

Donor Lymphocyte Infusion



What's involved



At all times patients should rely on the advice of their specialist who is the only person with full information about their diagnosis and medical history.

For further advice contact the clinical information team on 020 7269 9060.

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Introduction

This booklet has been written to explain treatment with donor lymphocytes after a bone marrow or stem cell transplant¹; a procedure called donor lymphocyte infusion (DLI). Not all of this information will be relevant to all patients. Patients should ask their treatment team about anything they are unsure about.

The aim of a stem cell transplant is either to replace diseased bone marrow with healthy functioning marrow or to restore marrow function after intensive anti-cancer therapy has destroyed the patient's original stem cells. When all new blood cells are derived from the donor stem cells, this is called full chimerism; sometimes there will be a mixture of donor and host stem cells, this is known as mixed chimerism. When a stem cell transplant is carried out for a haematological malignancy (blood cancer) the aim is to replace all the patient's marrow with donor cells i.e. achieving full chimerism.

¹ There is a separate publication on stem cell transplantation available from Leukaemia Research.

What are lymphocytes?

Lymphocytes are a type of white blood cell. A subset called T cells are used in DLI. Lymphocytes are vital components of the body's immune system; the defence against invading organisms. They help protect against infections by mounting an immune response to bacteria, fungi and viruses but they are also able to recognise abnormal or cancerous cells and kill them.

When a patient develops leukaemia or other type of blood cancer there is an excessive production of cancerous cells and this overwhelms the production of healthy blood cells, including lymphocytes. This means patients are prone to infection and are also unable to attack and destroy the leukaemia cells.

Why is DLI used?

Donor lymphocyte infusion is a procedure that can be carried out after a patient has received a stem cell transplant using donor stem cells.

The transplant consultant will decide if a patient needs to have donor lymphocyte infusions and when these should be given. Key differences between DLI and a stem cell transplant are that only lymphocytes (not stem cells) are collected from the donor. The patient does not require any conditioning treatment before receiving the donor lymphocytes, although if there are a large number of cancerous cells still present further chemotherapy may be given prior to the DLI infusion. For a CML patient, Glivec (imatinib) may be prescribed if there is haematological evidence of disease less than one year after transplant. This is usually continued until 12 months from transplant, when it is felt that the body is better able to tolerate DLI.

There are two main reasons why DLI may be given:

1) To destroy any residual disease

Patients are carefully monitored after a transplant to make sure that they are in remission. For some diseases there are very sensitive tests which show whether very low levels of the original blood cancer are still present. This is called residual disease. DLI may be considered if there is any residual disease after a transplant or if there are signs of relapse of the disease. Responses to DLI have been seen in patients with leukaemia, lymphoma and myeloma although the effectiveness varies from patient to patient.

The donor lymphocytes recognise the patient's cells as 'foreign' and can attack them causing a condition called graft versus host disease (GvHD), which may be severe and even life-threatening. However, there is also a beneficial aspect to this immune response by the donor cells because the same process can kill any residual leukaemia cells very effectively. This is known as the graft versus leukaemia effect (GvL).

2) To treat mixed chimerism

A mini-transplant uses lower doses of drugs and radiation to suppress a patient's immune system prior to a stem cell transplant from a donor. There is usually a stage in this approach when the patient has a mixture of their own and donor cells in the bone marrow. This is called mixed chimerism. This can happen even if the patient is in complete remission. If tests show that there is less than full chimerism then DLI may also be given to ensure that all the marrow cells originate from the donor. This may help to prevent the disease recurring in the future.

Collecting the donor lymphocytes

Donor lymphocytes are easy to collect from the blood of a donor as they are present in considerable numbers. No injections are required to increase the number of lymphocytes. The donor will be given a full physical examination and blood tests (including screening for viruses such as HIV and Hepatitis) that were undertaken before the bone marrow or peripheral blood stem cell harvest will be repeated. The donor will also have blood tests to ensure that there is no risk of clotting or bleeding problems before going on to the cell separator (apheresis) machine.

Specially trained nurses operate the apheresis machine. The donor has two intravenous lines put in, one in each arm. Blood is taken out via one line and goes through the machine. It is mixed with anti-coagulant to prevent the blood from clotting and to help separate the cells. The blood is spun in the machine and separated into red cells, white cells and plasma. Lymphocytes are collected by special pumps into a sterile bag attached to the machine. The remaining red and white cells and plasma are returned to the donor via the other line. The collection time can be two to three hours with a total lymphocyte volume of about 200mls (approximately one cupful).

The collection bag is then separated from the machine, labelled and taken to the laboratory to be checked and have cell numbers counted. Usually just one collection is required and the lymphocytes are frozen down in several small bags which contain different doses of cells. However, it is possible that the donor may need to go through this process again.

Donor and patient

If the donor and the patient are related an appointment will be given for a chosen day when both people can come to the hospital. An unrelated (volunteer) donor will be asked to attend a convenient hospital where apheresis facilities are available.

If the unrelated donor has not met the patient, but the cells are to be collected at the same hospital, it is important to respect the anonymity of both parties. This means that they will not be in the department at the same time. In the future, when treatment has been successful, both the patient and the donor may want to consider meeting. However some bone marrow registries will not allow this while others specify a minimum time period and will only permit the patient to instigate contact.

Receiving DLI

At some stage before receiving DLI the patient will have a full physical examination, a full blood count and a bone marrow biopsy in order to get a full picture of the stage or amount of disease present before starting the DLI. Blood tests will also be taken to check the function of other organs in the body, such as the kidneys and liver, and to screen for viruses.

A small line is inserted into a vein in the arm. This is temporary and will be removed before going home. The infusion can be given through a central line if there is one already in place. The donor cells will have been collected in the morning, however it is possible that cells will not be ready to be given to the patient until late afternoon, so it can be a long day.

The cells are given slowly over 10 to 30 minutes through a line or in a syringe depending on the number of cells being infused. If the cells have been frozen then there is a small chance of reacting to the preservative called DMSO. When the infusion is over the lines are taken out or the central line is flushed.

A doctor will supervise the procedure and check that there are no reactions to the infusion. An injection of anti-histamine is given before the infusion to minimise the risk of reaction. This may cause drowsiness so it is advisable not to drive to and from the appointment. Sometimes the patient needs to sleep off the effects of the anti-histamine before leaving. If the infusion is given late in the day then an overnight stay might be necessary.

It is very unusual for there to be any reactions to the transfusion but the nurses will be present at all times. Patients should not hesitate to tell them if they experience any discomfort or are worried about anything. A doctor is always available.

Side effects

GvHD

The ‘graft versus leukaemia’ (GvL) effect is part of the immune reaction against host tissues and therefore some GvHD is to be expected following DLI. It is important to note that the amount of GvHD does not correlate to GvL or the effectiveness of the DLI.

The early signs of GvHD are:

- Rashes or redness of the skin, most commonly on the hands and feet or around the neck and the top of the back.
- Upset stomach or loss of appetite, sickness or diarrhoea.
- The lining of the mouth and tongue can become sore and infections may develop in the mouth.
- Blood tests which show alterations in the function of the liver.

A doctor will decide if any treatment is needed. It is important to report any symptoms that develop either at clinic appointments or by telephone if the next clinic visit is some time away.

Treatment of GvHD might suppress the GvL response. For this reason medication to suppress GvHD is avoided if possible. Some patients with GvHD will only require monitoring as an outpatient while others will require treatment in hospital. Any drugs being given to suppress GvHD from the original transplant will usually have been stopped in preparation for DLI. If this has not been possible because of the need to control GvHD, the use of these drugs will be reviewed at each outpatient visit.

Low blood counts

DLI can suppress the bone marrow (myelosuppression), which leads to a reduced number of blood cells. This can lead to a range of symptoms including anaemia, increased bruising and bleeding and susceptibility to infection. If the red cell count or platelet count is low then this is monitored and infusions of red cells or platelets are given when necessary.

If the white cell count is very low then it may be necessary to check blood counts more regularly and monitor for any problems, such as infections. Most patients will continue to take antibiotics. There may be additional advice about preventative measures against serious infections such as pneumonia. If the low white cell count continues then G-CSF (a growth factor to help increase the number of white cells) may be prescribed.

If blood counts do not recover, usually over a period of seven to ten days, then it may be necessary to have a 'top-up' of stem cells (the cells given during the original transplant) from the donor, although this is rare. This will involve being admitted to hospital, for the infusion and close monitoring, until the cell count recovers and there is no longer a risk of infections and problems from low platelets. This could be for a period of two to four weeks.

The care team will explain about any extra precautions that may be necessary to take in the home. It should be perfectly safe to be at home with low blood counts if advice given about diet and hygiene is followed. Do not hesitate to ask for advice on this important topic.

Follow-up

It is very important that progress is monitored carefully by the transplant team, who have the experience to assess progress and recognise potential problems.

This means attending an outpatient clinic every two to four weeks, during the first three or four months after the first DLI. As before, blood samples will be taken and the doctor will do a physical assessment and discuss any side effects. It is unlikely that there will be any change in blood tests in the first one to four weeks but it is still important for blood samples to be taken. In fact, very little may feel different during this time.

Further doses of donor lymphocyte

Approximately eight weeks after the dose of donor lymphocytes has been given, the response is assessed in terms of the disease or chimerism status.

If there is still evidence of disease being present or if there is still mixed chimerism, and there has been no significant GvHD, then another slightly higher dose of donor lymphocytes may be given. Further doses are usually given at three monthly intervals. Sometimes several doses of donor lymphocytes are given until the desired effect is reached or until significant GvHD develops.

Support information

DLI offers the chance of curing disease without the huge upheaval of coming into hospital for long periods and without the risks and side effects associated with a repeat transplant. Unlike the transplant, this treatment may not have a significant impact on daily life. For some patients it is possible to work throughout the treatment, for others working or travelling may be difficult. Most patients are at home throughout most of this time and although this is better than being in hospital, it can leave people feeling vulnerable.

There should always be someone for patients to talk to such as support nurses or a doctor in-between clinic visits. If it is an emergency the haematology department should be contacted directly to speak to the haematologist on call. DLI therapy can take several months before the doctor can tell if it has been successful, so a positive approach is essential.

Please use the space below to record the contact details of your care team:

Support Nurses:

Haematology Outpatient Department:

Haematologist on call:

The following patient information booklets are available free of charge from Leukaemia Research. You can download them from our website or request copies by phone or post (see form inside):

Leukaemia and Related Diseases

Acute Promyelocytic Leukaemia

Adult Acute Lymphoblastic Leukaemia (ALL)

Adult Acute Myeloid Leukaemia (AML)

Aplastic Anaemia (AA)

Bone Marrow and Stem Cell Transplantation (BMT)

Childhood Acute Lymphoblastic Leukaemia (ALL)

Childhood Acute Myeloid Leukaemia (AML)

Chronic Lymphocytic Leukaemia (CLL)

Chronic Myeloid Leukaemia (CML)

Hodgkin's Lymphoma (HL)

Multiple Myeloma (MM)

Non-Hodgkin's Lymphoma (NHL)

The Myelodysplastic Syndromes (MDS)

The Myeloproliferative Disorders (MPD)

Clinical Trials

Chemotherapy – what do I need to know?

Donating stem cells – what's involved?

Donor Lymphocyte Infusion (DLI) - what's involved

Supportive care

The Seven Steps – Blood & Bone Marrow Transplantation

Young Adults with a blood cancer – what do I need to know?

Jack's Diary: an illustrated children's book to help young patients understand and deal with blood cancers, treatment and life changes

Leaflets on a range of associated blood disorders are also available

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