

Allogeneic stem cell transplantation in myeloma

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?

Despite its effectiveness, a major drawback of chemotherapy is the inability to give high doses safely. This is because high doses not only kill the myeloma cells but also 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 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 stem cell transplantation is to consolidate the response to initial (induction) treatment, helping 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 a donor with a matched tissue type (usually a sibling) are used for the transplant.

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.

Currently, allogeneic SCTs are only part of myeloma treatment in the UK for 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.

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

Full intensity allogeneic SCT

The full intensity allogeneic SCT uses high-dose chemotherapy - either alone or in combination with total body irradiation (radiotherapy) - to suppress the patient's immune system and reduce the number of myeloma cells in the bone marrow. 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 than the full intensity treatment. This aims to reduce the serious risks associated with the full intensity allogeneic SCT. However, mini-allogeneic SCTs are still associated with reasonably 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.

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 have a very close degree of HLA-matching). 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/registries 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 supportive care.

Allogeneic SCT – an overview of the process

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 at relapse.

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 treatment approach will depend on the intensity of the transplant and the preferences of the local transplant unit.

As well as potentially killing myeloma cells, the high-dose therapy also suppresses the normal healthy blood-producing cells in the bone marrow and your immune system.

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).

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.

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 and potential to prevent relapse that can be seen following an allogeneic SCT compared to an autologous SCT.

Studies have also suggested that allogeneic SCT may help to overcome the effects of high-risk myeloma (a more active or more difficult to treat myeloma, often associated with certain genetic abnormalities).

That said, there is still much to be discovered about harnessing the effectiveness of allogeneic stem cell transplantation, and doing so safely.

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. This 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 can develop 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.

Symptoms of acute GVHD include:

- Red spots on the hands, feet and face which then spread across the body into a rash (which may then develop into blisters)
- A fever of 38°C (100.4°F) or above
- Bloody or watery diarrhoea
- Stomach cramps
- Jaundice – yellowing of the skin and whites of the eyes (although this is a rare symptom of acute GVHD)

Symptoms of chronic GVHD include:

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

Severe GVHD is treated with drugs such as cyclosporine and high-dose steroids

which suppress the immune system. These drugs stop 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.

Who is eligible for an allogeneic SCT?

Generally the risks associated with allogeneic transplantation are reduced for younger patients who have a matched sibling donor and who have no other serious health conditions in addition to their myeloma.

If a full intensity allogeneic SCT is considered a suitable treatment option, patients with a matched donor up to the age of 40 – 45 years and who achieved a good response (very good partial remission or better) to their autologous SCT may be eligible.

The upper age limit at most accredited centres for a mini-allogeneic SCT is 55 – 60 years of age, though careful consideration of eligibility on a patient-by-patient basis is necessary irrespective of age.

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. On the other, even in ideal candidates, side-effects and complications can be life-threatening and relapses can still potentially occur.

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.

Future directions

Allogeneic stem cell transplantation 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. All Myeloma UK publications are extensively reviewed by patients and healthcare professionals prior to publication. For a list of references used to develop our resources, visit www.myeloma.org.uk/references

Other information available from Myeloma UK

Myeloma UK has a range of Essential Guides, Infoguides and Infosheets available covering many areas of myeloma, its treatment and management.

To order your free copies or to talk to one of our Myeloma Information Specialists about any aspect of myeloma, call the **Myeloma Infoline: 0800 980 3332** or **1800 937 773** from Ireland.

The Myeloma Infoline is open from Monday to Friday, 9am to 5pm and is free to phone from anywhere in the UK and Ireland.

Information and support about myeloma is also available around the clock at www.myeloma.org.uk

Published by: Myeloma UK
Publication date: September 2013
Last updated: March 2017
Review date: March 2019

Myeloma UK 22 Logie Mill, Beaverbank Business Park, Edinburgh EH7 4HG
T: 0131 557 3332 **E: myelomauk@myeloma.org.uk** Charity No: SC 026116

Myeloma Infoline: 0800 980 3332 or
1800 937 773 from Ireland
www.myeloma.org.uk

Myeloma Awareness Week 21 - 28 June