement of the bones?**
   
In some rare cases, there is just one single localised site (for example, femoral bone lesion*) of the body affected by abnormal plasma cells*. In this scenario, which is called solitary plasmocytoma, a systemic treatment* is not required. The therapy of choice is radiotherapy* or surgical excision of the lesion. Thereafter, a strict follow-up is required since this condition often evolves into multiple myeloma.

2) **Is the disease symptomatic*? Are symptoms* present?**
   
If the disease is asymptomatic* (smoldering myeloma), a strict follow-up, usually without treatment, is required. Once there is evidence of multiple disease sites (diffuse bone marrow involvement or multiple bone lesions*), it is crucial to understand if there are signs and symptoms* of disease. A systemic treatment* has to be started if the disease is symptomatic*.
   
The treatment will usually include therapies that:
   - treat multiple myeloma systemically (treating myeloma cells throughout the body).
   - treat multiple myeloma locally (i.e. in specific sites of the body), such as surgery or radiotherapy* if symptomatic* bone lesions* are present (e.g. backbone fractures).

3) **Is autologous stem cell transplantation* an option?**
   
Autologous stem cell transplantation* (with the patient’s own stem cells) gives the best disease responses when incorporated in the first-line of therapy. Even if it is now less toxic than in the past, this is reserved only for younger patients and those patients in good physical condition who can tolerate the side-effects of the procedure. Being older than 70 usually excludes patients from undergoing stem cell transplantation. An exception might be made if an older patient is in good physical condition without other relevant health issues. This depends on an accurate clinical evaluation of each case.

Treatments listed below have their benefits, their risks and their contraindications. It is recommended that you ask your doctor about the expected benefits and risks of every treatment in order to be informed about the consequences of the treatment. In cases where several treatment options are available, the choice should be discussed according to the balance between benefits and risks.
First-line treatment plan for autologous stem cell transplantation* candidates

Patients in good physical condition (or those younger than 65) who are candidates for autologous stem cell transplantation* usually receive an induction treatment*. The aim of this is to reduce the disease burden* before the transplantation. Once the disease burden* is reduced, the goal is to maintain a response for as long as possible with an autologous transplant*.

Induction treatment* is usually composed of a three-drug regimen:
- Bortezomib* (V)/thalidomide* (T)/dexamethasone* (D) (VTD)
- Bortezomib* (V)/cyclophosphamide* (C)/dexamethasone* (D) (VCD)
- Bortezomib* (P)/doxorubicin* (A)/dexamethasone* (D) (PAD)
- Lenalidomide* (R)/bortezomib* (V)/dexamethasone* (D) (RVD - this combination is not approved yet in Europe).

One treatment cycle usually lasts 21 or 28 days. Response to treatment is assessed before each cycle. The total number of cycles required to complete the induction treatment* ranges from 4 to 6, depending on the type of response, therapy and your health status.

After the induction therapy*, a consolidation* phase is necessary to prolong the interval that patients remain free from disease. In multiple myeloma, consolidation* is obtained with autologous stem cell transplantation*. This process is preceded by the collection of autologous (of the patient) stem cells by a procedure called apheresis*. To stimulate the release of stem cells from the bone marrow to the bloodstream, the patient receives a growth factor* (granulocyte-colony stimulating factor, G-CSF) alone or in combination with chemotherapy* (cyclophosphamide*). After a few days, when the number of stem cells rises, the patient receives the apheresis* procedure. The number of stem cells can be determined by means of blood tests. Peripheral blood* is filtered and stem cells are collected and frozen. Once the collection has been done and the patient has recovered from the procedure, he or she can be admitted for the autologous transplantation*. This procedure consists of administering high dose chemotherapy* (usually with a drug called melphalan*) followed by reinfusion of the patients' own stem cells.

If the first transplant does not give a complete or almost complete response, a second autologous transplantation* can be performed usually within 3-6 months after the first.

Allogeneic stem cell transplantation* (from a donor) should only be carried out in the context of a clinical trial.

First-line treatment plan for NON transplant candidates

Patients who are not candidates for autologous stem cell transplantation* (70 years and older or patients in poor physical condition) are usually treated with a three-drug induction regimen. Frailer patients can be treated with a two-drug regimen.

Three drug regimens:
- Bortezomib* (V)/melphalan* (M)/prednisone* (P) (VMP)
- Melphalan* (M)/prednisone* (P)/thalidomide* (T) (MPT)
Two drug regimen:
- Lenalidomide*(R)/dexamethasone* (D) (RD)
- Bendamustine*/prednisone*
- Melphalan*/prednisone*

**Second-line treatment plan for relapsed** or **refractory** disease
Participation in clinical trials should be encouraged to allow patients to benefit from new drugs or combinations of drugs which are currently being tested.

Considerations that should be taken into account when choosing first-line treatment still apply to second-line or subsequent therapies. Choice depends on several factors regarding the patient (age, health status) and previous treatments (type, efficacy, tolerance).

The following therapies can be used in this setting:
- Lenalidomide*/dexamethasone*
- Pomalidomide*/dexamethasone*: only for patients who have already failed on lenalidomide* and bortezomib*
- Bortezomib* alone or in combination with dexamethasone* or pegilated doxorubicin*
- Carfilzomib*/lenalidomide*/dexamethasone* or carfilzomib*/dexamethasone*
- Ixazomib*/lenalidomide*/dexamethasone*: only for patients who have already failed one of previous therapies
- Panobinostat*/bortezomib*/dexamethasone*: only for patients who have already failed on bortezomib* and an immunomodulatory drug* (thalidomide*, lenalidomide*, pomalidomide*)
- Elotuzumab*/lenalidomide*/dexamethasone*
- Daratumumab* alone for patients who have already failed on proteasome inhibitors (bortezomib*, carfilzomib*, ixazomib*) and immunomodulatory agents* (thalidomide*, lenalidomide*, pomalidomide*), and in combination with lenalidomide* and dexamethasone*, or bortezomib* and dexamethasone*, for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.

Autologous stem cell transplantation* could also be used in selected cases (in those with good response to previous autologous transplant* and with disease response of longer than 2 years).

Allogeneic stem cell transplantation* (from a donor) should be carried out only in the context of a clinical trial.

**Treatment of multiple myeloma complications**
It is very important for the treatment of multiple myeloma to cure its organ-related complications. Timing is fundamental to prevent chronic organ damage or life-threatening events.

**Impaired kidney function:** almost fifty percent of patients affected by multiple myeloma have impaired kidney function. Treatment may vary depending on the grade of kidney impairment. Along with systemic therapy*, oral and intravenous hydration* or even dialysis* could be part of the treatment. It is fundamental to avoid the use of non-steroidal anti-inflammatory drugs, such as aspirin or nimesulide, as they may cause kidney damage.
**Bone pain or bone lesions**: bone damage is frequent in multiple myeloma. It can be asymptomatic* or it may cause pain. In some cases, bone fractures can be the initial manifestation of multiple myeloma and in this case an orthopaedic intervention is necessary. Besides surgical intervention, radiotherapy* can also be useful.

If bone lesions* are not present but there are early signs of bone erosion, a therapy with bone strengthening drugs is suggested. Bisphosphonates* are the main drugs used for this purpose. Zoledronate* or pamidronate* are given by intravenous infusion. This treatment should be done for two years and infections of the jaw should be excluded before starting these drugs.

**Increased blood calcium level**: this is due to bone erosion. The extent of the increase can vary. Intravenous fluids and bisphosphonates* are required in case of very high calcium levels.

**Anaemia**: this is related to low red blood cell count. There are several causes of anaemia* in multiple myeloma. Bone marrow infiltration by abnormal plasma cells* and/or kidney damage are the most frequent causes. Blood transfusions can be necessary in very severe cases. Administration of erythropoietin*, a drug which stimulates red blood cell production, may decrease the need for transfusions.

**Infections**: both chemotherapy* and multiple myeloma can weaken the immune system. For this reason, your doctor may give you some anti-infective drugs to prevent infection. In case of fever or other signs of infection, do not hesitate to contact your doctor as it could be important to start the correct treatment. The influenza vaccine is helpful in decreasing the rate of respiratory infection.

**Spinal cord compression**: the cause of this complication is the presence of a localised mass (plasmocytoma) at backbone level which compresses the spine. This can also be caused by backbone fractures. Symptoms* are localised pain or nervous symptoms* such as tingling in the legs or muscular weakness. You should seek medical attention immediately if you experience these symptoms* as this complication can lead to irreversible paralysis if not treated. Corticosteroids*, radiotherapy* or even surgery are therapies available to treat this condition.
WHAT ARE THE POSSIBLE SIDE EFFECTS OF THE TREATMENTS?

Side effects vary according to treatment type. A few of the most common side effects caused by multiple myeloma therapies are as follows:

- **Appetite loss**: some treatments may cause appetite loss which can last for a few days after the treatment ends or sometimes longer. Try to eat smaller meals more often than usual, since they are easier to digest. Avoid fatty foods and drink plenty of liquids (approximately 1.5-2 L/day).

- **Constipation**: some drugs, such as thalidomide*, bortezomib* or dexamethasone*, can cause constipation. This is a very common symptom* and your doctor can prescribe special medication (laxatives) in case this occurs. It is very important to prevent constipation. If constipation is present, drink plenty of liquids (2 litres/day of water/soda/tea etc.) and include exercise in your daily routine.

- **Diarrhoea**: this symptom* can be related to certain drugs, such as lenalidomide*, or bortezomib*, or to an unrelated infection. There are several remedies that can be used depending on the cause of the diarrhoea. It is important to notify your doctor if this occurs.

- **Hair loss**: older chemotherapy* drugs can cause hair thinning or loss. Depending on the therapy, it may last until therapy is completed. Once the treatment is finished, your hair will grow back.

- **Infertility**: Alkylating agents*, such as melphalan* (used for autologous transplantation*) and cyclophosphamide* (used for stem cell collection), are more likely to cause this side effect. If you are taking thalidomide* or lenalidomide*, teratogenic* effects may occur. If you are planning to have children or this could be an option in your future, remember to ask your doctor about this issue. Today there are some ways to reduce the chance of becoming infertile and to collect sperm or eggs before starting treatment.

- **Infections**: virtually all chemotherapy* agents can increase the incidence of infections. This happens because of a reduced number or altered function of white blood cells. These cells defend our body from bacterial, viral or fungal infections. Bacterial infections and viral reactivations are the most common infectious complications during a treatment and in the following months after it is completed. Some drugs are usually prescribed during this phase to reduce the incidence* of this complication. Neutropenia* is a reduction of neutrophils, the fraction of white blood cells whose function is to protect us from bacterial and fungal infections. If you have a fever or any other symptom* while you are neutropenic (with a low number of neutrophils), it is important to contact a doctor as soon as possible since it is possible to develop a severe infection requiring hospitalization. There are a few tips to follow to reduce the chances of becoming ill:
  1. **Avoid crowded places**: the higher the number of people, the more likely the chances of becoming ill. This is especially true during the flu season (autumn/winter).
  2. **Eat healthily**: this means avoiding foods that may carry infections. Follow standard hygiene rules and do not eat raw meat or fish/seafood or unpasteurised dairy products.
3) Stay active: doing light physical activities, such as walking, can help you recover from chemotherapy*-related fatigue and it will keep your heart, lungs and muscles in good shape. This reduces the risk of infection and helps your body to cope with stressful conditions.

- **Nausea and vomiting**: this side effect is usually related to traditional chemotherapy* agents. Antiemetic agents* are commonly used to prevent this side effect. Sometimes, if prevention is not enough, other drugs can be prescribed to treat nausea and vomiting.

- **Peripheral neuropathy**: this is commonly related to bortezomib* and thalidomide*. Damage to peripheral nerves can cause both sensory deficit (palms and soles tingling) and pain. This damage usually arises gradually, starting with feet and hands. It is important to tell your doctor if you have any of these symptoms*. Adjusting drug dosage and how the drug is administered (subcutaneous instead of intravenous bortezomib*) is usually sufficient to reduce or stop these symptoms*. There are a few drugs available to reduce peripheral neuropathy*.

- **Thrombosis**: the risk of developing a blood clot is higher when thalidomide* or lenalidomide* are combined with dexamethasone*. Swelling, pain and occurrence of a red warm area are signs and symptoms* of thrombosis*. If you notice this in your arms or legs, contact your doctor immediately. To reduce the chance of thrombosis, a prophylaxis* with anti-coagulant drugs (heparin or low-dose aspirin) is usually prescribed and may be recommended when the above combinations are used.
**WHAT HAPPENS AFTER THE TREATMENT?**

**Follow-up with doctors**
In patients with multiple myeloma, a long term follow-up is necessary to detect disease relapse* before it becomes symptomatic*. Blood tests, e.g. complete blood cell count*, measurements of creatinine* and calcium levels, serum and urine electrophoresis* and/or serum-free light chain ratio* determination, should be carried out every 2-3 months. Radiological exams* and bone marrow examination* may be done on an individual basis.

**Back to daily activities**
The diagnosis of multiple myeloma may cause changes in your daily life and also in the daily activities of those close to you. Patient support groups may help you to cope with these changes. It can be hard to live with the idea that multiple myeloma can come back. Based on what is currently known, there are no specific recommendations to decrease the risk of recurrence* after completion of treatment. As a consequence of the treatment and the multiple myeloma itself, return to normal life may not be easy for some people. Questions related to body-image, sexuality, fatigue, work, emotions or lifestyle may be a concern for you. Discussing these questions with relatives, friends, other patients or doctors may be helpful. Patient support groups may also be able to help by providing advice on dealing with the effects of treatments. Psycho-oncologists or telephone information services and helplines are available in many countries to provide additional support.

**What if the multiple myeloma comes back?**
If the multiple myeloma comes back this is called a relapse* or recurrence*. Treatment in this case depends on the age and health status of the patient and prior treatments.

There are currently several effective therapies available for relapsed* multiple myeloma and it is of utmost importance to find the most appropriate one in terms of efficacy and toxicity. More drugs are expected to arrive into clinical practice in the next few years.

Generally, the goal of a second-line therapy for multiple myeloma is to obtain a second response, the longer the better, in order to offer the patient another period of time without disease symptoms*. This could be compared to the concept of a chronic disease, such as diabetes or hypertension, where the aim of treatment is not to cure the disease itself but its symptoms*. In both cases, the aim is to allow the patient to live a normal life for as long as possible.
Should I consider clinical trials?

Despite the best therapies that are currently available, the majority of patients will have disease relapse* after first-line treatment. During the last few years, an increasing number of new drugs have been developed and tested world-wide. Drugs proven to be effective in laboratory experiments are eligible to be tested in humans, in what is known as clinical trials. Not all clinical trials will result in better treatment and may show that the treatment being tested isn’t as good as those already in use. However, participating in clinical trials is important as it gives patients access to drugs which would not otherwise be available for a number of years. It is important to talk with your doctor about the possibility of participating in such a clinical trial. You can also find information about clinical trials on Internet (clinicaltrials.gov, or clinicaltrialsregister.eu).
DEFINITIONS OF DIFFICULT WORDS

**Albumin**
A type of protein found in blood, egg white, milk, and other substances.

**Alkylating agent**
A type of drug that is used in the treatment of cancer. It interferes with DNA and inhibits cell growth.

**Allogeneic transplant (transplantation)**
A procedure in which a person receives stem cells (cells from which all blood cells develop) from a genetically similar, but not identical, donor.

**Amyloidosis**
A group of diseases in which protein builds up in certain organs (localised amyloidosis) or throughout the body (systemic amyloidosis). Amyloidosis may be either primary (with no known cause), secondary (caused by another disease, including some types of cancer, such as multiple myeloma), or hereditary (passed down from parents to children). Many organs are affected by amyloidosis. The organs affected may depend on the form (primary, secondary, or hereditary) of the amyloidosis.

**Anaemia**
A condition characterised by the shortage of red blood cells or haemoglobin. Haemoglobin is the part of the red blood cell that carries oxygen from the lungs to the whole body and in patients with anaemia this process is diminished.

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

**Antibody/antibodies**
A protein made by plasma cells* (a type of white blood cell) in response to an antigen (a substance that causes the body to make a specific immune response). Each antibody can bind to only one specific antigen. The purpose of this binding is to help destroy the antigen. Some antibodies destroy antigens directly. Others make it easier for white blood cells to destroy the antigen. An antibody is a type of immunoglobulin*.

**Antiemetic agent**
A drug that prevents or reduces nausea and vomiting.

**Apheresis**
A procedure in which blood is collected, part of the blood such as platelets* or white blood cells is taken out, and the rest of the blood is returned to the donor. Also called pheresis.

**Asymptomatic**
In a disease, this is the absence of symptoms*, such as pain, or subjective manifestations of the illness.
Autologous transplant (transplantation)
Autologous stem cell transplantation is a procedure in which stem cells (cells from which all blood cells develop) are removed, stored, and later given back to the same person. Autologous bone marrow transplantation is a procedure in which bone marrow is removed from a person, stored, and then given back to the person after intensive treatment.

Bendamustine
The active ingredient in a drug that is used to treat multiple myeloma and other haematological malignancies. Bendamustine may damage the DNA in cancer cells and cause them to die. It is a type of alkylating agent* and a type of antimetabolite.

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

Beta-2-microglobulin
A small protein normally found on the surface of many cells, including lymphocytes, and in small amounts in the blood and urine. An increased amount in the blood or urine may be a sign of certain diseases, including some types of cancer such as multiple myeloma or lymphoma.

Bisphosphonates
Drugs or substances used to treat hypercalcemia* and bone pain caused by some types of cancer. Forms of bisphosphonates are also used to treat osteoporosis and for bone imaging. Bisphosphonates inhibit a type of bone cell that breaks down bone. Also called diphosphonate.

Bone lesion(s)
A bone lesion is an abnormality in the growth or structure of a bone. Bone lesion(s) may be cancerous or non-cancerous. Bone lesions result in destruction of the bones in patients with multiple myeloma and primarily affect the spine, pelvis or rib cage. In patients with multiple myeloma, bone lesions weaken the bone, causing pain and increasing the risk of fractures.

Bone marrow aspirate
Bone marrow aspiration removes a small amount of bone marrow fluid and cells through a needle put into a bone. The bone marrow fluid and cells are then examined for problems with any of the blood cells made in the bone marrow.

Bone marrow biopsy
A procedure in which a small sample of bone with bone marrow inside it is removed, usually from the hip bone. A small area of skin and the surface of the bone underneath are numbed with an anaesthetic. Then a special, wide needle is pushed into the bone and rotated to remove a sample of bone with the bone marrow inside it. This procedure may be done at the same time as a bone marrow aspiration. The removed cells or tissues will be examined by a pathologist. The pathologist may study the tissue under a microscope or perform other tests on the cells or tissue. The pathologist will determine if the bone marrow is affected by or is free of myeloma.
Bone marrow aspiration and biopsy. After a small area of skin is numbed, a Jamshidi needle (a long, hollow needle) is inserted into the patient’s hip bone. Samples of blood, bone, and bone marrow are removed for examination under a microscope.

**Bone marrow examination/evaluation**
Bone marrow examination refers to the pathologic analysis (evaluation of cells and tissues made by a pathologist using microscope) of samples of bone marrow obtained by bone marrow aspiration and bone marrow biopsy.

**Bortezomib**
A drug used to treat multiple myeloma. It is also used to treat mantle cell lymphoma in patients who have already received at least one other type of treatment and is being studied in the treatment of other types of cancer. Bortezomib blocks several molecular pathways in cells and may cause cancer cells to die. It is a type of proteasome inhibitor - it blocks the action of enzymes called proteasomes, which may help keep cancer cells from growing and may kill them.

**Carfilzomib**
A drug used alone or with other drugs to treat multiple myeloma that has gotten worse or come back after treatment with other anticancer therapy. It is also being studied in the treatment of other types of cancer. Carfilzomib is a type of proteasome inhibitor – it blocks the action of enzymes called proteasomes, which may help keep cancer cells from growing and may kill them.

**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.
Comorbidity
The condition of having two or more diseases at the same time.

Complete blood cell count
A complete blood cell count is a blood panel requested by a doctor or other medical professional that gives information about the cells in a patient's blood, such as the cell count for each cell type and the concentrations of various proteins and minerals. The cells that circulate in the bloodstream are generally divided into three types: white blood cells (leukocytes), red blood cells (erythrocytes), and platelets* (thrombocytes). Abnormally high or low counts may indicate the presence of many forms of disease, and hence blood counts are among the most commonly performed blood tests in medicine as they can provide an overview of a patient's general health status.

Computed tomography (CT) scan
A form of radiography in which body organs are scanned with X-rays* and the results are put together by a computer to generate detailed images of parts of the body. A dye may be injected into a vein or swallowed to help the tissues and organs show up more clearly. It may be used to help diagnose disease, plan treatment, or find out how well treatment is working.

Consolidation (treatment)
Treatment that is given after cancer has disappeared following the initial therapy. Consolidation therapy is used to kill any cancer cells that may be left in the body. It may include radiation therapy, a stem cell transplant, or treatment with drugs that kill cancer cells.

Corticosteroids
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 leukaemias.

Creatinine
A compound that is excreted from the body in urine. Creatinine levels are measured to monitor kidney function.

Creatinine clearance
The creatinine clearance test helps provide information about how well the kidneys are working. The test compares the creatinine* level in urine with the creatinine* level in blood.

Cyclophosphamide
A drug that is used to treat many types of cancer and is being studied in the treatment of other types of cancer. Cyclophosphamide attaches to DNA in cells and may kill cancer cells. It is a type of alkylating agent*.
Cytogenetics
The study of chromosomes, which are long strands of DNA and protein that contain most of the genetic information in a cell. Cytogenetics involves testing samples of tissue, blood, or bone marrow in a laboratory to look for changes in chromosomes, including broken, missing, or extra chromosomes. Changes in certain chromosomes may be a sign of a genetic disease or condition or some types of cancer. Cytogenetics may be used to help diagnose a disease or condition, plan treatment, or find out how well treatment is working.

Daratumumab
A drug used to treat multiple myeloma. Daratumumab binds to a protein called CD38, which is found on some types of immune cells and cancer cells, including myeloma cells. Daratumumab may block CD38 and help the immune system kill cancer cells. It is a type of monoclonal antibody.

Dexamethasone
A synthetic steroid (similar to steroid hormones produced naturally in the adrenal gland). Dexamethasone is also used to treat leukaemia and lymphoma and may be used to treat some of the problems caused by other cancers and their treatment.

Dialysis
The procedure is used to filter the blood when the kidneys are not working properly and are unable to complete this task.

Disease burden
The total effect of a disease on an individual or on a society. In the context of this guide, disease burden refers to the extent of myeloma spread.

Doxorubicin
A drug that is used to treat many types of cancer and is being studied in the treatment of other types of cancer. Doxorubicin comes from the bacterium *Streptomyces peucetius*. It damages DNA and may kill cancer cells. It is a type of anthracycline antitumour antibiotic.

Echocardiography
A procedure that uses high-energy sound waves (ultrasound) to look at tissues and organs inside the chest. Echoes from the sound waves form a picture of the size, shape, and position of the heart on a computer screen (echocardiogram). The pictures can also show the parts of the inside of the heart, such as the valves, and the motion of the heart while it is beating. Echocardiography may be used to help diagnose heart problems and damage to the heart muscle. It may also be used to check for an infection on or around the heart valves, blood clots or tumours inside the heart, and fluid buildup in the sac around the heart.

Electrocardiogram
A line graph that shows changes in the electrical activity of the heart over time. It is made by an instrument called an electrocardiograph. The graph can show if there are abnormal conditions, such as blocked arteries, changes in electrolytes (particles with electrical charges), and changes in the way electrical currents pass through the heart tissue. Also called ECG and EKG.
Electrophoresis
A laboratory technique that uses an electric current to separate substances, such as proteins or nucleic acids. The size and electrical charge (either positive or negative) of a substance determines how far it moves with the current. Electrophoresis may be used to help diagnosis certain diseases. There are many different types of electrophoresis.

Elotuzumab
A drug used to treat multiple myeloma. It is used in patients whose cancer has been treated with one to three previous anticancer therapies. Elotuzumab binds to a protein called CS1, which is found on myeloma cells and some types of immune cells. Elotuzumab may block CS1 and help the immune system kill cancer cells. It is a type of monoclonal antibody.

Erythropoietin
A substance that is naturally produced by the kidneys and that stimulates the bone marrow to make red blood cells. When erythropoietin is made in the laboratory, it is called epoetin alfa or epoetin beta.

Fluorescence In situ Hybridization (FISH) test
A cytogenetic* technique that uses fluorescent probes to detect and localize the presence or absence of specific DNA sequences on chromosomes. Fluorescence microscopy can be used to find out where the fluorescent probe is bound to the chromosomes. It can help define the patterns of gene expression within cells and tissues.

Growth factor
A substance made by the body that regulates cell division and cell survival. Some growth factors are also produced in the laboratory and used in biological therapy.

Haemoglobin
A protein inside red blood cells that carries oxygen from the lungs to tissues and organs in the body and carries carbon dioxide back to the lungs. Testing for the amount of haemoglobin in the blood is usually part of a complete blood cell test. It is used to check for conditions such as anaemia, dehydration, and malnutrition.

Haematoma(s)
A pool of clotted or partially clotted blood in an organ, tissue, or body space, usually caused by a broken blood vessel.

High risk disease
In medicine, risk groups are used to describe people who are alike in important ways. For example, patients with the same type of cancer may be divided into different risk groups that depend on certain aspects of their disease. These risk groups may be based on the patients’ chance of being cured (good versus poor) or the chance that their disease will come back (high versus low). Treatment may be based on which risk group a patient falls into.
Hydration
A process of giving fluids needed by the body.

Hypercalcemia
Higher than normal levels of calcium in the blood. Some types of cancer increase the risk of hypercalcemia.

Immune system
A complex network of cells, tissues, organs, and the substances they make that helps the body fight infections and other diseases. The immune system includes white blood cells and organs and tissues of the lymph system, such as the thymus, spleen, tonsils, lymph nodes, lymph vessels, and bone marrow.

Immunofixation
Immunofixation is a technique that allows the detection and typing of monoclonal antibodies or immunoglobulins in serum or urine. A typical antibody is composed of two immunoglobulin* heavy chains and two immunoglobulin* light chains. Immunofixation is important for the diagnosis and monitoring of certain blood related diseases such as multiple myeloma.

Immunoglobulin
A protein that is made by B cells and plasma cells (types of white blood cells) and helps the body fight infection. Some immunoglobulins may be found in higher than normal amounts in patients with certain conditions or certain types of cancer, including multiple myeloma and Waldenstrom macroglobulinemia. Measuring the amount of specific immunoglobulins in the blood and urine may help diagnose cancer or find out how well treatment is working or if cancer has come back. Some immunoglobulins may be used as tumour markers. Also called Ig.

Immunomodulatory drug (agent)
A therapeutic agent that suppress the immune system.

Incidence
The number of new cases of a disease diagnosed each year.

Induction treatment
The first treatment given for a disease. It is often part of a standard set of treatments, such as surgery followed by chemotherapy and radiation. When used by itself, induction therapy is the one accepted as the best treatment. If it doesn’t cure the disease or it causes severe side effects, other treatments may be used as a substitute or in addition to the one used as induction therapy.

Ixazomib
A drug used to treat multiple myeloma. It is used in patients who have received at least one other anticancer treatment. It is also being studied in the treatment of other types of cancer. Ixazomib blocks enzymes called proteasomes, which may help keep cancer cells from growing and may kill them. It is a type of proteasome inhibitor.
Kidney function
A term used to describe how well the kidneys work. The kidneys remove waste and extra water from the blood (as urine) and help keep chemicals (such as sodium, potassium, and calcium) balanced in the body. They also make hormones that help control blood pressure and stimulate bone marrow to make red blood cells. Also called renal function.

Lenalidomide
A drug that is similar to thalidomide*, and is used to treat multiple myeloma and certain types of anaemia. It is also used to treat mantle cell lymphoma that has come back or has not gotten better after other treatment. It is being studied in the treatment of other conditions and types of cancer. Lenalidomide may help the immune system kill abnormal blood cells or cancer cells. It may also prevent the growth of new blood vessels that tumours need to grow. It is a type of antiangiogenesis agent and a type of immunomodulating agent*.

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

Melphalan
A drug used to treat multiple myeloma. It is also being studied in the treatment of other types of cancer. Melphalan may kill cancer cells by damaging their DNA and stopping them from dividing. It is a type of alkylating agent*.

Monoclonal Gammopathy of Uncertain Significance (MGUS)
Most multiple myelomas arise from a benign* condition known as Monoclonal Gammopathy of Uncertain Significance (MGUS). People affected by this condition have a little abnormal production of monoclonal protein* without any symptoms*. The majority of people with this condition will never develop symptomatic* multiple myeloma. In most cases MGUS is discovered by accident during routine blood tests.

Monoclonal protein
An antibody found in unusually large amounts in the blood or urine of people with multiple myeloma and other types of plasma cell* tumours. Also called M protein.

(Peripheral) neuropathy
A nerve problem that causes pain, numbness, tingling, swelling, or muscle weakness in different parts of the body. It usually begins in the hands or feet and gets worse over time. Peripheral neuropathy may be caused by cancer or cancer treatment, such as chemotherapy. It may also be caused by physical injury, infection, toxic substances, or conditions such as diabetes, kidney failure, or malnutrition. Also called neuropathy.

Neutropenia
A condition in which there is a lower-than-normal number of neutrophils (a type of white blood cell).
Non-Hodgkin lymphoma(s)
Any of a large group of cancers of lymphocytes (white blood cells). Non-Hodgkin lymphomas can occur at any age and are often marked by enlarged lymph nodes, fever, and weight loss. There are many different types of non-Hodgkin lymphoma. These can be divided into aggressive (fast-growing) and indolent (slow-growing) types formed from either B-cells or T-cells. B-cell non-Hodgkin lymphomas include Burkitt lymphoma, chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL), diffuse large B-cell lymphoma, follicular lymphoma, immunoblastic large cell lymphoma, precursor B-lymphoblastic lymphoma, and mantle cell lymphoma. T-cell non-Hodgkin lymphomas include mycosis fungoides, anaplastic large cell lymphoma, and precursor T-lymphoblastic lymphoma. Lymphomas that occur after a bone marrow or stem cell transplantation are usually B-cell non-Hodgkin lymphomas. Prognosis* and treatment depend on the stage and type of disease.

Pamidronate
A drug used to treat hypercalcemia (high levels of calcium in the blood) caused by certain types of cancer. It is also used with other anticancer drugs to treat multiple myeloma and breast cancer that has spread to the bone and is used to treat Paget’s disease of bone. Pamidronate may help keep bone from breaking down and prevent the loss of calcium from the bones. It is a type of bisphosphonate.

Panobinostat
A drug used with bortezomib and dexamethasone to treat multiple myeloma. It is used in patients who have already been treated with bortezomib and an immunomodulating agent*. It is also being studied in the treatment of other types of cancer. Panobinostat blocks certain enzymes needed for cells to grow and divide and may kill cancer cells. It may also prevent the growth of new blood vessels that tumours need to grow. It is a type of histone deacetylase inhibitor and a type of antiangiogenesis agent.

Peripheral blood
Blood circulating throughout the body.

Peripheral neuropathy
A nerve problem that causes pain, numbness, tingling, swelling, or muscle weakness in different parts of the body. It usually begins in the hands or feet and gets worse over time. Peripheral neuropathy may be caused by cancer or cancer treatment, such as chemotherapy. It may also be caused by physical injury, infection, toxic substances, or conditions such as diabetes, kidney failure, or malnutrition. Also called neuropathy.

Plasma cells
Plasma cells, also called plasma B cells, plasmocytes, plasmacytes, are white blood cells that secrete large volumes of antibodies. They are transported by the blood plasma and the lymphatic system. Once released into the blood and lymph, these antibody molecules bind to the target antigen (foreign substance) and initiate its neutralization or destruction. Plasma cells originate in the bone marrow from B cells.
Platelet
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.

Pomalidomide
A drug that is a form of thalidomide*, and is used to treat multiple myeloma that has not gotten better with other anticancer drugs. It is also being studied in the treatment of other types of cancer. Pomalidomide may help the immune system kill cancer cells. It may also prevent the growth of new blood vessels that tumours need to grow. It is a type of immunomodulating agent* and a type of antiangiogenesis agent.

Positron emission tomography (PET) scan
A procedure in which a small amount of radioactive glucose (sugar) is injected into a vein, and a scanner is used to make detailed, computerized pictures of areas inside the body where the glucose is taken up. Because cancer cells often take up more glucose than normal cells, the pictures can be used to find cancer cells in the body.

Positron emission tomography-computed tomography (PET-CT) scan
A procedure that combines the pictures from a positron emission tomography (PET) scan and a computed tomography (CT) scan. The PET and CT scans are done at the same time with the same machine. The combined scans give more detailed pictures of areas inside the body than either scan gives by itself. A PET-CT scan may be used to help diagnose diseases (such as cancer), plan treatment, or find out how well treatment is working.

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.

Prophylaxis
An attempt to prevent disease.

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

Prognostic
A situation or condition, or a characteristic of a patient, that can be used to estimate the chance of recovery from a disease or the chance of the disease recurring (coming back).

Radiological exam(s)
A test that uses imaging technology (such as radiography, ultrasound*, computed tomography* and nuclear medicine) to visualize organs, structures and tissues within the body to both diagnose and treat diseases.
Radiotherapy
A therapy in which radiation is used in the treatment of cancer. It is always oriented to the specific location of the cancer.

Recurrence
Cancer that has recurred (come back), usually after a period of time during which the cancer could not be detected. The cancer may come back to the same place as the original (primary) tumour or to another place in the body. Also called recurrent cancer.

Refractory disease
Cancer that does not respond to treatment. The cancer may be resistant at the beginning of treatment or it may become resistant during treatment. Also called resistant disease or resistant cancer.

Relapse (relapsed disease)
Return of the manifestations of a disease after a period of improvement. In cancer, return of the cancer after a remission*.

Remission
A decrease in or disappearance of signs and symptoms of cancer. In partial remission, some, but not all, signs and symptoms of cancer have disappeared. In complete remission, all signs and symptoms of cancer have disappeared, although cancer may still be present in the body.

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.

Serum free light chain level
Immunoglobulin* light chains that are circulating in serum in a free (unbound) state are called free light chains. Using a blood test to measure the serum level of free light chains can help to diagnose and monitor multiple myeloma and related disorders. There are two types of immunoglobulin* light chain produced in humans, designated by the Greek letters kappa (κ) and lambda (λ).

Serum free light chain ratio
Comparing the ratio of kappa (κ) free light chains to lambda (λ) free light chains in the blood against reference ranges indicates whether that person may have a plasma cell tumour such as multiple myeloma or AL amyloidosis*.

Staging
Performing exams and tests to learn the extent of the cancer within the body, especially whether the disease has spread from the original site to other parts of the body. It is important to know the stage of the disease in order to plan the best treatment.
Symptom
A physical or mental problem that a person experiences that may indicate a disease or condition. Symptoms cannot be seen and do not show up on medical tests. Some examples of symptoms are headache, fatigue, nausea, and pain.

Symptomatic
Having to do with symptoms, which are signs of a condition or disease.

Systemic treatment (therapy)
Treatment using substances that travel through the bloodstream, reaching and affecting cells all over the body.

Teratogenic
A teratogen is a substance or process that causes birth defects. Teratogens include certain drugs (such as thalidomide), infections and ionizing radiation.

Thalidomide
A drug used to treat multiple myeloma. It is being studied in the treatment of other types of cancer. Thalidomide may help the immune system to kill cancer cells. It may also prevent the growth of new blood vessels that tumours need to grow. It is a type of antiangiogenesis agent and a type of immunomodulating agent*.

Thrombosis
The formation or presence of a thrombus (blood clot) inside a blood vessel.

Ultrasound
A procedure that uses high-energy sound waves to look at tissues and organs inside the body. The sound waves make echoes that form pictures of the tissues and organs on a computer screen (sonogram). Ultrasound may be used to help diagnose diseases, such as cancer. It may also be used during medical procedures, such as biopsies. Also called ultrasonography.

X-ray
A type of radiation used in the diagnosis and treatment of cancer and other diseases. In low doses, X-rays are used to diagnose diseases by making pictures of the inside of the body. In high doses, X-rays are used to treat cancer.

Zoledronate
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. It belongs to a class of drug 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 Patient Advocates Working Group.

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