

WE ASPIRE TO:
SUPPORT
STRENGTHEN
HELP

Multiple Myeloma

Disease, diagnosis and therapy



Our service for people with cancer and their caregivers



Dear Reader,

The diagnosis of multiple myeloma frequently gives rise to many questions for those affected and their caregivers. “What exactly is multiple myeloma?”, “How is multiple myeloma diagnosed?” and “What will happen next?”.

This brochure covers three central topics and is intended to help you to understand the disease better.

1. The section “**Multiple Myeloma**” explains what lies behind the disease and the effect it has on our body.
2. “**The Diagnosis**” deals with the various investigational methods, the diagnostic criteria and the classification of the disease.
3. In the third section “**The Therapy**” we present the various treatment methods.

The contents of the three sections have also been converted into short explanatory films. You can find these on our website www.takeda-onkologie.de/multiples-myelom/service.

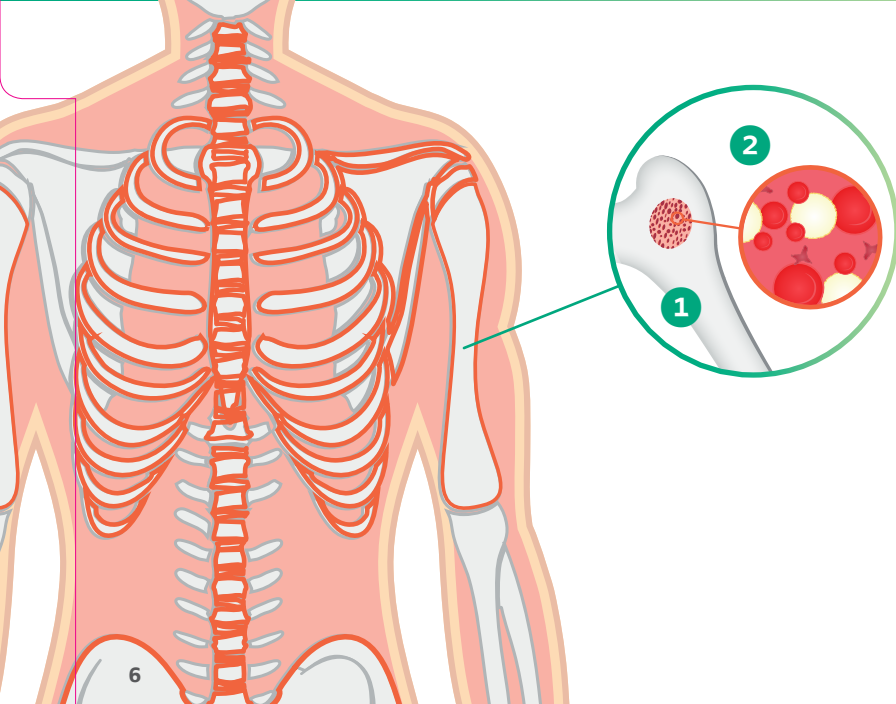
We hope that we will be able to answer some of your questions. You can obtain further information from the doctor treating you.

Your team from
Takeda Oncology



Multiple Myeloma

The functions of the bone marrow

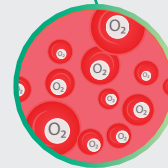


The bone marrow plays an important role in the origin of multiple myeloma.

- 1 The **bone marrow** is a sponge-like tissue in the large bones of our body.
- 2 It is responsible for **producing blood cells**: the **erythrocytes** (red blood cells), the thrombocytes (blood platelets) and the **leukocytes** (white blood cells).

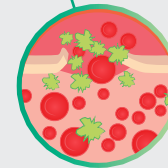
The blood cells fulfil vital tasks in our organism.

Erythrocytes



Oxygen transport

Thrombocytes



Blood clotting

Leukocytes

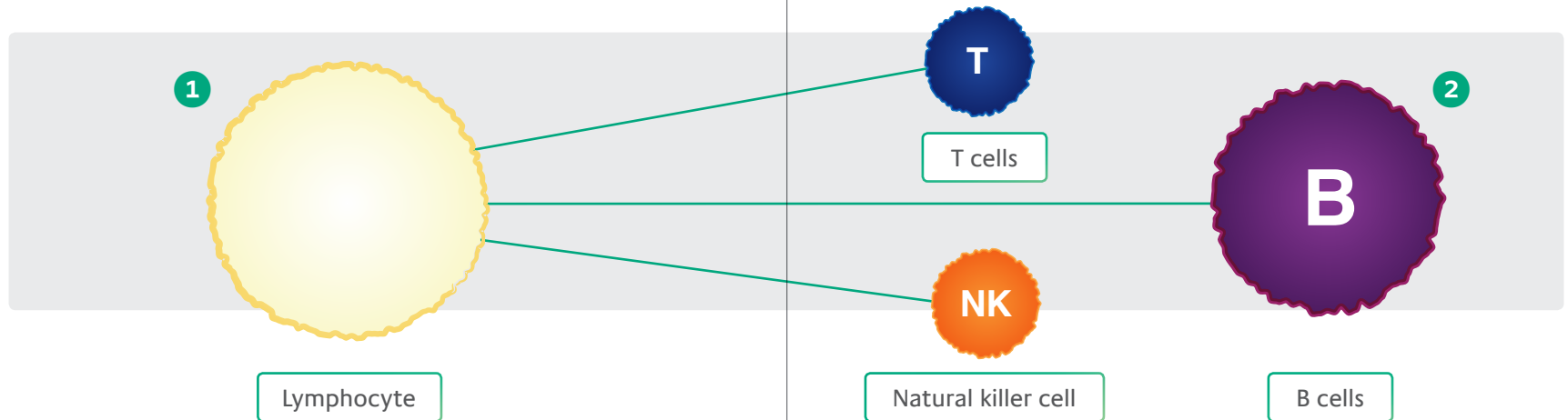


Defence against infection

The white blood cells: part of our body's powers of resistance

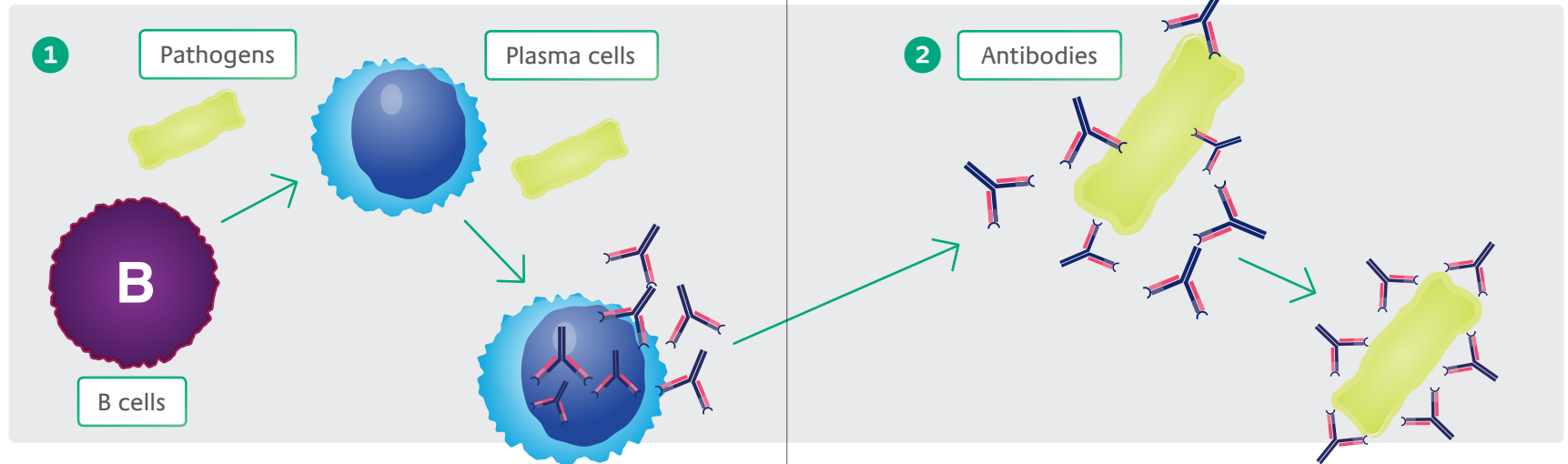
The **white blood cells** fight off infections, for example. They identify and eradicate pathogens.

- 1 One of their subgroups is formed by the **lymphocytes**. Lymphocytes are further divided into T cells, B cells and natural killer cells.
- 2 In **multiple myeloma**, the **B cells** are particularly important.

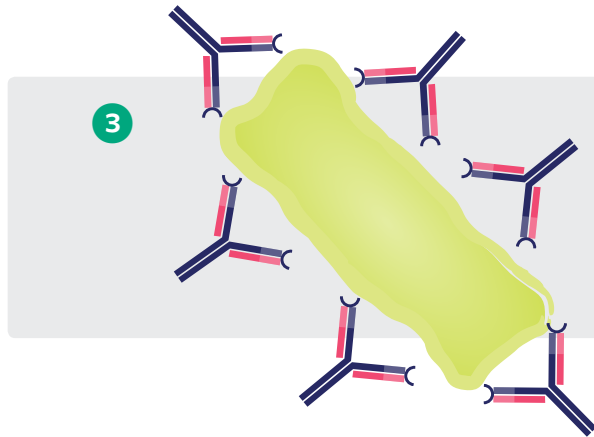


The immune defence of our body

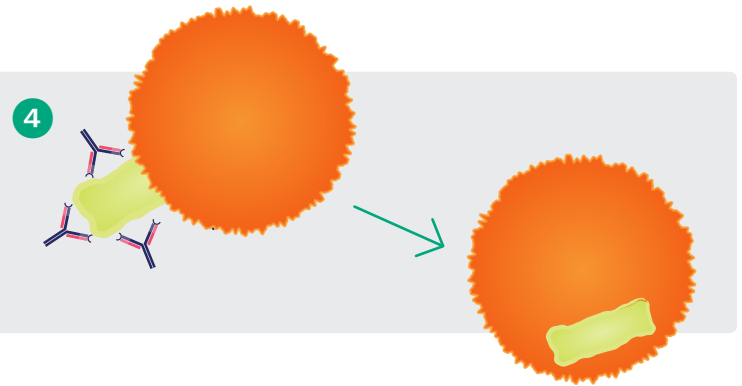
- 1 In the healthy immune system, B cells identify pathogens and form plasma cells. These produce antibodies against the pathogen and release them into the blood.
- 2 The antibodies bind to the pathogen and mark it.



The immune defence of our body



- 3 The pathogens have now been identified by the antibodies.
- 4 Specialised immune cells can now find, destroy and break down these pathogens



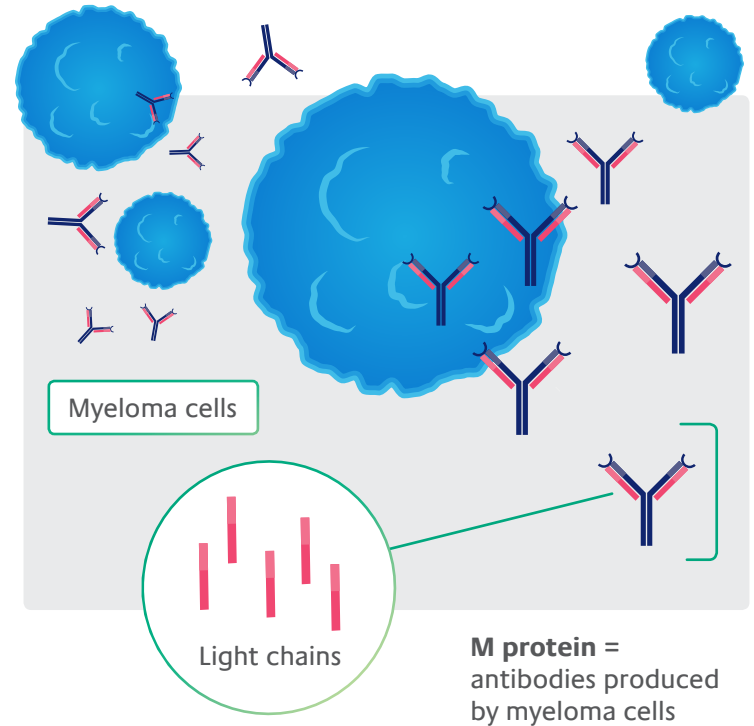
Specialised immune cells

Degenerated plasma cells in multiple myeloma

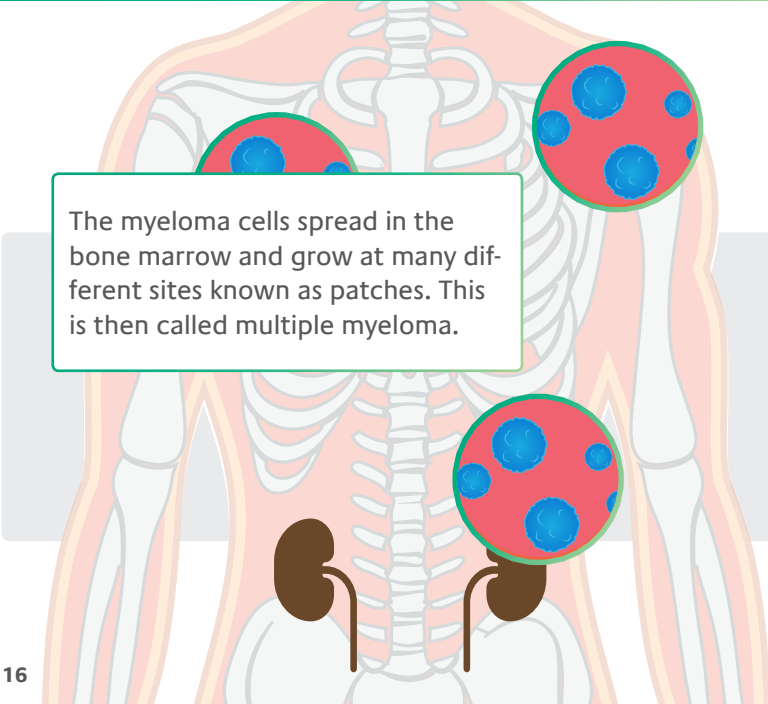
In multiple myeloma, the plasma cells have degenerated: They divide in an uncontrolled way and, even without any pathogens, produce vast numbers of identical and non-functional antibodies. Doctors call these antibodies **monoclonal** or **M proteins**.

The degenerated plasma cells are called **myeloma cells**.

Some myeloma cells produce only fragments of antibodies, known as **light chains**.



How multiple myeloma causes symptoms

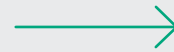


The myeloma cells spread in the bone marrow and grow at many different sites known as patches. This is then called multiple myeloma.

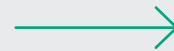
The M proteins and light chains produced by the myeloma cells flood the body and block the kidneys. This can lead to kidney damage.

Due to the displacement of healthy blood-forming cells in the bone marrow, sufficient numbers of red blood cells can no longer be formed. This leads to anaemia.

In addition, if the immune system is weakened because there are too few white blood cells, infections become more frequent.



Kidney damage

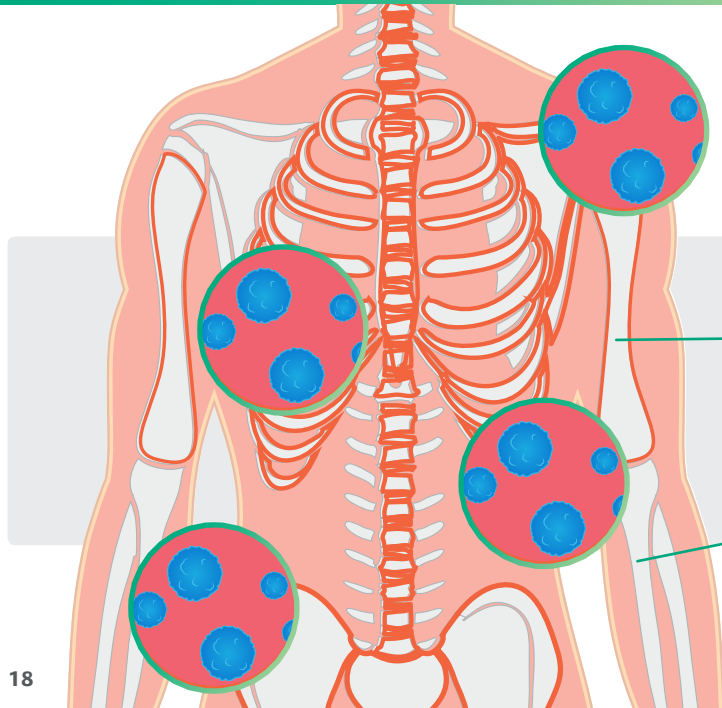


Anaemia



Weak immune system

How multiple myeloma damages the bones



Bone loss

Bone fractures

The myeloma cells, growing in patches, damage the structure of the bone marrow and lead to bone loss, known as osteolysis.

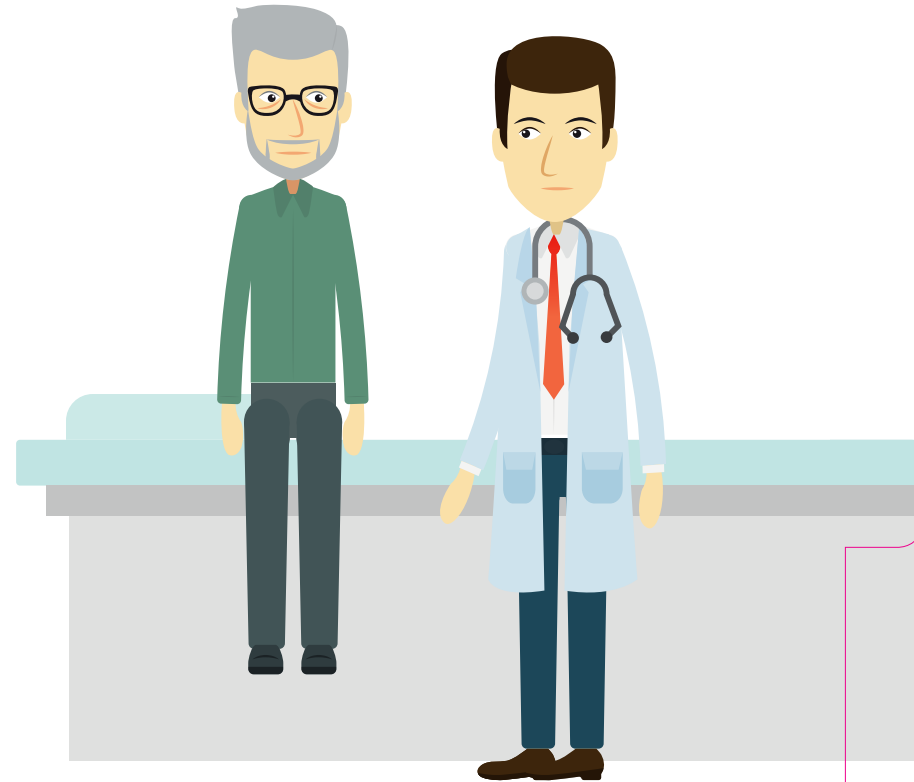
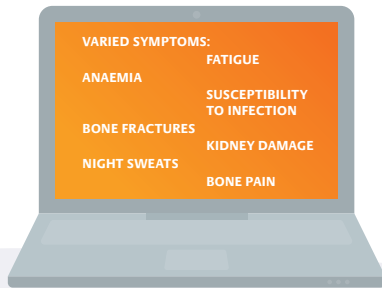
As a result, the bones become unstable at these sites, they can break and severe pain can occur.

In addition, the increased bone loss can disturb the calcium balance in the blood.

The varied symptoms of multiple myeloma

The symptoms of multiple myeloma can vary considerably, e.g. fatigue, anaemia, bone pain or frequent infections.

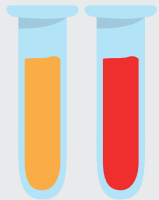
It is therefore important that the doctor carries out various investigations, in order to have a suspicion confirmed by the diagnosis and to determine the exact stage of the disease.



Possible investigations

Blood and urine investigations

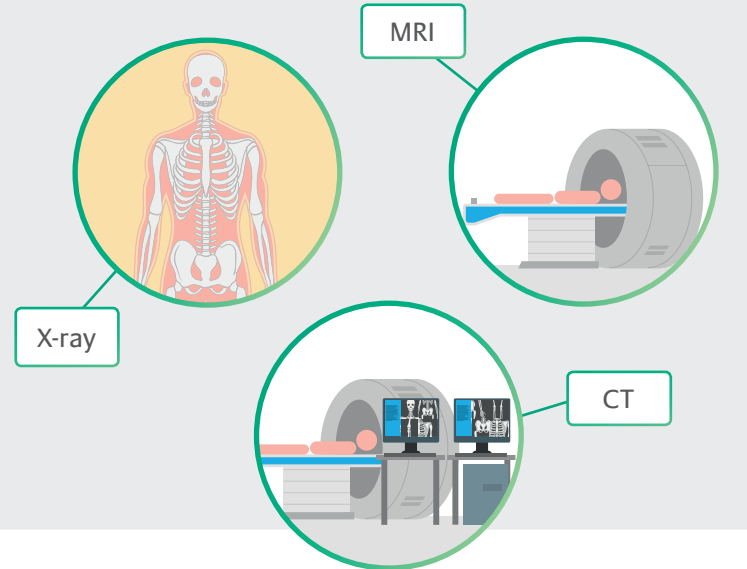
The results of blood and urine tests can give indications of multiple myeloma, because the M proteins and light chains, for example, can be detected here.



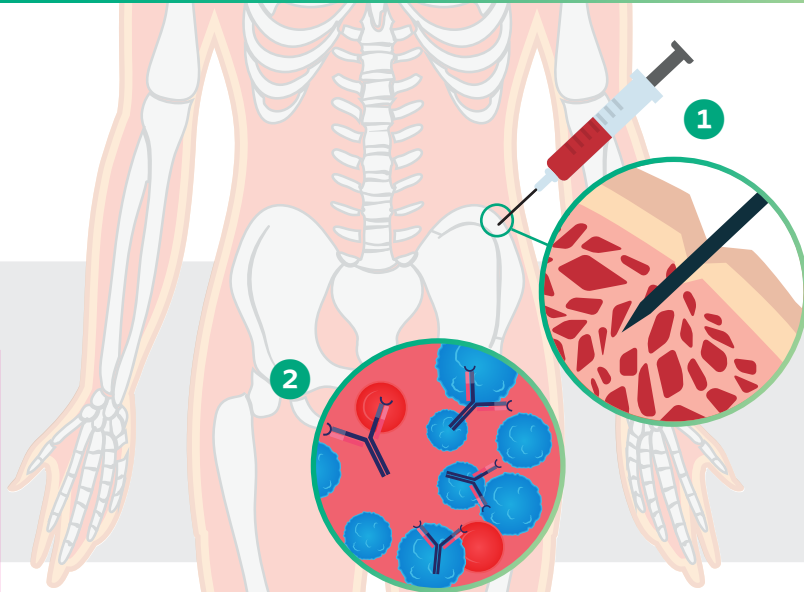
_____	CRP [C-REACTIVE PROTEIN]	_____
_____	DIFFERENTIAL BLOOD COUNT	_____
_____	SERUM ELECTROPHORESIS	_____
_____	BETA-2 MICROGLOBULIN	_____
_____	LLDH [LACTATE DEHYDROGENASE]	_____
_____	ALBUMIN AND FREE KAPPA AND LAMBDA LIGHT CHAINS IN THE SERUM	_____
<input checked="" type="checkbox"/>	_____	<input checked="" type="checkbox"/>
<input type="checkbox"/>	UREA	<input type="checkbox"/>
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Medical imaging

X-rays of the bones, computed tomography (CT) or magnetic resonance imaging (MRI) help to detect changes to the bone structure and accumulations of myeloma cells, known as patches.



Confirming the diagnosis by means of a bone marrow biopsy



Confirming the diagnosis

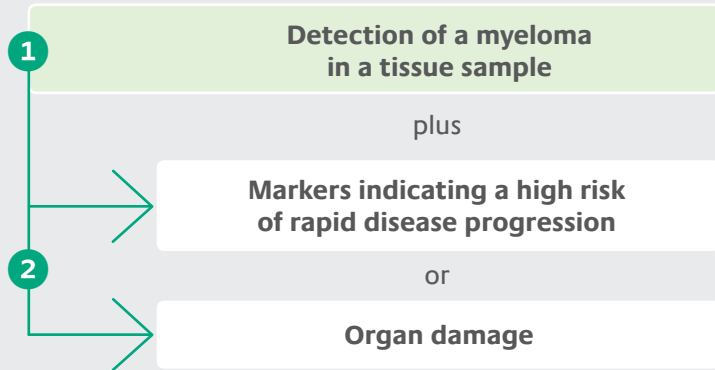
- 1 In order to confirm a diagnosis, a bone marrow biopsy is also necessary - on an outpatient basis, with an anaesthetic or under a general anaesthetic, if desired.
- 2 It allows the doctor to determine the proportion of degenerated plasma cells in the bone marrow.

Determining particular genetic features

By means of a biopsy, the doctor can also investigate the particular genetic feature of the disease. This can provide information about the possible course of the disease and potentially influence the choice of therapy.

The diagnostic criteria

New diagnostic criteria of multiple myeloma from the IMWG



Based on all the test results, the doctor can determine the precise diagnosis. This is based on the criteria of the “International Myeloma Working Group” (IMWG).

- 1 By means of a tissue sample, usually from the bone marrow, a certain proportion of myeloma cells is detected.
- 2 Either a so-called biomarker, indicating a high risk of rapid progression of the disease, or organ damage, according to the CRAB criteria, can be determined.



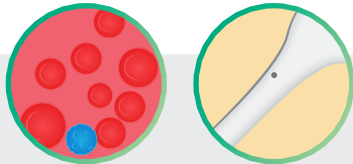
Once the diagnosis has been made, the disease is classified into stages.

The Durie-Salmon classification

The Durie-Salmon classification system divides the multiple myeloma into 3 stages after determining various values, in order to make a subsequent decision on whether treatment is necessary.

At Stages II and III, therapy is usually necessary.

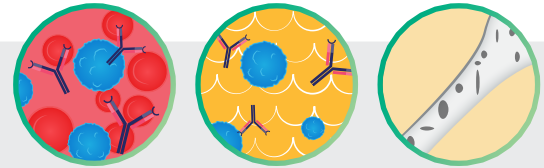
1



At Stage 1, no symptoms have yet occurred.

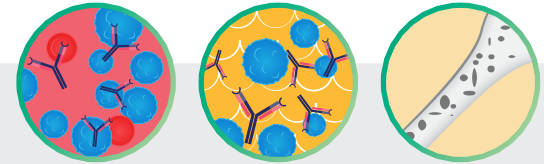
The only evidence of the disease are slightly altered blood values and a maximum of one lesion in the bones.

2



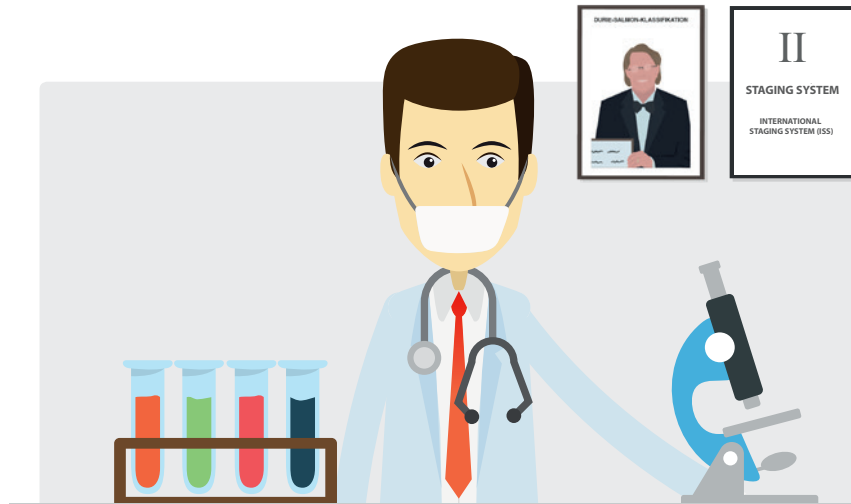
At Stage II, symptoms of the disease can occur. Blood values have changed and, in addition, more protein components are evident in the blood and urine. The bones already show signs of deterioration.

3



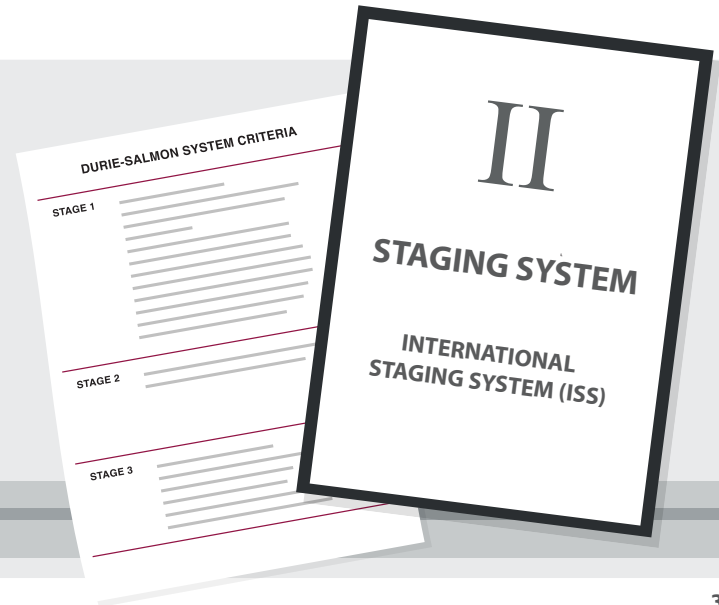
At Stage III, many myeloma patches are present or the blood values have changed greatly. In addition, very high numbers of non-functional protein components are found in the blood/urine or the bone loss is clearly visible at various places.

The International Staging System (ISS)

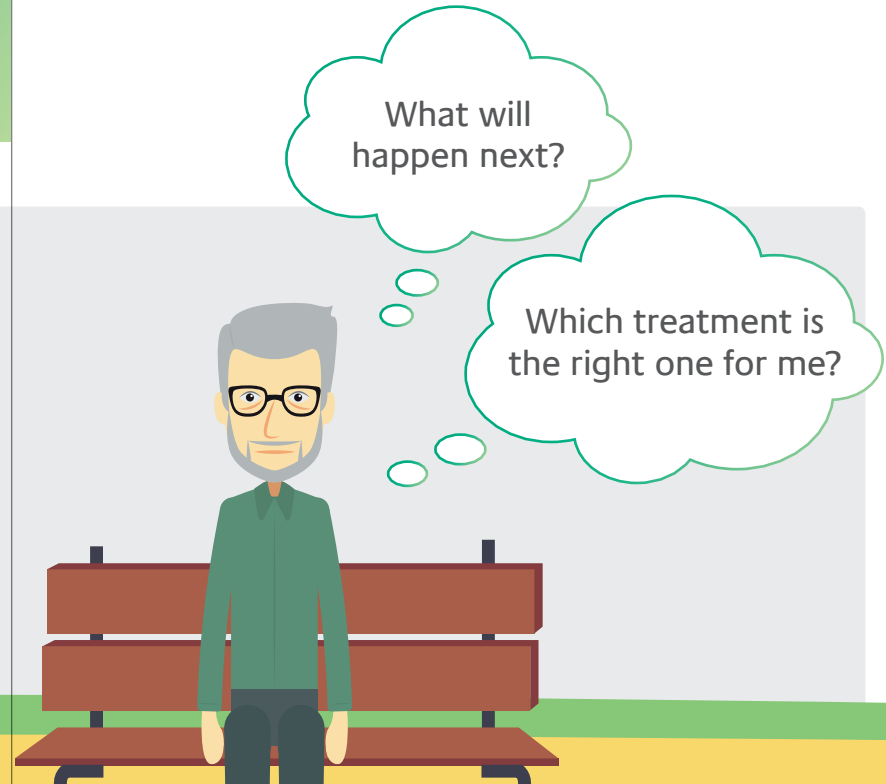


The “International Staging System ISS” determines the stage on the basis of certain blood values and also divides multiple myeloma into 3 stages.

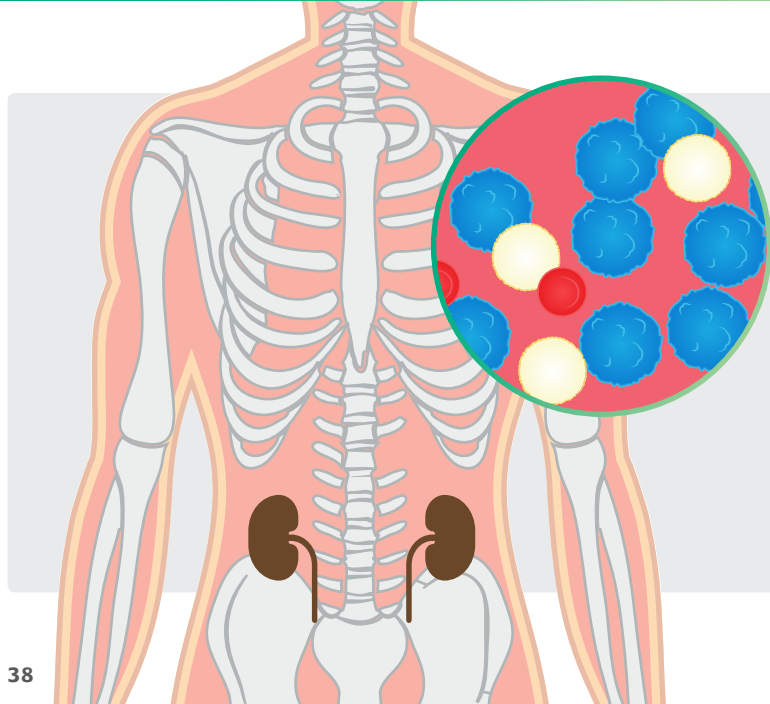
These give indications of how quickly the disease can progress.



Pressing questions after the diagnosis



When does multiple myeloma have to be treated?



Not every myeloma requires treatment. Treatment of multiple myeloma is usually only started if there is a risk of the disease leading to organ and kidney damage, i.e., for example, when at least one of the so-called “CRAB criteria” is met.

C

Increased calcium in the blood

C = Calcium

R

Impaired kidney function

R = Renal/kidney

A

Anaemia

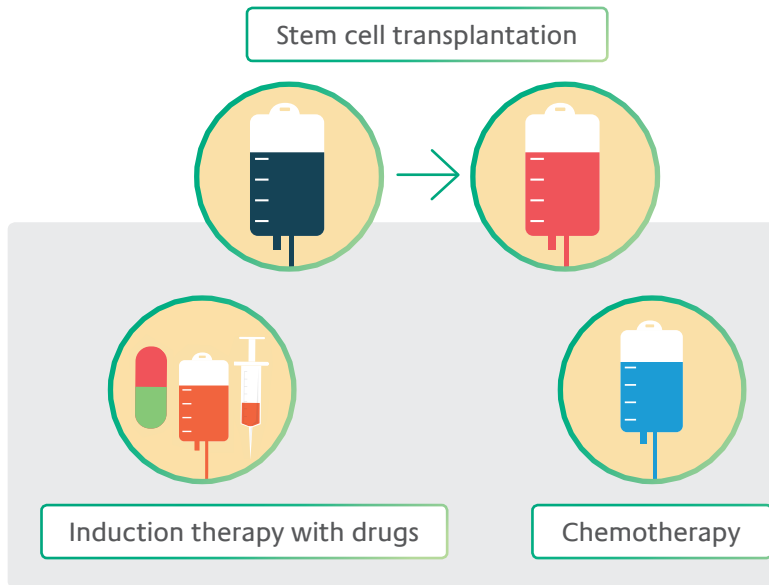
A = Anaemia

B

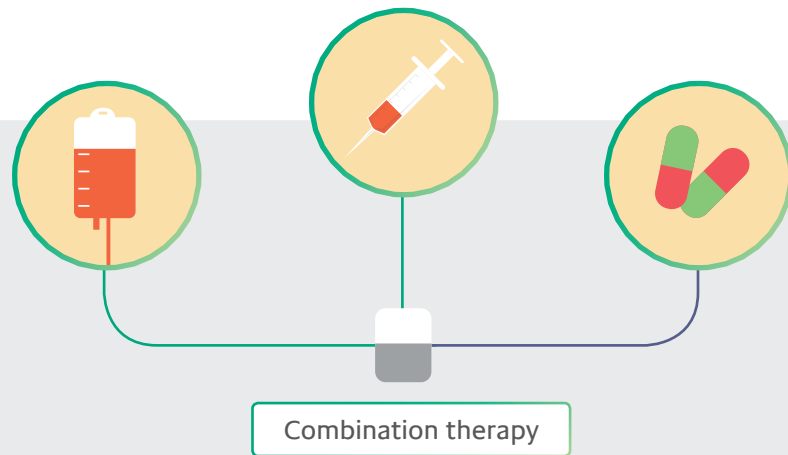
Bone damage

B = Bone

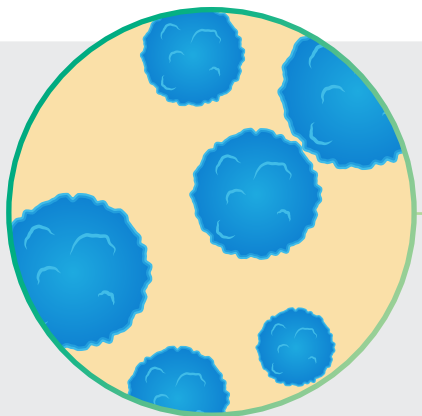
Therapy options



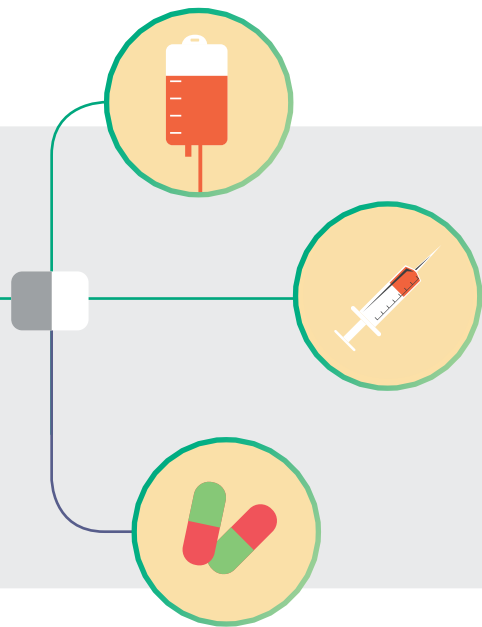
A wide range of treatment options is available, depending, for example, on the stage of the disease, the genetic change or the patient's physical condition.



Combination therapies



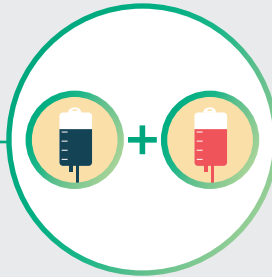
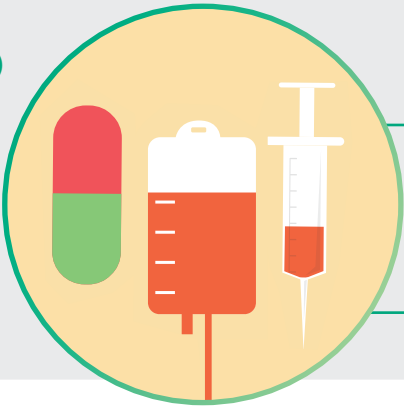
In order to achieve the greatest effect against the tumour cells, combinations of different medicines are often used, which attack the myeloma cells at various sites.



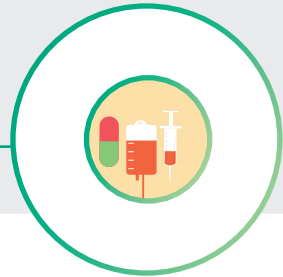
Induction therapy

- 1 An initial treatment, known as induction therapy, aims to suppress the multiple myeloma.
- 2 Subsequently, a decision can be made on how to proceed: One possibility is high-dose therapy with an autologous stem cell transplantation, i.e. with the patient's own cells. In addition, the therapy already started can be continued, possibly at a lower dose.

1

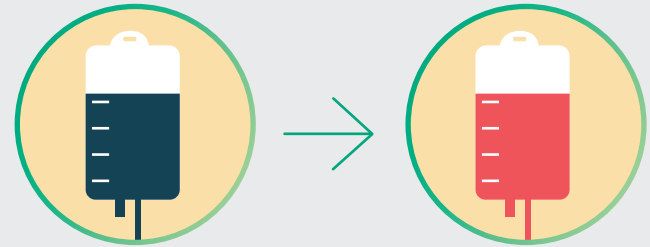


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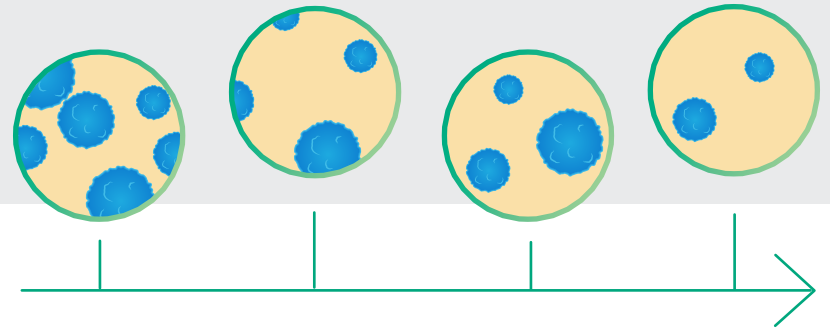


High-dose chemotherapy with SCT

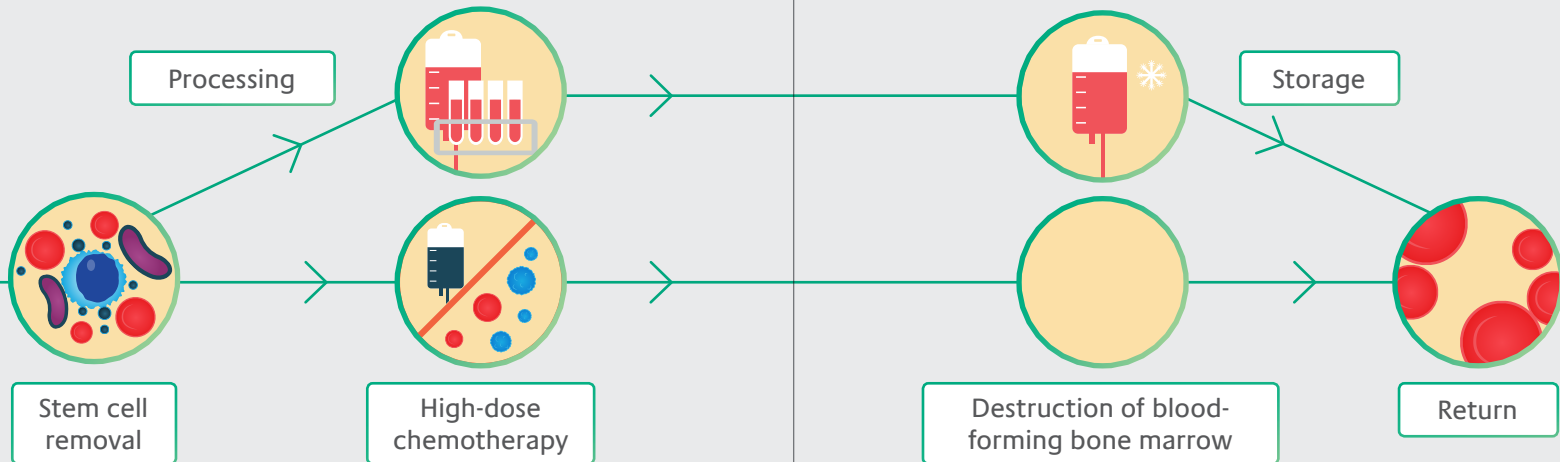
Today, high-dose chemotherapy with subsequent transplant of the patient's own stem cells, (autologous stem cell transplantation, SCT) is the standard therapy for patients in good general health, including the elderly.



It is a very effective therapeutic procedure:
Disease progression can often be delayed for a long period.



Autologous stem cell transplantation

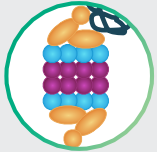


In order to try and destroy all existing tumour cells, a very high dose of chemotherapy is administered. In this process, the blood-forming bone marrow, i.e. including the healthy cells, is destroyed.

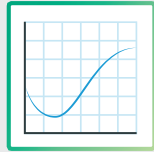
Before starting the high-dose chemotherapy, therefore, stem cells are removed from the patient's blood, the high-dose chemotherapy is then performed and the stem cells are returned after the end of treatment.

Innovative therapies and therapeutic approaches

Promising new substances:



1 Proteasome inhibitors



2 Immunomodulatory substances



3 Monoclonal antibodies



4 HDAC inhibitors



5 Chemotherapy

Intensive research has produced a number of new active substances and innovative therapeutic approaches in recent years. They have now become an important component of treatment and are often administered in combination. But traditional chemotherapies also remain firmly established in the treatment of multiple myeloma and are generally well tolerated.

How the different substances work:

- 1 Proteasome inhibitors block the breakdown of proteins in the myeloma cells and thus lead to their death
- 2 The role of immunomodulatory substances includes stimulating the body's own immune system against the myeloma cells
- 3 Monoclonal antibodies bind to special structures of the myeloma cells and thus cause the cells to die via various mechanisms
- 4 HDAC inhibitors inhibit various enzymes of the HDAC type and thus lead to the death of the myeloma cells
- 5 Chemotherapy blocks cell division, thereby leading to the death of the myeloma cells

Supportive treatments

Supportive treatments are used as an accompaniment to the chosen therapy.

Radiotherapy



Selectively destroys myeloma patches in the bone

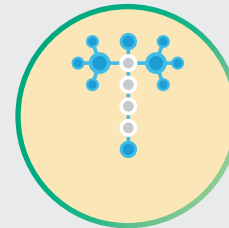
Aims: rapid pain relief, prevention of bone destruction

Bisphosphonates

Retain the calcium in the bones

Prevent the loss of bone substance

Aims: stabilisation of the bones, pain relief, prevention of bone fractures

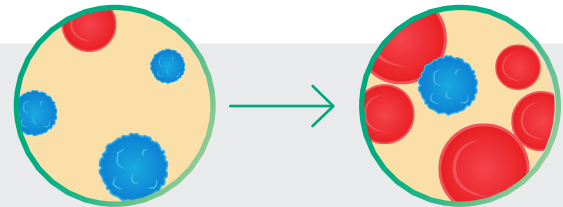


Follow-up examinations



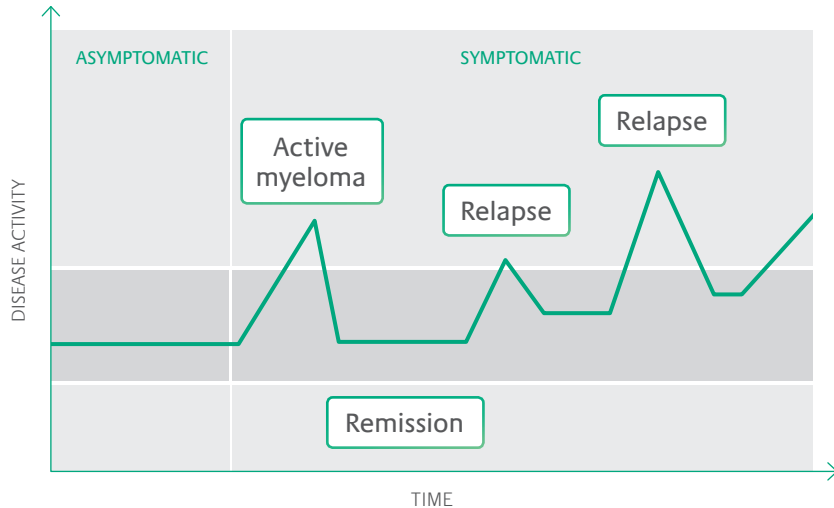
How well the tumour is actually responding to therapy can be checked by taking blood samples at follow-up examinations.

In addition to the blood values, it is becoming increasingly important to determine the residual cancer cells in the body, known as minimal residual disease.



Treating relapses

Typical course of the disease

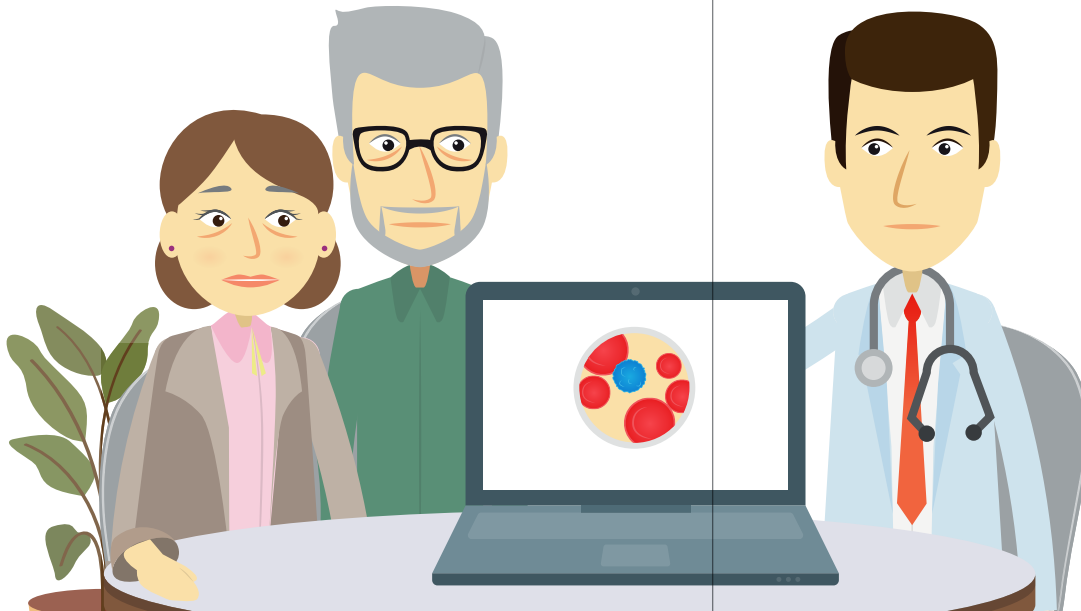


Multiple myeloma is usually a progressive and recurring disease. Despite intensive therapy after the initial diagnosis, the disease eventually recurs in most patients. This is known as a relapse.

Nowadays, a variety of modern treatment options are available for the therapy of such a relapse, which can at least temporarily halt the multiple myeloma again.

Achieving the treatment target together

As multiple myeloma is not yet curable, the aim of treatment is a rapid reduction in the disease symptoms and the optimal suppression of the multiple myeloma. In agreement with the patient, the doctor will decide which treatment method is most suitable for each patient, while also taking maintenance of their quality of life into account.



Notes and questions

Make a note here of questions for your doctor's appointment.



More brochures from this series
and our explanatory videos for
multiple myeloma can be found on:

**[www.takeda-onkologie.de/
multiples-myelom/service](http://www.takeda-onkologie.de/multiples-myelom/service)**

The videos are also available with subtitles
in English, Russian and Turkish.



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