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Multiple Myeloma – Patient's Booklet

National University
Cancer Institute, Singapore

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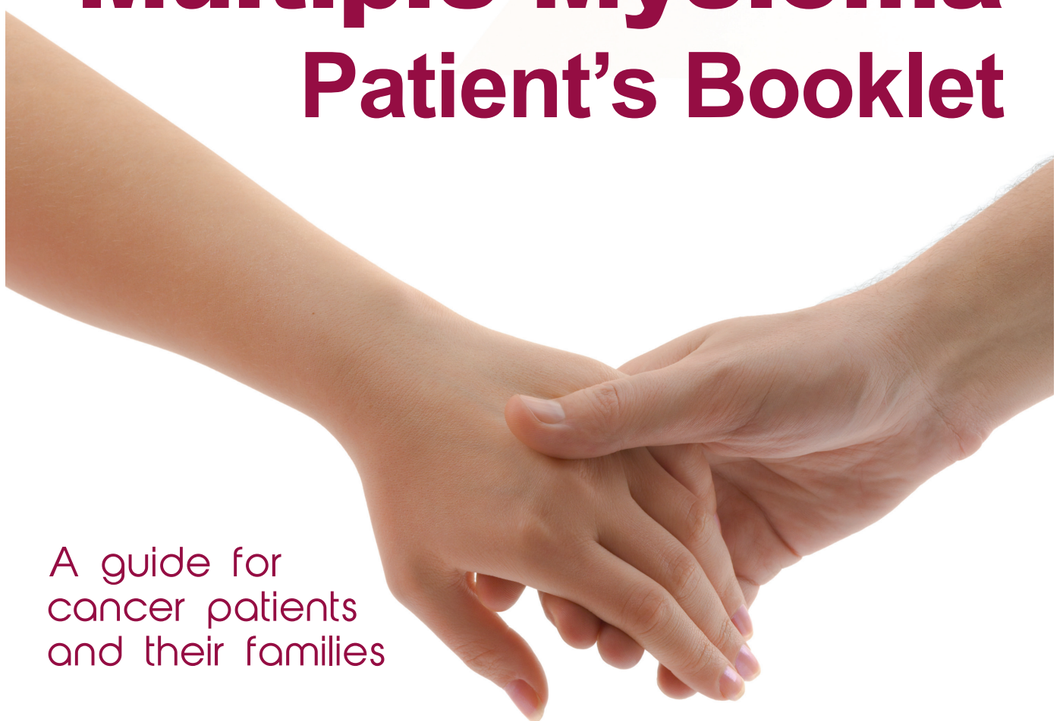
Multiple Myeloma
Patient's Booklet



A guide for
cancer patients
and their families

A member of the NUHS

Made possible by educational grant from

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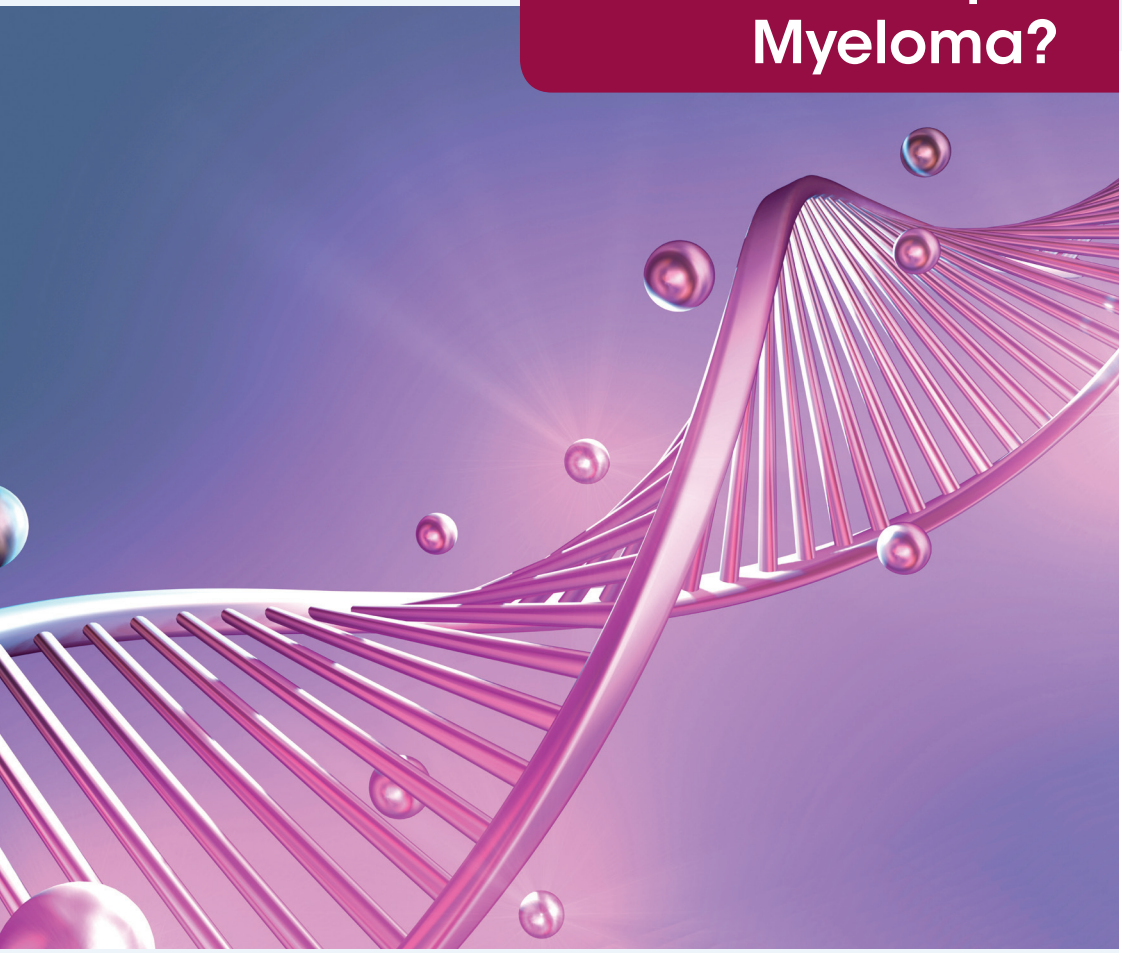
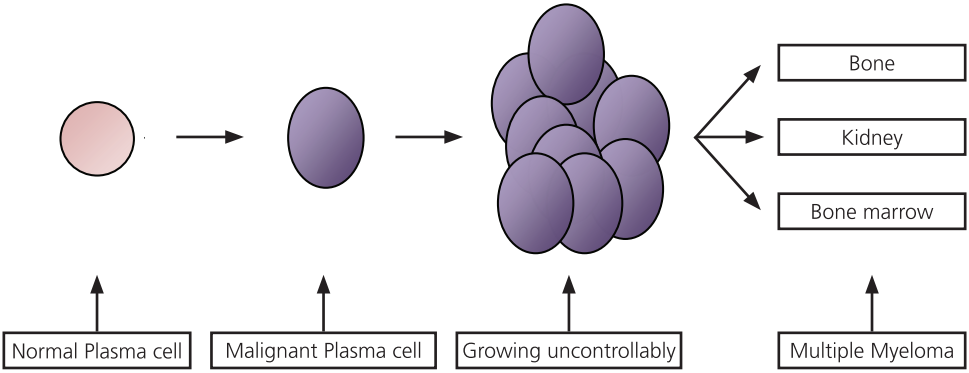
What is Multiple Myeloma?



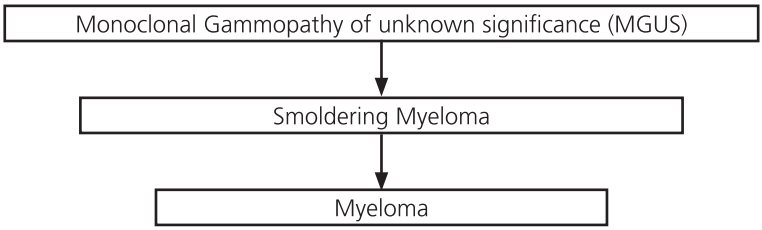
1. What is Multiple Myeloma?

Multiple Myeloma is a form of cancer that accounts for approximately one percent of all cancers. It is a disease that originates from plasma cells – a type of blood cells living in the bone marrow. The role of a plasma cell is to produce antibodies (also known as *immunoglobulins*), which aid in the fight against infection. Myeloma occurs when normal plasma cells become malignant, multiplying uncontrollably. These malignant plasma cells produce monoclonal immunoglobulins (also known as M-proteins), and will eventually disrupt the functions of bone marrow cells and kidneys, while destroying bones.



2. What are MGUS and Smoldering Myeloma?

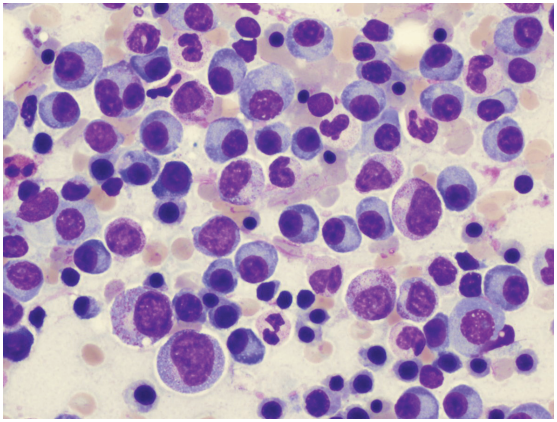
Monoclonal Gammapathy of Undetermined Significance (MGUS) is a benign condition that resembles Multiple Myeloma. The differences are that in MGUS, the level of M-proteins is lower, and there is only a slight increment of plasma cells in bone marrows. Patients with Smoldering Myeloma, however, have a higher level of M-proteins and plasma cells in their bone marrow. Both MGUS and Smoldering Myeloma are pre-cancerous conditions – patients suffering from them are asymptomatic and do not require any active treatment. These conditions can progress gradually to Myeloma though, and thus periodic monitoring of both conditions is recommended.



3. What is a plasma cell and what are plasma cell disorders?

A plasma cell is a special type of white blood cell that produces *immunoglobulins* (also known as antibodies), which are involved in the body's fight against infections. Plasma cells are found primarily in the bone marrows, and are developed from B-lymphocytes. In times of an infection, the B-lymphocytes are triggered to differentiate into plasma cells. The plasma cells then produce antibodies, which help to destroy the invading microorganisms. Plasma cells are capable of producing five classes of antibodies: IgG, IgA, IgM, IgE and IgD. A typical antibody consists of two *immunoglobulin* heavy chains and two light chains. The heavy chain will determine the classes of the antibodies – IgG, IgA, IgM, IgE and IgD, while the light chain can be classified into two distinct groups – kappa (κ) chain and lambda (λ) chain.

In normal conditions, the body produces plasma cells only in times of an infection. Plasma cells are short-lived, and they die after the body has been cleared of an infection. Certain mutations can cause these plasma cells to acquire the ability to continue multiplying infinitely and uncontrollably. In myeloma patients, plasma cells can account for more than 20% of the total cell population in the bone marrow. These abnormal plasma cells produce a specific class of antibodies known as M-proteins. The most common class of antibodies overproduced by an abnormal plasma cell is the IgG or IgA. Usually, a complete monoclonal antibody is produced by an abnormal plasma cell. However, in about 20% of the cases, only light chain antibodies are produced by the abnormal cells.



Bone Marrow Plasma Cells

4. What is Amyloidosis?

In medicine, Amyloidosis refers to a variety of conditions wherein normally soluble proteins become insoluble, and are deposited in the extracellular spaces of various organs or tissues (such as the heart, kidney etc.), disrupting their normal functions. This condition may develop into Myeloma, or both conditions can happen simultaneously.

5. Why do I have Multiple Myeloma?

At present, the cause of Myeloma is still poorly understood. It has been speculated that smoking, diet, alcohol consumption, occupation as well as exposure to ionising radiation may all contribute to Myeloma. However, all these speculations remain inconclusive, and further research is required to provide more insights on the etiology (cause) of this disease. Although we do not know the exact cause of Myeloma, we do know this disease is non-infectious.

Nevertheless, age remains the most significant risk factor for this disease. The majority of Myeloma patients are over 50 years old, with only a small proportion of them being under 40 years of age.

6. Is Multiple Myeloma hereditary?

There has been no strong correlation between the development of Myeloma and one's family history. A family history of Myeloma shows no significant increase in the risk of the disease developing in another family member. Only 3% to 5% of Myeloma patients present with history of Myeloma within the extended family.

7. Is Multiple Myeloma curable?

There is no known cure at present. However, Multiple Myeloma is a treatable disease and the treatment outcomes are continuously improving. The vast advancements in treatments have greatly improved the survival rates and quality of life for most patients.

8. How long can a Multiple Myeloma patient live?

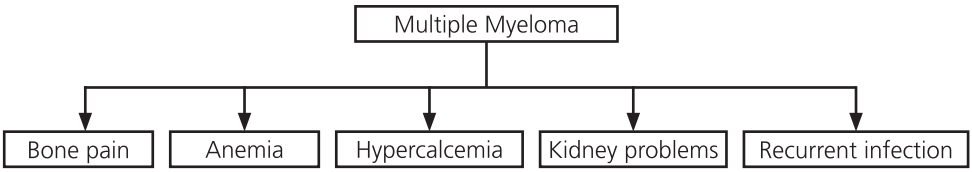
The life expectancy of Myeloma patients differs greatly from one individual to another. Factors such as age, gender, overall health condition and the disease stage at which the patient is diagnosed with contribute to the overall life expectancy. Survival rates are also complicated by the response of the patients to the given treatments, and how well the individual can withstand the treatment procedure.

The average life expectancy, from the time of diagnosis, is often predicted to be from 5 to 10 years. However, it is important to note that this is but a mere estimation, and an accurate gauge for life expectancy can be made only after taking into consideration all contributing factors related to the disease.

9. What are the signs and symptoms of Myeloma?

Signs and symptoms may vary from one individual to another. During the early stages of the disease (either MGUS or Smoldering Myeloma), there is often no symptoms, and the disease is usually discovered through routine blood tests. As the disease progresses, common symptoms include:

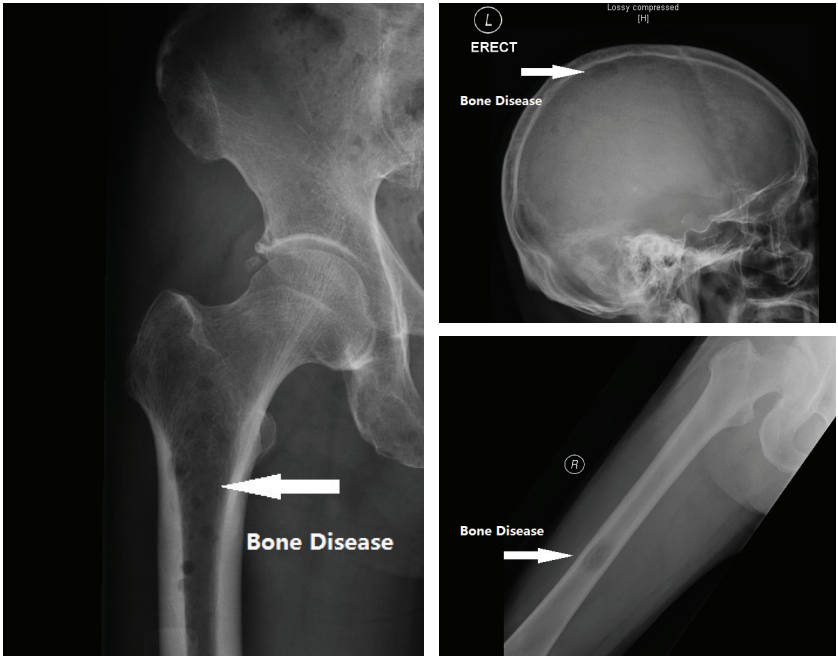
- **Bone pain**. Mostly in the back and the rib cage.
- **Anemia**. This can cause fatigue, dizziness and shortness of breath.
- **Hypercalcemia**. High levels of calcium in the blood may result in muscle weakness, increased thirst, nausea, loss of appetite, constipation as well as mental confusion.
- **Kidney problems**. Damage to the kidneys will impair the body's ability to remove excess salt, fluid and waste, resulting in the swelling of the lower limbs and weakness.
- **Recurrent infection**. Myeloma patients are more prone to infections and take longer periods of time to recover from them, due to weakened immune systems.



Multiple Myeloma and its symptoms

10. Why do I have bone pain?

Bone pain is the most prominent clinical presentation of Multiple Myeloma. The malignant plasma cells trigger other cells in the bone marrow to attack and destroy the bones, causing soft spots known as *osteolytic lesions. Osteolytic lesions* weaken the bones, increasing the incidences of fractures.



Bone disease

11. What is plasmacytoma?

Plasmacytoma refers to a single clump of malignant plasma cells that has proliferated, forming an isolated tumour. *Plasmacytoma* can be found growing within soft tissues or within the skeleton. *Plasmacytoma* of the bone often becomes Multiple Myeloma along with time. It is not uncommon to feel pain at where the *plasmacytoma* has developed. Depending on various factors, of which your doctor should be discussing with you, radiation therapy, surgery and/or chemotherapy are some possible treatment options.

12. Why do I need to undergo dialysis?

Approximately 20% of all Myeloma patients develop progressive kidney failures during the course of their illnesses. The production of monoclonal proteins (by the Myeloma cells) increases as the tumour burden gets heavier, resulting in increased stress on the kidneys, being the ones tasked with the removal of these monoclonal proteins. For patients who develop kidney failure, dialysis is an effective way to clear unwanted wastes from their bodies.

13. Why do I get infections easily?

In a healthy person, there are many plasma cells producing different types of antibodies, so as to protect us from a wide range of pathogens (infectious agents) that can potentially cause infections. In a Myeloma patient, only the malignant plasma cells producing one type of antibody is growing, overwhelming the rest of the normal cells. Myeloma patients thus have a limited range of antibodies and become more prone to infections. In addition, if a patient is receiving chemotherapy, the production of white blood cells in the bone marrow may be reduced, making this another possible cause of infection. Myeloma patients should watch out for symptoms like fever, chills or rigors, and to check their temperatures if they feel unwell. Crowded areas should also be avoided.

14. Why do I have a high calcium level?

As Myeloma cells attack the skeleton, the breakdown of bones release calcium into the bloodstream. This results in an abnormally high level of calcium in your blood – a situation known as hypercalcemia. Symptoms you may experience include muscle weakness, mental confusion and tiredness. Severe hypercalcemia can also lead to kidney complications. Apart from bisphosphonates, your doctor may also prescribe you fluid hydration. You should feel better soon after the treatments have been administered.

15. What is anemia?

The healthy bone marrow is involved in the production of red blood cells. When Myeloma affects the bone marrow, the production of red blood cells decreases. This situation is known as anemia. The chemotherapy which you might be receiving could also be a cause of anemia. If you feel tired, giddy and breathless or your heart is beating rapidly, you might be experiencing symptoms of anemia. Do ask for help when you are moving about, should you be experiencing symptomatic anemia. Your doctor might give you injections of a protein called erythropoietin and/or blood transfusion.

16. Do Myeloma patients with seeming similar presentations and diagnosis share the same prognosis?

Studies have shown that some common genetic abnormalities in Myeloma patients lead to different outcomes. The table below lists the common abnormalities and their prognoses:

Abnormalities	Frequencies	Prognosis
t(4;14)	10-15%	Poor
t(11;14)	15-20%	Neutral
t(14;16)	3-5%	Poor
1q21 Gain	30-35%	Poor
13q14 del	45-50%	Neutral
17p13 del	5-10%	Poor

Diagnosis

17. Which tests should I be going for if my doctor suspects I have Multiple Myeloma?

When your doctor suspects you have Multiple Myeloma, they will usually perform a series of tests to confirm the diagnosis, and to assess the status of the disease. These tests include:

Blood tests:	
Full blood count	Provides information on whether you have anemia, which is an important symptom associated with Myeloma. It also provides information on your white blood cell count and its differentiation, as well as your platelet count.
Chemistry	Provides information on your blood chemistry levels, especially your calcium level.
Organ function	Monitors your kidney function and liver function statuses.
M-band (spike)	Measures the amount of abnormal (monoclonal) proteins.
Immunofixation (IFE)	Tells information related to the presence or absence of monoclonal proteins, and the type present, i.e. heavy chain (G, A, D, or E) and/or light chain (kappa or lambda).
Quantitative immunoglobulin	Assesses the total amount of IgG, IgA, and IgM, including both normal and abnormal immunoglobulin.
Serum free light chain assay (sFLC)	For some subtypes of Myeloma, the patients' myeloma cells secrete very little or no monoclonal protein, which renders the cell undetected by the above mentioned tests. This sFLC test measures the amount of free kappa or free lambda light chains (fragments of monoclonal proteins).

Article continued on next page...

17. Which tests should I be going for if my doctor suspects I have Multiple Myeloma?

Urine tests:	
Urine immunofixation (IFE)	Like the abovementioned IFE, Urine IFE also indicates both presence and absence of monoclonal proteins and the type, if present.
Routine urinalysis	Shows the presence of protein and/or indicates evidences of kidney damage or infection.
Imaging study:	
X-ray (skeletal survey)	This test is used to identify lytic lesions in the bones caused by Myeloma. In addition, this test can also detect any weakened bone areas or fractures that may require surgery.
Pathology study:	
Bone marrow biopsy	Assesses the percentage of Myeloma plasma cells in the bone marrow.
Other tissue biopsy	May be performed if your doctor is concerned about amyloidosis (a disorder related to Myeloma, characterised by the deposition of abnormal light-chains amyloid proteins in the organs or tissues) or extramedullary (outside the bone marrow) disease.
Genetic studies	
Cytogenetic	This test shows the arrangement of chromosomes in cells (an organised structure of DNA and proteins). The result of this test can tell a physician your risk groups, and help in the decision of a treatment plan.
Fluorescence In Situ Hybridization (FISH)	This test goes hand in hand with the cytogenetic test. In this test, specific genetic abnormalities are assessed (see point no.16 above).

18. What are the diagnostic criteria for Multiple Myeloma?

International criteria for the diagnosis of Myeloma have been established, as follows:

Diagnosis	Diagnostic Criteria: All three below are required
Symptomatic Multiple Myeloma 	◆ Monoclonal plasma cells in the bone marrow > 10% and/or presence of a biopsy-proven plasmacytoma ◆ Monoclonal proteins present in the serum and/or urine ◆ Myeloma-related organ dysfunction (at least one of the following:) • **[C]** Calcium elevation in the blood (serum calcium > upper limit of normal) • **[R]** Renal insufficiency (serum creatinine > 177 µmol/L) • **[A]** Anemia (haemoglobin <10 g per 100 ml or 2 g <normal) • **[B]** Lytic bone lesions or osteoporosis
Monoclonal Gammopathy of Undetermined Significance (MGUS)	◆ Serum monoclonal protein <30g/l ◆ Monoclonal bone marrow plasma cells <10% ◆ No evidence of end-organ damage attributable to the clonal plasma cell disorder: • Normal serum calcium, haemoglobin level and serum creatinine • No bone lesions on full skeletal X-ray survey and/or other imaging if performed • No clinical or laboratory features of amyloidosis or light chain deposition disease

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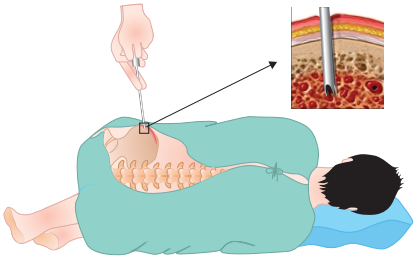
18. What are the diagnostic criteria for Multiple Myeloma?

Smoldering or Indolent Myeloma	◆ Monoclonal protein present in the serum 30 g/l or higher or ◆ Monoclonal plasma cells 10% or greater present in the bone marrow and/or a tissue biopsy ◆ No evidence of end-organ damage attributable to the clonal plasma cell disorder: • Normal serum calcium, haemoglobin level and serum creatinine • No bone lesions on full skeletal X-ray survey and/or other imaging if performed • No clinical or laboratory features of amyloidosis or light chain deposition disease
Solitary Plasmacytoma of Bone	◆ Biopsy-proven plasmacytoma of bone in a single site only. X-rays and magnetic resonance imaging and/or ◆ FDG PET imaging (if performed) must be negative outside the primary site ◆ The primary lesion may be associated with a low serum and/or urine M-component ◆ The bone marrow contains no monoclonal plasma cells ◆ No other myeloma-related organ dysfunction

19. What is a bone marrow test and what are the side effects?



Bone marrow is a sponge-like, flexible tissue found in bone interiors. Blood cells, including plasma cells, reside in the bone marrow.

A bone marrow examination refers to the pathologic analysis of bone marrow samples, obtained via a bone marrow biopsy – the process where a small, cylindrical piece of bone is extracted using a needle (often called a trephine biopsy) – and bone marrow aspiration – the process where a small amount of blood (about 5 to 10 mls) is aspirated (sucked out) from the bone marrow. The bone marrow examination is most commonly performed on the back of the hipbone.

Bone marrow examinations may be done in outpatient clinics or in hospital wards. Informed consent for this procedure is required. You will be asked to lie on your abdomen or on your side. After the skin is cleansed, a local anesthetic will be injected into the area around the bone, where the bone marrow needle will be inserted later, to numb the skin. You may also be pre-treated with pain killers and/or anti-anxiety medications, although this is not a routine practice.

Typically, aspiration is performed first. An aspirate needle is inserted, through the skin, using manual pressure. It is inserted into the bone marrow cavity by twisting motions of the clinician's hand and wrist. Once the needle is in the cavity, a syringe will be attached to aspirate liquid bone marrow. This step may be repeated several times, depending on the nature of the tests ordered. There is usually some discomfort when blood is aspirated from the bone marrow, but this procedure is usually over within a few seconds.

Subsequently, a biopsy will be performed, if required. In a biopsy, the needle will be advanced further inwards by a twisting motion, before it is rotated to obtain a solid piece of bone marrow about 1cm long. This bone marrow is then removed, along with the needle. The entire procedure, factoring in preparation time, typically takes about 30 to 45 minutes.

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19. What is a bone marrow test and what are the side effects?

After the procedure is completed, you will be asked to lie flat for two to four hours usually, so as to apply pressure over the procedure site. Thereafter, assuming no bleeding is observed, you can then get up and go about your normal activities. Paracetamol (Panadol) or other common painkillers can be used to ease soreness – which is not uncommon two to three days post-procedure. Any worsening pain, redness, fever, bleeding or swelling may suggest a complication. You should also avoid washing the procedure site for at least 24 hours after the completion of your procedure.

20. What information can a bone marrow test tell?

A bone marrow test can confirm if you have the disease, and if so, the status of the disease. It is also through this procedure that samples required for cytogenetic and FISH tests can be obtained, so as to find out more information on your condition.

21. What is a skeletal survey test and what are the side effects?

A skeletal survey is a series of bone x-rays done on different areas of your body, including the skull, the vertebral column, the ribcage, limbs and pelvic bone. The procedure should take approximately 30 minutes. During the procedure, you would need to stay still, and might be asked to hold your breath for a few seconds.

As with any forms of procedures involving ionising radiation, x-rays carry potential risks to our health, but the effects are negligible. In reality, we are exposed to natural radiation in our surroundings every day. These come from the sun, the food we eat and the ground. Each x-ray examination you undergo simply adds on a little to the amount of natural radiation you are already exposed to. Should your doctor request for you to undergo a skeletal survey, he/she is confident that the benefits of the test far outweighs any small risks the test might pose. That being said, the risks of radiation are slightly higher when it comes to unborn children. Female patients aged 10 to 55 years will thus be asked if they are having their periods prior to the x-rays, to find out if there is a chance of pregnancy. Details like these are to be verified before the test, in a bid to safeguard and minimise the amount of x-rays you will be exposed to.

22. How do I read my test results?

You can ask your physician for a copy of your test results. Normal lab values (usually expressed as a range of values in parentheses next to your lab results) vary from lab to lab. Do note that the metric system units (grams or milligrams, liters or deciliters etc.) used might also vary from lab to lab. Do ensure that you only compare results expressed in the same unit. If your lab result falls below the lower limit of the normal range, or above the upper limit of the normal range, your reported lab value will be assigned a symbol denoting that it is out of range: usually an "H" for high or an "L" for low. You should discuss the significance of any abnormal lab value with your physician. In general, a trend or a pattern observed from a series of test results gathered over time often reveals more information about your condition, as compared to looking at results from just one particular test.

23. What is International Staging System (ISS)?

The International Staging System (ISS) is a measure of the severity (or stage) of the disease, used for the prognosis of Myeloma.

The International Staging System utilises a combination of serum β2 microglobulin and serum albumin to provide a simple, powerful, and reproducible three-stage classification. By using easy to use variables in a simple manner, the International Staging System can be used internationally, at a relatively low cost.

Stage	Criteria
I	Serum β2-microglobulin (β2M) < 3500 ug/L and albumin >= 35 g/L
II	Not I or III
III	β2M >= 5500 ug/L

There are two possibilities for stage II:

- Serum β2 microglobulin <3500 ug/L, but serum albumin <35 g/L

OR

- Serum β2 microglobulin 3500 – 5500 ug/L irrespective of the serum albumin

24. What is Durie-Salmon Staging System?

Dr. Brian Durie and Dr. Sydney Salmon published the Durie-Salmon Staging System in 1975, and it has been used throughout the world in the last 30 years. Like the ISS mentioned above, this system is also a measure of the severity (or stage) of the disease used in the prognosis of Myeloma, but it is based on more complex clinical and laboratory criteria, as shown in the table below:

Durie-Salmon Staging System

Stage	Criteria	Measured Myeloma Cell Mass *(myeloma cells in billions/m²)**
Stage I (low cell mass)	All of the following: ◆ Haemoglobin value > 10g/dL ◆ Serum calcium value normal or < 10.5mg/dL ◆ Bone x-ray, normal bone structure (scale 0), or solitary bone plasmacytoma only ◆ Low M-component production rates IgG value < 5g/dL; IgA value < 3g/dL ◆ Urine light chain M-component on electrophoresis < 4g/24h	600 billion*
Stage II (intermediate cell mass)	Fitting neither Stage I nor III	600 to 1,200 billion* **myeloma cells in whole body*

Article continued on next page...

24. What is Durie-Salmon Staging System?

Stage III (high cell mass)	One or more of the following: ◆ Haemoglobin value < 8.5g/dL ◆ Serum calcium value > 12mg/dL ◆ Advanced lytic bone lesions (scale 3) ◆ High M-component production rates IgG value > 7g/dL; IgA value > 5g/dL ◆ Bence Jones protein > 12g/24h	>1,200 billion*
Subclassification (either A or B)	◆ A: relatively normal renal function (Serum creatinine value) < 2.0mg/dL ◆ B: abnormal renal function (Serum creatinine value) > 2.0mg/dL *Examples: Stage IA (low cell mass with normal renal function) Stage IIIB(high cell mass with abnormal renal function)*	

25. How do we differentiate Myeloma from other diseases?

Multiple Myeloma and other diseases may have similar signs and symptoms, such as cancer metastatic to bone, *Waldenström Macroglobulinemia* (a type of lymphoma), kidney disease (for those patients who present with abnormal kidney functions) and so on. Tests mentioned in point 19 above could help your physician confirm your diagnosis.

Treatment

26. Do I need to take calcium pills?

The calcium level in a Myeloma patient may be elevated, so the use of calcium pills cannot be recommended as per under normal circumstances. However, if bisphosphonate is prescribed to a patient with bone disease, consumption of the drug may lead to a lower calcium level, in which the intake of calcium pills will then be required. Your physician will make this decision based on the results of your blood test.

27. How many treatment options do I have?

Nowadays, patients with Myeloma have many treatment options. In general, a strong treatment plan is preferred at the start, so as to get the disease under control as quickly as possible. These harsher treatments usually include one or more of the following drugs: Thalidomide, Velcade, Revlimid and Dexamethasone. The combination of drugs may differ, depending on the patient's overall condition as well as the disease characteristics, e.g. stage and genetics. For the younger patients, stem cell transplants are usually involved after the initial months of treatment.

28. What are the costs of the different treatment options?

The costs of the treatment options vary, and may differ between the various institutions. More costly treatments are usually those involving the use of Velcade, Revlimid or stem cell transplantations. It is important to find out the cost of the various treatment options available for you.

29. What is Velcade?

Velcade is a drug that inhibits the proteasome – a component in the cell that removes unwanted protein. As Myeloma cells produce high levels of protein, they are very sensitive to this blockade, resulting in deaths of these cancer cells. Velcade is thus a very effective treatment for Myeloma. It is given via an intravenous or subcutaneous injection, either once or twice a week, over the course of two weeks, with one week of rest after each course. Used only in targeted therapy, Velcade is not a conventional chemotherapy drug.

30. What are some possible side effects of Velcade?

The main side effect noted affects the nerves, resulting in sensations of numbness or 'pins and needles' in the hands and feet. Sometimes, the side effect can be more severe, causing pain or affecting functions of the limbs. However, these symptoms are potentially reversible with early intervention, so it is important that you report the symptoms to your physician when you first notice them. Another common side effect affects the digestive system, resulting in nausea, vomiting and/or diarrhea. Again, these symptoms are manageable along with early detection and intervention. The last side effect might be a dip in your blood count, especially a drop in your platelet level, while on the Velcade treatment. However, these effects are usually mild and do not require intervention.

31. What precautions in my diet should I take while on the Velcade treatment?

Studies have shown that high levels of vitamin C and green tea extract, epigallocatechin gallate (EGCG), affect the efficacy of Velcade. Do avoid food containing these compounds in your daily diet, while on any Velcade-based treatments.

32. What drugs will interfere with Velcade?

While on Velcade, there are some medications which you cannot take. However, if you are required to take any new medication, it is important to inform your doctor.

33. What are the differences between subcutaneous and intravenous Velcade?

With subcutaneous injections, the drugs are injected under the skin, whereas for intravenous injections, the drugs are injected into the veins. The other main difference is the frequency of side effects. It has been found that subcutaneous injections are associated with much lower incidences of nerve problems. When it comes to the effectiveness of Velcade, there is no difference between the subcutaneous and intravenous method.

34. What are the differences between the two administration schedules of Velcade?

There are two common administration schedules of Velcade. One is 21 days per cycle: the drug will be given on day 1, 4, 8, 11. The other is 28 days per cycle: the drug will be administered weekly. Studies have shown that the weekly Velcade administrations have the same efficacy but with lesser side effects (especially peripheral neuropathy), when compared to the 21 days administration schedule.

35. What is Thalidomide?

Thalidomide belongs to a group of drugs called immunomodulatory agents or IMiDs. IMiDs are a type of drugs that enhances the body's immune system, increasing its ability to kill off Myeloma cells. Thalidomide is thus used in various combinations and at varied times during the course of the disease. It can be used during first-line therapy (upfront therapy), during the maintenance phase or after the Myeloma cells become active again after a period of control (relapse). It can be given as a treatment on its own, or more commonly, given together with a steroid (Dexamethasome or Prednisolone) and/or Velcade and/or a chemotherapy drug (Melphalan or Cyclophosphamide).

36. What are some possible side effects of Thalidomide?

Side effects vary according to the dose and duration of treatment. It is important to remember that everyone's reaction to Thalidomide differ, and that side effects, if any, are temporary and should go away when the Thalidomide dosages stop.

Most patients taking Thalidomide complain of constipation and fatigue. Should you be suffering from severe constipation, do get your physician to prescribe you some medication. You are also recommended to take your Thalidomide before sleep, so as to have sufficient rest and energy when the day comes.

37. What is Lenalidomide (Revlimid ®)?

Lenalidomide falls under the category of immunomodulatory agents or IMiDs too. While it is chemically similar to Thalidomide, it has shown to be more effective. Lenalidomide is used to treat Myeloma, usually after a relapse or after the initial treatment. These treatment plans also include the use of Thalidomide, high dose therapies and stem cell transplants (if suitable), so as to maintain the response.

38. What are some possible side effects of Lenalidomide (Revlimid ®)?

Lenalidomide is generally well tolerated by patients and has fewer side effects compared to Thalidomide. The most common side effects of Lenalidomide are:

- Lowered white cell count (making you more susceptible to infections). In most cases, your physician will request for you to do a blood test midway through your first cycle of Lenalidomide, to ensure that your blood count falls within the safe level.
- Risk of blood clots. You may be required to take a blood thinning agent.
- Fatigue and tiredness. You are recommended to take Lenalidomide before sleep, so as to have sufficient rest and energy when the day comes.
- 50% of patients develop skin rashes during their first and second cycles of Lenalidomide usage. Your physician may then prescribe you anti-histamine drugs, to relieve the itch and other symptoms associated with skin rashes.

39. What is peripheral neuropathy?

Peripheral neuropathy refers to the condition where the nerves connecting the brain and spinal cord to the rest of the body are damaged or diseased. Patients with peripheral neuropathy may experience tingling, numbness, weakness, burning pain or other unusual sensations in the affected areas. Often, these symptoms are symmetrical and extend to both hands and feet. Because the symptoms are often present in areas where we wear gloves and stockings, patients experiencing peripheral neuropathy are often described to be having a "glove and stocking" distribution of symptoms.

40. How can I manage peripheral neuropathy caused by the intake of Velcade or Thalidomide?

Early drug dosage reduction is probably the most useful method in reducing the symptoms of peripheral neuropathy. The use of weekly or subcutaneous injections of Velcade is also associated with decreased chances of peripheral neuropathy. If painful neuropathy occurs, you physician may prescribe you vitamin B complex and medications like Pregabalin and Amitiptylline.

41. What are Dexamethasone, Prednisolone and steroids?

Dexamethasone and Prednisolone are steroids commonly used in the treatment of Myeloma. They are usually part of a combination treatment, used together with other novel agents such as Velcade, Thalidomide or Lenalidomide. Steroids are prescribed in the form of oral medications.

42. What are some possible side effects of Dexamethasone?

Steroid treatments can result in short and long term side effects. Common **short term side effects** include:

- Inability to sleep. You are recommended to take this drug in the day.
- Confusion in the elderly.
- Hiccups.
- Elevation of blood glucose level (diabetic patients may need to adjust their anti-diabetic tablet dosage while undergoing steroid treatments).
- Gastritis. Patients are usually given medications to ease the discomfort.
- Reduced immunity. Patients are usually prescribed with Prophylactic antibiotics such as Bactrim and acyclovir to prevent common infections.
- Water retention.

Long term side effects include:

- Osteoporosis.
- Hormonal problems, resulting in a condition called Cushing's Syndrome.
- Avascular necrosis. This is a condition where hindered blood supply to hip joints result in the death of bone cells, causing pain.
- Limb weakness (muscles in arms and legs are weakened).

Long term side effects of steroid treatments are uncommon in Myeloma patients; as such treatments are administered in short durations.

43. What is chemotherapy?

Chemotherapy involves drugs that modify the DNA of cells and stop them from producing new DNA, resulting in cell deaths. Cancer cells grow quickly and need increased productions of new DNA for their rapid growth. Chemotherapy is thus effective in killing off these cancerous cells. Unfortunately, normal fast growing cells such as stem cells and hair cells will also be affected by the effects of chemotherapy.

44. What are some possible side effects of chemotherapy?

The common side effects experienced are hair loss, nausea, vomiting and the suppression of blood production – resulting in increased risks of infection, bleeding and symptoms of anemia such as shortness of breath, fatigue and dizziness.

45. What are Alkylating agents (Melphalan, Cyclophosphamide)?

Alkylating agents kill cancer cells by attaching an alkyl group to their DNA, resulting in cell DNA damage. Unfortunately, they cause damage to normal, non-cancerous cells as well.

46. What are Anthracyclines (Doxorubicin, Liposomal doxorubicin)?

Anthracyclines are used in many cancer treatment plans. These agents kill cancerous cells by inhibiting their DNA and RNA syntheses, or by damaging their DNA, proteins and cell membranes. A common side effect of Anthracyclines is cardiotoxicity (adverse effects to the heart), and usage of this drug in cancer treatments are to be monitored carefully.

47. What are Bisphosphonates?

A common complaint of Multiple Myeloma patients is bone pain, caused by the destruction of bone material. Bisphosphonates slow down the bone destruction process and help strengthen the bones. They are often used in the treatment and prevention of osteoporosis too. Commonly used Bisphosphonates include Zometa and Pamidronate. These are usually administered intravenously and on a monthly basis. Pamidronate is given over the span of two to four hours, while Zometa is given over the course of 15 minutes.

48. What are some possible side effects of Bisphosphonates?

Side effects of Bisphosphonates are usually mild. Some patients may experience fever and flu like symptoms, muscle cramps or numbness and tingling sensations due to hypocalcaemia, changes in bowel movements and bone, muscle or joint pain. Although rare, Bisphosphonates can also cause severe side effects like kidney problems and osteonecrosis of the jaw (ONJ). The onset of ONJ seemed to be related to the length of Bisphosphonate treatment, and is more frequent in patients who are on Zometa.

49. What is radiation therapy?

Radiation therapy uses high-energy radiation to shrink tumors and kill cancer cells. X-rays, gamma rays and charged particles are types of radiation used for cancer treatments.

The radiation may be delivered by a machine outside the body (external-beam radiation therapy), or it may come from radioactive materials placed in the body, near the cancer cells (internal radiation therapy, also called brachytherapy).

Systemic radiation therapy uses radioactive substances, such as radioactive iodine, that travel via the bloodstream to kill cancer cells.

The type of radiation most commonly used to treat Myeloma patients is the external beam radiation therapy. Radiation may be used to treat areas of bone damaged by Myeloma, which have not been responding to chemotherapy, and are causing pain. It is also the most common treatment for solitary Plasmacytomas. Hence not every Myeloma patient needs radiation therapy.

50. What are some possible side effects of radiation therapy?

Radiation therapy can cause both early (acute) and late (chronic) side effects. Acute side effects occur during treatment, while chronic side effects occur months or even years after the treatment ends. The side effects that develop depend on the area of the body that underwent radiation therapy, the dosage given per day, the total dosage given, the patient's general medical condition and other treatments he/she is given at the same time.

Acute side effects of radiation therapy are caused by damage to rapidly dividing normal cells in the area undergoing treatment. These effects include skin irritation or damage at regions exposed to the radiation beams. Examples include damage to the salivary glands, hair loss (when the head or neck areas are being treated), or urinary problems (when the lower abdomen is being treated).

Most acute side effects disappear after treatment ends, though some (like salivary gland damage) can become permanent.

Fatigue is a common side effect of radiation therapy, regardless of which part of the body is being treated. Nausea with or without vomiting is common when the abdomen is being treated, and it occurs sometimes when the brain is being treated too. Medications are available to help prevent or alleviate nausea and vomiting during the course of treatment.

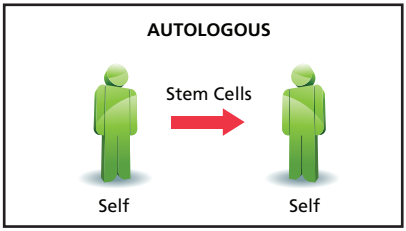
Chronic side effects of radiation therapy may or may not occur in patients. Depending on the area of the body being treated, chronic side effects can include:

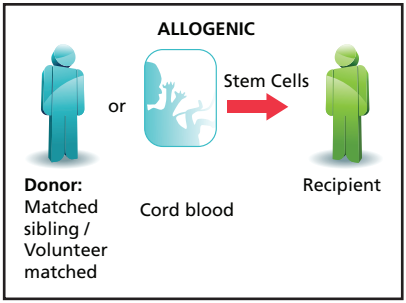
- Fibrosis (the replacement of normal tissues with scar tissues, leading to restricted movement of the affected area).
- Damage to the bowels, causing diarrhea and bleeding.
- Memory loss.
- Infertility.
- Another cancer, caused by radiation exposure (in very rare cases).

51. What is Haematopoietic Stem Cell Transplantation (HSCT)?

Haematopoietic Stem Cell Transplantation (HSCT) is a form of treatment which involves the taking of stem cells from the donor or from cord blood, before infusing it into the recipient. Sources of stem cells can be from:

- The patient (autologous)
- A relative (allogeneic)
- A matched, unrelated donor (MUD)
- A banked, unrelated cord blood unit appropriately matched to the patient's (cord blood transplant)





Majority of the Myeloma patients would undergo Autologous Stem Cell Transplantation (ASCT). Although ASCT does not provide a cure, overall survival and progression-free survival of the patients are prolonged, as compared to them undergoing treatments with conventional chemotherapy alone.

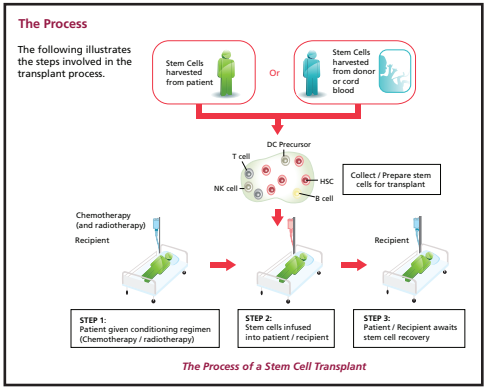
52. What is Haematopoietic Stem Cell?

Haematopoietic Stem Cells are produced in the bone marrow, and are responsible for the daily production of new blood cells. Stem cells are pluripotent, i.e. they have the ability to divide and differentiate into three different types of cells (white blood cells, red blood cells and platelets) that can be found in our blood.

53. What is the process of Autologous Stem Cell Transplantation (ASCT)?

The following gives a brief illustration on the process of HSCT.

Step 1: Stem cell mobilisation



The Process of a Stem Cell Transplant

The first step involves the collection of stem cells from the patient's body. Stem cells can be found from the bone marrow. In stem cell mobilisation, stem cells are transported from the bone marrow into the bloodstream, where they can then be easily collected. The two techniques used for mobilisation are:

1) Growth factor injection (GCSF): GCSF is a hormone that stimulates the bone marrow to increase their produce of white blood cells.

2) GCSF plus chemotherapy: Certain types of chemotherapy can cause stem cells to move out of the bone marrow and into the bloodstream for easy collection, and may also help in the removal of some cancer cells.

Step 2: Stem cell collection (Apheresis)

The process is carried out via a Central Venous Catheter (CVC), which is inserted, through the skin, into a large vein found near the groin, or via the large veins found in the forearms. The patient's blood is then passed through an apheresis machine, which removes the stem cells before returning the blood back to the patient's body. This process takes approximately four to six hours daily, and may have to be carried out through several days to collect enough stem cells for a transplant.

Step 3: Conditioning phase

High dose chemotherapy is administered to the patient before the stem cells are infused. This is essential in the preparation of the bone marrow for the new cells. The aim of the chemotherapy is to destroy as many cancer cells found in the body as possible, so as to create more "space" for the new stem cells.

Article continued on next page...

53. What is the process of Autologous Stem Cell Transplantation (ASCT)?

Step 4: Stem cell infusion

The stem cell infusion process is similar to that of a blood transfusion. Bags of stem cells will be infused into the patient over the span of one to two hours. For some individuals, this process may take longer.

54. What should I do after the transplant?

The transplant experience differs for different individuals. Some patients will experience more complications than the others, while some may experience none. Your immune system after the transplant will be weak, rendering you more prone to infections. Hence, it is necessary to practise good hygiene and to minimise your exposure to bacteria, fungi or viruses post-transplant.

You will be monitored closely by your transplant doctor, and on a frequent basis, the first few months post-transplant. This is to keep a close monitor on your progress, and to treat any complications early.

55. Is there any traditional Chinese medicine/acupuncture that can help improve my condition?

We suggest patients NOT to take any traditional Chinese medicine during their treatment, as we cannot be sure if ingredients found in the medication will not interfere with the drugs used during treatment. Though some studies have shown positive results when it comes to treating peripheral neuropathy with acupuncture, you should consult your physician first, to evaluate how safe it is for you to go for acupuncture (as your platelet count may be low during treatment).

56. Should I go to the hospital if I experience any of the side effects mentioned above while undergoing treatment?

Some of the side effects mentioned above are expected, and are related to the treatment you are under. You might have already been advised to take certain medication to prevent, lessen or treat these side effects. It is important to monitor the side effects and to inform your doctor if they get worse, or affect your daily activities. You may wish to contact your doctor and describe your symptoms to get his professional opinion first, before deciding if you should make a trip down to the hospital.

57. What is a clinical trial?

Clinical trials are research studies involving people. The aim of each trial is for doctors and pharmaceutical companies to gather more information on how they can improve on current prevention, screening and treatment methods for a particular health condition. The trials usually involve the testing of new methods and/or new drugs. Clinical trials can take place only after satisfactory information has been gathered from non-clinical research conducted in a laboratory. You can be assured that locally, clinical trials involving patients are approved by the Institutional Ethics Review Board and Health Sciences Authority of Singapore (HSA). This is done to ensure protection and safety to your health.

58. Why should I consider joining a clinical trial?

At some stage(s) of your medical treatment, your doctor may approach you and ask if you would like to participate in a clinical trial. Your doctor is aware of possible and suitable clinical trials available to you, with your best interests in mind. Each trial has its own set of criteria to determine a participant's suitability. If you choose to take part in a clinical trial, you may be one of the first few patients to benefit from a new treatment method. You also have the opportunity to contribute to the future of science and treatment for cancer. A doctor and a clinical research coordinator will explain to you, in greater detail, should you be offered the opportunity to partake in a clinical trial.

59. How is treatment response assessed?

The International Myeloma Working Group (IMWG) has developed a set of uniformed response criteria, which are used to assess the effectiveness of a treatment. You can refer to the table below for reference:

(taken from: http://myeloma.org)

Response	IMWG criteria
sCR	CR as defined below plus normal FLC ratio and absence of clonal cells in bone marrow by immunohistochemistry or immunofluorescence
CR	Negative immunofixation on the serum and urine and disappearance of any soft tissue plasmacytomas and < 5% plasma cells in bone marrow
VGPR	Serum and urine M-protein detectable by immunofixation but not on electrophoresis or > 90% reduction in serum M-protein plus urine M-protein level < 100 mg/24 h
PR	> 50% reduction of serum M-protein and reduction in 24 hours urinary M-protein by >90% or to < 200 mg/24 h If the serum and urine M-protein are unmeasurable, a > 50% decrease in the difference between involved and uninvolved FLC levels is required in place of the M-protein criteria If serum and urine M-protein are not measurable, and serum free light assay is also not measureable, > 50% reduction in plasma cells is required in place of M-protein, provided baseline bone marrow plasma cell percentage was > 30% In addition to the above listed criteria, if present at baseline, a > 50% reduction in the size of soft tissue plasmacytomas is also required
No change/ Stable disease	Not meeting criteria for CR, VGPR, PR, or progressive disease

Article continued on next page...

59. How is treatment responses assessed?

Progressive disease	Increase of > 25% from lowest response value in any one or more of the following: ◆ Serum M-component and/or (the absolute increase must be > 0.5 g/dL) ◆ Urine M-component and/or (the absolute increase must be > 200 mg/24 h) ◆ Only in patients without measurable serum and urine M-protein levels; the difference between involved and uninvolved FLC levels. The absolute increase must be > 10 mg/dL ◆ Bone marrow plasma cell percentage; the absolute percentage must be > 10% ◆ Definite development of new bone lesions or soft tissue plasmacytomas or definite increase in the size of existing bone lesions or soft tissue plasmacytomas ◆ Development of hypercalcaemia (corrected serum calcium > 11.5 mg/dL or 2.65 mmol/L) that can be attributed solely to the plasma cell proliferative disorder

60. What is consolidation therapy?

After their transplants, some patients may be given additional cycles of treatment. This is known as consolidation therapy, and the aim of it is to further reduce the disease condition, helping to achieve a complete treatment response.

61. What is maintenance therapy?

Some patients (regardless of if patients who have undergone stem cell transplants) may be given long periods of treatment (usually years) involving Thalidomide, Velcade or Revlimid. This is called maintenance therapy, and the aim of it is to delay potential disease relapses.

62. Are consolidation and maintenance therapies required?

Clinical trials have shown the benefits of both consolidation and maintenance therapies. However, as with all treatments, there are bound to be side effects. Some of these therapies are costly too. It is hence important to take all these factors into consideration and to consult your doctor for his/her advice, when deciding if you need these therapies.

63. What questions should I be asking my physician?

You may wish to find out more about your condition, prognosis, treatment options and costs involved from your physician. It is also important to know the potential side effects you may experience with each treatment, as well as the chances of positive response.

64. What is relapse or refractory Myeloma?

The majority of Multiple Myeloma patients who have completed their initial treatments will experience relapses, requiring further treatment. Relapsed Myeloma is the condition where one is required to undergo treatment again, after being off-therapy (because of an improved condition) for a period of time. Refractory Myeloma refers to the condition where the patient does not respond to the given treatment or see his/her condition progressing within 60 days from last treatment.

65. If my disease relapses, what treatment options are available for me?

Treatment options for patients with relapsed or refractory Multiple Myeloma include HSCT, a re-challenge of the previous chemotherapy regimen or a trial of a new regimen. Your doctor will decide, for you, the choice of therapy, by considering the severity of your disease, the prior treatments used, and the duration of positive response to these treatments.

Other FAQs on Myeloma

66. How do I handle the mental stress that comes with the diagnosis of Multiple Myeloma?

Individuals cope differently when they are first diagnosed with Myeloma. However, it is normal to feel angry, helpless and confused. At times, you may feel in control of your emotions at one moment, while feeling overwhelmed by them the next. These feelings are common, and are all part of the process of coming to terms with your diagnosis.

It is worth remembering that knowledge of the disease often helps take away some of the fear of the unknown. Ask your doctor any questions you might have regarding the disease or treatment options.

Emotional support is also important when it comes to living with Myeloma. It is often easy for patients and their family members to feel a sense of isolation, as the strong emotions they may be feeling often make it difficult for them to discuss their worries and fears openly. Talking to someone who understands what is going on can ease these feelings of isolation. If you are finding it hard to talk about your situation, you may ask your doctor to refer to you a counselor, or someone who can help.

Support groups provide an informal and comfortable atmosphere in which members can share their experiences and information. Many people assume that support group members are cynical and emotionally unstable, but this is usually not the case. On the contrary, they are often a supportive group of people who are facing the same issues as you, and you should consider joining such a support group.

Lastly, it is useful if you are able to set yourself a target in life, after your diagnosis of Myeloma. Working towards the target can serve as a good source of motivation, and a positive frame of mind is important in the achievement of success when it comes to treatment.

67. Can I exercise during treatment?

You can engage in mild exercises such as walking, cycling and hiking during your treatment. If you are suffering from severe bone pain, you should consult with your orthopedic doctor or your cancer rehabilitation physician/therapist on the kind of exercises suitable for your condition. Because of the weakened immune system during treatment and post-transplantation, swimming is not recommended, as you may develop infections.



68. Where can I find more information on Multiple Myeloma?

You can find more information on the disease from the internet. You can also visit the International Myeloma Foundation website at www.myeloma.org

Reference:

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