

General information for patients, families and carers considering Haematopoietic Stem Cell Transplantation (HSCT) for a severe autoimmune disease (AD):

A position statement from the EBMT Working Party for Autoimmune Diseases and JACIE

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Autoimmune Diseases (ADs): what are they?

Autoimmune diseases are a broad group of illnesses where body's immune system reacts against its own tissues and organs. The immune attack is followed by chronic inflammation and abnormal healing and scar tissue, which may be associated with permanent damage, disability, and poor quality of life. In some cases, severe ADs may shorten life expectancy or even be immediately life-threatening.

The types of tissues and organs affected vary between ADs. For example, systemic sclerosis, lupus, vasculitis and other connective tissue diseases affect many organs, typically causing inflammation and scarring of the skin, heart, lungs, kidneys and other organs. Multiple sclerosis (MS), affects the brain and spinal cord, whereas Crohn's disease affects the gut.

Treatment with immunosuppressant drugs, disease modifying treatments (DMTs) and steroids may be successful in controlling the AD, but there is an increased susceptibility to infection and organ damage, which add to the problems of living with an AD.

Some patients have very aggressive forms of AD and are poorly controlled by standard therapies. In some of these severely affected patients, there may be benefit in considering bone marrow transplantation, or, as it is now more commonly known, haematopoietic stem cell transplantation (HSCT).

Haematopoietic Stem Cell Transplantation (HSCT) for Autoimmune Diseases (ADs): background

HSCT is commonly used for the treatment of serious blood diseases, including leukaemia, myeloma and lymphomas. Many haematology departments will provide it as a routine treatment in most European countries for these common indications. It involves giving high doses of chemotherapy and/or radiotherapy and then use blood or bone marrow derived (i.e. 'haematopoietic') stem cells from the patients themselves ('auto-transplant') or from donors ('allo-transplant') to rebuild the bone marrow and immune system, hopefully without the malignant disease.

Over the last 20 years, HSCT has also been used to treat severe ADs, as it is an effective means by which to suppress the abnormal inflammation and scarring and re-build an altered immune

system which does not regenerate the AD, or leads to a milder form and better disease control. To date, over 3000 patients with ADs have been treated worldwide with HSCT, with around 2000 patients registered in Europe. The main ADs treated are currently relapsing remitting MS, systemic sclerosis, lupus and other connective tissue diseases, and Crohn's disease, but other rarer immune disorders have been treated in smaller numbers.

It should be emphasized that HSCT is not a form of 'regenerative' stem cell therapy in the same way as many scientists hope that stem cells may be used to rebuild new organs. Although HSCT is common in many haematology departments, its use in ADs is relatively rare and only a small number of transplant centres in each country have a good level of experience in working with disease specialists to select the most appropriate patients with AD and then delivering the HSCT treatment as safely as possible.

The type of HSCT virtually always used in severe ADs is 'auto-transplant', which is more safely delivered than 'allo-transplant', which is a much more complex procedure requiring a donor. Even so there are significant risks and toxicities with 'auto-transplant', which are an important consideration, especially if the AD has already caused significant organ damage and disability. In view of these toxicities and risks, it is very important that patients have a full discussion with their haematology and autoimmune disease specialist teams. Ideally, the transplant centres should have external accreditation (by JACIE) and have a good track record of experience and academic publication in the disease for which HSCT is being considered.

It is too early to say whether HSCT is curative in severe ADs, but some patients have had very profound responses lasting many years, far more than expected from treatment with standard therapies. The response is dependent on the specific AD and the stage of the disease when it has been treated e.g. the disease process has been 'switched off' before it became irreversible or caused permanent damage. The benefit of HSCT in some ADs (Systemic Sclerosis, Multiple Sclerosis and Crohn's disease) has been shown in some ADs have been in randomized controlled trials against the best available conventional therapy. However, there is always need for more evidence to help improve outcomes, and, where possible, patients should be treated on ethically approved clinical studies.

Specific advice to patients considering HSCT for their autoimmune disease

The European Society of Blood & Marrow Transplantation (EBMT) has published guidelines and recommendations for the use of HSCT in autoimmune diseases (see reference below). Whereas these guidelines are primarily intended for a professional readership and therefore written in a technical language, they are openly accessible to all to read.

The EBMT recommend that you can ask your haematologist and disease specialist to explain any aspect of the guidelines, including whether you are being treated in line with the published recommendations. One exception is treatment on an ethically approved clinical trial, which may, for example, be testing whether a new technique might provide an advantage over existing treatments. In this instance, you will be counseled to provide fully informed consent for the trial.

Your clinicians should be active in the EBMT and/or other national and international professional societies, which means that they should follow published guidelines, report their outcomes to the EBMT (or equivalent professional society) and maintain their professional competencies in this highly specialized field.

You should also ask your haematologist and disease specialist about the experience of their transplant unit in general, whether the transplant unit is accredited (by JACIE or equivalent) and their specific experience of treating your AD with the HSCT approach. Importantly, you should ask about short and long term side-effects of the treatment and the level of risk of death from the treatment and the severe AD so that you can make a balanced decision. You may also want to ask for an independent specialist opinion or whether your case has had a documented discussion with a wider group of professionals within a multidisciplinary setting. Even if you are not on a clinical trial, full informed consent for treatment and also for data reporting is an EBMT requirement for good clinical practice.

If you are planning treatment outside your home country, you should ask yourself why the treatment is not available within your own health service. It may be that treatment is available under specific circumstances that do not cover your specific illness or your disease specialist may not consider it as the best option. If so, think carefully about your decision, as it may affect you not only financially, but you may also be exposing yourself to unnecessary risks. If treatment is unavailable in your home country, it is more satisfactory if you travel and receive treatment with the full support of a disease specialist and haematologist in your home country. This may enable direct communication with haematology and disease specialist teams undertaking the transplant. Even if the initial phase of the transplant is a success, you should be aware that risks of treatment, such as infection risk and organ damage last for many months and years after the transplant procedure. Ongoing follow up and support is recommended, along with the need for rapid self-referral to a haematology unit in case of infections and other emergencies. These aspects may be compromised if treatment is delivered outside of your country of origin, especially if communication between clinicians is limited.

For more information or any request, please send an email to Manuela Badoglio, ADWP Study Coordinator at the EBMT Paris office: manuela.badoglio@upmc.fr
Manuela will forward it to the relevant disease specialist working in the nearest hospital from your home address.

You are also welcome to join the next EBMT Annual Meeting – www.ebmt2016.org – and participate in the Patients, Family and Donor Day or attend the scientific sessions which would be of interest for you.

REFERENCE

Snowden JA, Saccardi R, Allez M, Ardizzone S, Arnold R, Cervera R, Denton C, Hawkey CJ, van Laar JM, Labopin M, Mancardi G, Martin R, Moore JJ, Passweg J, Peters C, Rabusin M, Rovira M, Farge D on behalf of the EBMT Autoimmune Disease (ADWP) and Paediatric Diseases (PDWP) Working Parties. Haematopoietic stem cell transplantation (HSCT) in severe auto-immune diseases (ADs): updated guidelines of the European Group for Blood and Marrow Transplantation (EBMT). *Bone Marrow Transplantation* 2012;47:770-90.