

Allogeneic stem cell transplantation in myeloma

Treatments and tests Infosheet

This Infosheet provides information on allogeneic stem cell transplantation, a type of transplant using stem cells from a donor, which is occasionally considered in the treatment of myeloma.

What is the principle behind stem cell transplantation?

Chemotherapy is a group of drugs used in cancers including myeloma. High doses of chemotherapy are effective in killing myeloma cells. However, high doses also kill the blood-forming stem cells in the bone marrow. This results in blood cell production being severely affected causing potentially life-threatening problems.

High-dose therapy and stem cell transplantation (HDT-SCT) provides a solution to this drawback. It involves giving high doses of chemotherapy to kill the myeloma cells and then giving stem cells to the patient to 'rescue' the bone marrow. This allows the bone marrow to recover and blood cell production to continue. The aim of HDT-SCT is to achieve a deeper, more durable response and ultimately improve the quality and duration of life.

If the patient's own stem cells are harvested and then given back to them it is called an autologous stem cell transplant. This is by far the most common type of transplant carried out in myeloma.

More rarely, a patient may receive stem cells from a donor. This is known as an allogeneic stem cell transplant.

What is an allogeneic stem cell transplant?

For a small number of younger patients, an allogeneic stem cell transplant (SCT) may be considered. This is where stem cells from another person (a "donor") are used for the transplant. The donor will have stem cells which are as closely matched as possible to those of the patient.

Allogeneic SCTs aim to use the immune system of the donor to help fight against the patient's myeloma. This represents the main advantage of allogeneic SCTs compared to autologous SCTs – the donated stem cells have the potential to attack myeloma cells and delay or prevent relapse.

There are two main types of allogeneic transplant: full intensity allogeneic SCT and the mini-allogeneic (or reduced intensity) SCT.

Full intensity allogeneic SCT

Full intensity allogeneic SCT uses high-dose chemotherapy – either alone or in combination with total body irradiation (radiotherapy). As well as reducing the number of myeloma cells in the bone marrow, the high dose treatment strongly suppresses the patient's immune system. The patient's immune system needs to be suppressed to prevent it attacking or 'rejecting' the donor's immune system.

However, the very high doses of chemotherapy/radiotherapy used as part of a full intensity allogeneic SCT – in association with the serious side effects/complications that may occur – can be life-threatening.

The use of this type of allogeneic transplant is therefore limited in myeloma since, even in ideal patients, there is a high risk of treatment-related death.

Mini-allogeneic SCT

A mini-allogeneic (or reduced intensity) SCT involves giving lower doses of chemotherapy/radiotherapy than used in the full intensity allogeneic SCT.

The lower doses still suppress the immune system within the patient's bone marrow but to a lesser extent.

This aims to reduce the serious risks associated with the full intensity allogeneic SCT. However, mini-allogeneic SCTs are still associated with significant risks.

Whilst still uncommon, mini-allogeneic SCTs are performed more often than full intensity allogeneic SCTs in myeloma because of their improved safety profile.

A common way to receive an allogeneic SCT in the UK is about three to six months after having had an autologous SCT. This is sometimes called a 'double' or 'tandem' transplant.

Allogeneic SCT can also be performed on its own at relapse.

How is a donor matched to you?

Doctors search for a suitable stem cell donor who matches your tissue type, specifically your human leukocyte antigen (HLA) tissue type. HLAs are proteins – or markers – found on most cells in your body. Your immune system uses these markers to recognise which cells belong in your body and which do not. HLA tissue type can be determined through a simple blood test.

Donors may be related to you (usually a closely HLA-matched brother or sister) or unrelated (a volunteer donor who is not related to you but who is found to be a very close HLA match). Around one in three people have a close relative with a matching HLA tissue type. For those that don't have a matched related donor, bone marrow registers exist that include volunteers who are willing to donate their bone marrow stem cells if required.

Allogeneic SCTs using stem cells from matched unrelated donors can carry higher risks than when the donor is related, though the risks are reducing with improvements in post-transplant care.

Once a suitable donor has been found, their stem cells will be collected just before you are ready to receive them. The cells usually come from the donor's blood, or are sometimes taken directly from their bone marrow.

What will happen during the allogeneic SCT process?

At the beginning of the allogeneic SCT process, you will receive high-dose chemotherapy (e.g. cyclophosphamide, fludarabine or melphalan), possibly in combination with radiotherapy.

The exact treatments will depend on the intensity of the transplant and the preferences of the local transplant unit.

Within a day or so of receiving the high-dose therapy, the donor's stem cells are introduced into your blood system via an intravenous infusion (into a vein).

Once the donated stem cells are in the bloodstream, they travel to the bone marrow where they develop into new blood and immune system cells. Since these cells are not your own but your donor's, they can recognise myeloma cells as foreign and therefore attack them. However, the new immune cells can also potentially identify your normal cells as foreign and attack them. This is known as 'graft-versus-host disease' (described on page 5).

Until the stem cells have developed into new blood cells, you will be at risk from infection, bleeding/bruising, and anaemia. You will be closely monitored during this time, and preventive drug treatments will be given. You are also likely to be given blood transfusions and platelets, which will be specially treated to make them safe for you.

Given the greater potential for serious side effects and complications following an allogeneic SCT, the

supportive care and recovery period is generally longer than with an autologous transplant. You can expect to stay in hospital for around 4 – 6 weeks following an allogeneic SCT (longer in cases of serious side effects). There will also be more frequent trips to the transplant unit as an outpatient following an allogeneic SCT, with a recovery period of more than six months, depending on whether any late complications occur.

For more information about the processes involved in stem cell transplantation see the [High-dose therapy and autologous stem cell transplantation Infoguide](#) from Myeloma UK

What are the possible advantages and disadvantages of an allogeneic SCT?

Advantages

Allogeneic SCTs aim to use the immune system of the donor to help fight against the patient's myeloma. Consequently, the main advantage of an allogeneic SCT is that the donated stem cells have the potential to attack the myeloma cells – this is known as the 'graft-versus-myeloma' effect.

The graft-versus-myeloma effect is thought to be responsible for the prolonged period of plateau/remission that can be seen in some patients following an allogeneic SCT.

Disadvantages

The main disadvantage of an allogeneic SCT is the risk of graft-versus-host disease (GVHD), which is a potentially life-threatening condition. GVHD can occur when the donated cells not only attack the myeloma cells but also attack the patient's own body tissue. The risk of this happening is less when the donor is more closely matched to the patient. But it can occur even if the donor and patient are HLA-identical because the immune system can still recognise other differences between their tissues. Immunosuppressive drugs are given to limit this threat.

Acute GVHD usually develops within 100 days of transplantation whereas chronic GVHD usually develops later and lasts longer than acute GVHD. Both can cause mild to moderate symptoms, though potentially these can be serious and life-threatening.

Acute GVHD

Symptoms include:

- Red spots on the hands, feet and face which then spread across the body into a rash (which may then develop into blisters)
- Bloody or watery diarrhoea
- Stomach cramps, nausea or vomiting
- Jaundice – yellowing of the skin and whites of the eyes

Chronic GVHD

Chronic GVHD can affect almost any organ of the body, and patients may have symptoms affecting several organs. Common symptoms include:

- An itchy, dry rash that can spread over the entire body
- Dry and sensitive mouth
- Dry eyes
- Hardening of the skin
- Hair loss
- Breathlessness or cough

Patients will be monitored for GVHD and treated early to try to prevent severe GVHD from developing. GVHD is treated with drugs such as cyclosporine and corticosteroids which suppress the immune system. You may be given

other drug treatments as well if the GVHD is not improving despite the corticosteroids. All these drugs help to prevent the transplanted donor cells attacking the rest of your body. However, the drugs also affect the rest of your immune system, placing you at higher risk of infection. You will be given antibiotics and infection prevention measures. You may also receive treatments to help with specific GVHD symptoms.

How is allogeneic SCT currently used in myeloma?

Allogeneic SCTs are part of myeloma treatment in the UK for only a small number of younger patients, and investigations are still ongoing to determine their benefit. Most are carried out at the doctor's discretion, if a matched donor is available, or within a clinical trial.

Allogeneic SCT is more likely to be carried out in younger and fitter patients with high-risk disease and early relapse after their first myeloma treatment. The risks associated with the treatment are generally considered to be lower for younger and fitter patients who have a matched sibling donor and who have no other serious health conditions in addition to their myeloma. The upper age limit for a mini-allogeneic SCT is likely to be

about 55-60 years, although careful consideration of eligibility is on a patient-by-patient basis.

Allogeneic SCT is not considered to be a part of routine treatment as currently there is not enough evidence to show that it definitely benefits myeloma patients. Some studies show that allogeneic SCT is of benefit and can achieve long-term remission in some patients, whereas other studies suggest that the risk of complications such as GVHD, which can be serious or life-threatening, outweigh any potential benefit.

Deciding to have an allogeneic SCT

Treatment decisions that involve allogeneic SCTs are some of the most difficult for patients and their families. On the one hand, allogeneic SCTs have the potential to provide long-term remission in some patients. On the other, even in ideal candidates, side effects and complications can be life-threatening.

You should take as much time as you need before making a decision, carefully weighing up the pros and cons and seeking more than one opinion if you like. Myeloma UK can put you in touch with another patient who has had an allogeneic

SCT – please call the Infoline for more information if you think this would help. Our website also has discussion forums on different topics including SCT, which may be helpful.

Future directions

It is believed that allogeneic SCT has a role to play in carefully selected patients.

The challenge is how to make the procedure safer and more effective, and thus applicable to more patients.

This is the intention of current clinical trial research in this field.

A number of clinical trials are ongoing which are attempting to determine how best to use allogeneic transplantation in myeloma, including how to reduce the risks associated with GVHD and whether certain subgroups of patients may benefit more than others.

Ongoing research should also help to better define the role of allogeneic SCTs in the era of new and emerging drugs.

About this Infosheet

The information in this Infosheet is not meant to replace the advice of your medical team. They are the people to ask if you have questions about your individual situation.

For a list of references used to develop our resources, visit myeloma.org.uk/references

We value your feedback about our patient information.

For a short online survey go to myeloma.org.uk/pifeedback or email comments to myelomauk@myeloma.org.uk

Other information available from Myeloma UK

Myeloma UK has a range of publications available covering all areas of myeloma, its treatment and management. Download or order them from myeloma.org.uk/publications

To talk to one of our Myeloma Information Specialists about any aspect of myeloma, call our Myeloma Infoline on **0800 980 3332** or **1800 937 773** from Ireland.



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