IPOPI
INTERNATIONAL
PATIENT ORGANISATION
FOR PRIMARY IMMUNODEFICIENCIES

PRIMARY **IMMUNODEFICIENCIES**

# HAEMATOPOIETIC **STEM CELL TRANSPLANTATION**

## KEY ABBREVIATIONS

| | |
|---|---|
| CID | Combined immunodeficiency |
| GvHD | Graft-versus-host disease |
| HSCT | Haematopoietic stem cell transplantation |
| IPOPI | International Patient Organisation for Primary Immunodeficiencies |
| PID | Primary immunodeficiency |
| SCID | Severe combined immunodeficiency |
| BMT | Bone Marrow Transplant |
| HSC | Haematopoietic stem cell |

Primary immunodeficiencies and hematopoietic stem cell transplantation (1st edition).



Published by IPOPI: www.ipopi.org

# INTRODUCTION

**This booklet explains how haematopoietic stem cell transplantation (HSCT) can help some people with primary immunodeficiencies.**

Primary immunodeficiencies (PIDs) are rare diseases that occur when components of the immune system are either not present or not functioning normally. The immune system is a complex system that protects the body from infections, immune dysregulation (autoimmunity, allergies) and malignancies. When it is not functioning normally, the body is susceptible to recurrent infections, autoimmunity or malignancies, which can be life-threatening.

Haematopoietic stem cell transplantation (HSCT) may, for some patients, correct the underlying dysfunction of the immune system. However, there are a number of risks associated with the procedure itself and not all patients will be suitable candidates for this type of intensive treatment.

The following sections explain in more detail who might be eligible for this type of treatment, the risks associated with the procedure and the long-term effects patients can expect.

# WHAT IS HAEMATOPOIETIC STEM CELL TRANSPLANTATION?

## WHAT IS HSCT

HSCT, also known as bone marrow transplantation, is a potential cure for certain PIDs although it is not currently available in all countries.

The process involves harvesting the bone marrow (BMT) – the soft spongy tissue found in the center of the bones – from a donor and introducing it into a person with PID. The bone marrow contains the stem cells that are responsible for making the three main types of blood cells (red cells, white cells and platelets) including the cells of the immune system. By collecting the stem cells from a healthy donor and giving these to a person with PID it is expected that the healthy stem cells will take up residence in the recipient's bone marrow and start to generate healthy immune cells capable of fighting infections.

The actual process can take 3–4 months or more during which time the person receiving the transplant must remain in hospital and, for part of that time, in an isolation room to protect them from infection while the transplanted cells settle into their new home. A conditioning regimen (usually consisting of chemotherapy, sometimes combined with immunotherapy, but rarely with radiation) precedes the actual procedure by around 2 weeks.

Further information about HSCT can be obtained from organisations such as the Anthony Nolan Bone Marrow Trust (**https://www.anthonynolan.org/**) in the Uk, the Bone Marrow Trust (**http://bonemarrow.org/**) in the US and the **World Marrow Donor Association**, based in The Netherlands, but with worldwide scope.

## WHO MIGHT BE SUITABLE FOR HSCT?

The most suitable PIDs that can be treated with HSCT include severe combined immunodeficiency (SCID), combined immunodeficiency (CID), HLA class II deficiency, disease of immune dysregulation and a range of other well-defined PIDs such as Wiskott-Aldrich syndrome and Chronic Granulomatous Disease.

For early onset conditions such as SCID, the greatest success occurs when the transplant is carried out within the first few months of life, before major infections occur, making the early diagnosis of PIDs vital. For older children or adults, the best outcomes are for those with limited damage to organs such as the liver, heart and lungs from the infections associated with PIDs.

## WHO COULD BE A DONOR FOR SOMEONE UNDERGOING HSCT?

The person donating their bone marrow (the donor) is usually a 'match' for the person who will receive it (the recipient). This means that they share the same tissue type, and this reduces the risk of the recipient's body rejecting the donor bone marrow and destroying it before it can take up residence in the bone marrow – a condition called graft-versus-host disease (GvHD). The donor can sometimes be a mismatch donor (down to a semi-match donor in case one parent is used as the donor, in that case, it is called a haplo-identical donor).

Siblings of the person with PID are the best matched in terms of tissue type although well-matched unrelated or mismatched (related or unrelated) donors can also often be found. Bone marrow transplants have been successfully carried out with matched siblings since 1968.

## WHAT ARE THE RISKS ASSOCIATED WITH HSCT?

The main risks associated with HSCT are infection, GvHD, rejection or failure of the transplant and death (there's a higher risk of death during the first week post-HSCT).

Before a person can receive the donor's Haematopoietic stem cells (HSC), their defective bone marrow must be removed to make space. This is called the conditioning period and is achieved using powerful chemotherapy drugs, after which the person has no protection at all against infections until the donor cells start to generate healthy new immune cells. This process can take up to a maximum of 6 months during which time the person remains at risk from serious infections and might need to take prophylactic antibiotics and immunoglobulins.

GvHD can cause problems usually with the skin, liver and bowels. For this reason, the recipient often has to take drugs to modulate their immune system while the new immune cells grow and mature.

Failure of the transplant occurs when the HSCs do not engraft or when the recipient's residual immune system rejects and destroys the new cells.

Given the potentially serious consequences, the risks and benefits of HSCT must be considered on an individual basis and discussed with the attending physician (including the potential dangers of HSCT in people with little or no immune cells, such as PID patients).

# THE IMPORTANCE OF A SUPPORT NETWORK

HSCT is an intensive and prolonged intervention that requires extended hospital stays. For this reason, it is important for patients to have a network of family and friends who can support them, and each other, through this intensive treatment. Such a network may be particularly important for patients who need to travel outside their home country to receive treatment as they are likely to be away for weeks or even months.

# IS HSCT A CURE FOR PIDs?

## CAN HSCT CURE PIDs?

The outcomes for patients with PIDs who receive a HSCT from a matched sibling or well-matched unrelated donor are very good. However, as with any complex procedure there is always the risk that the procedure will fail and a second HSCT procedure may be required. The reasons that HSCT may fail depend on many factors and the possibility of a second procedure will depend on the patient's status and the reasons for the initial failure.
Even after a successfull HSCT procedure, patients with low or poor B cells count might still require immunoglobulin replacement therapy.

## WHAT ARE THE ADVERSE EFFECTS OF THIS TREATMENT?

The adverse effects of HSCT relate mainly to the occurrence of GvHD which can lead to skin rashes, hair loss, dry eyes, conjunctivitis, mouth ulcers, lung and liver damage, arthritis and chronic nausea/vomiting. Long-term potential complications include hypofertility, endocrine issues and secondary malignancies.

# WHAT IS BEING DONE SO THAT MORE PEOPLE CAN ACCESS HSCT?

SCID newborn screening campaigns and improved diagnosis of PIDs in early childhood have enabled more patients to be evaluated for HSCT. New conditioning regimens have improved the effectiveness of the initial stage of removing the dysfunctional bone marrow. New and improved supportive care continues to alleviate the adverse effects of the procedure so that more patients can access HSCT as a potential cure.

National and regional policy makers should take measures to foster the creation and improvement of HSC donor registries as this will facilitate patient's access to treatment.

## OTHER CURATIVE TREATMENTS

Gene therapy, while not currently available everywhere, holds potential as an alternative curative treatment for some patients with PID, especially when there aren't matching donors. The first ever licensed gene therapy product has been available since 2016 in the European Union for the treatment of SCID ADA.

The SCIDNet (**https://scidnet.eu/**) and Recomb (**http://www.recomb.eu/**) programmes are actively developing gene therapy for the treatment of SCID and it is hoped that this approach will be available for patients within the next few years.

## HAEMATOPOIETIC STEM CELL TRANSPLANTATION FOR PIDs

- HSCT offers a potential cure for patients with otherwise fatal PIDs.
- HSCT is an invasive procedure not suitable for all patients.
- Suitably matched or closely matched donors are considered to be the best donors for the success of HSCT.
- Early diagnosis of PIDs before significant damage is sustained from infections and evaluation for HSCT is essential to achieve the best outcomes for patients with PIDs.

# FURTHER INFORMATION AND SUPPORT

This booklet has been produced by the International Patient Organisation for Primary Immunodeficiencies (IPOPI). Other booklets are available in this series. For further information and details of PID national patient organisations active worldwide, please visit **www.ipopi.org**.

Shire

Supported by an educational grant from Shire.