

Donor Lymphocyte Infusion (DLI)

Information for patients



Leeds Cancer
Centre

This booklet has been written to explain, a procedure called Donor Lymphocyte Infusion (DLI). Not all of this information will be relevant to you. Patients should ask their treatment team about anything they are unsure about.

The aim of an Allogeneic stem cell transplant is to replace diseased bone marrow with healthy functioning marrow. 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 (patient) 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.

What are Lymphocytes?

Lymphocytes are a type of white blood cell. Subsets called T cells are used in DLI. Lymphocytes are vital components of the body's immune system. 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.

Why is DLI used?

DLI 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.

There are two main reasons why DLI may be given:

- **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 Measurable Residual Disease (MRD). DLI may be considered if there is any residual disease after a transplant or if there are signs of relapse of the disease.

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 Tumour (GvT) effect.

- **To treat mixed chimerism**

A reduced intensity 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. It is important to note that the chimerism can be 100% and then fall after a period of time. The transplant team will monitor the chimerism in all patients after allogeneic transplant up to one or sometimes two years after the transplant

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). 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.

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.

Sometimes the transplant centre will have been able to collect donor lymphocytes at the time of the original stem cell harvest and freeze and store these. If this is the case then there will be no need to collect additional cells.

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. If fresh donor cells are being collected, this will have been done in the morning, however it is possible that fresh cells will not be ready to be given to the patient until late afternoon.

The cells are given slowly over 10 - 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 nurse 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. 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.

Side-effects

Graft versus Host Disease (GvHD)

The 'Graft versus Tumour' (GvT) 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 GvT or the effectiveness of the DLI.

The early signs of GvHD are:

- Rashes or redness of the skin.
- 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.

Your team 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 GvT 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.

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, 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.

The healthcare team will explain about any extra precautions that may be necessary to take in the home.

Follow-up

It is very important that progress is monitored carefully by the transplant team, who have the experience to assess 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 first 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

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.

Please use the space below to record the dates and times of your DLI infusions or any questions you may have:

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