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About the European Group for Blood and Marrow Transplantation

Mission and activities

The EBMT is the leading, non-profit, scientific society representing 563 transplant centres from 57 countries in and outside Europe.

Fourty years ago, bone marrow or stem cell transplantation was an experimental procedure carried out as a last resort in terminally ill patients. Stem Cell Transplantation (SCT) then progressively advanced to a frequent treatment for patients with malignant and non-malignant diseases. Using this procedure, blood cancers and other previously life-threatening and incurable diseases have become curable.

EBMT's mission is to save the lives of patients with blood cancers and other life-threatening diseases by advancing the fields of blood and marrow transplantation and cell therapy worldwide through science, education and advocacy.

To this end, the society works to the highest scientific standards, promoting all activity aimed at improving SCT and cellular therapy: basic and clinical research, education, standardisation, quality control and management, and accreditation. For 40 years, the EBMT has significantly contributed to the success of SCT in the following ways:

Measuring trends in transplant activity – Initiated in 1990, the EBMT Annual Activity Survey collects data on the number of patients treated with HSCT according to indication, donor type and stem cell source and has become a tool for illustrating HSCT trends in Europe. This survey has been extended to a worldwide survey through the Worldwide Network for Blood and Marrow Transplantation (WBMT).

The collection and analysis of patient transplant data in Europe – EBMT has registered all transplant activities in Europe with a view to improving treatment outcomes for patients. By January 2014, EBMT's extensive registry has data on over 478,586 transplants and forms the backbone of the groups' retrospective studies and prospective clinical trials protocols.

Initiating pioneer prospective studies - employing new ideas and techniques within the field of HSCT and cellular therapy to improve clinical outcomes and advance patient care – EBMT is currently performing over 115 retrospective studies and 7 clinical trials underway (in set-up, accruing patients or in follow-up), and has published over 150 articles, including as many as 93 scientific reports in peer reviewed journals in four years.

Networking and educating professionals – EBMT is dedicated to sharing the latest information with all parties involved through its working parties, annual congress and training courses.

Establishing strict standards in transplantation procedures including data gathering via quality management and accreditation. The group, along with the US-based FACT accreditation organisation, has established international standards designed to provide minimum guidelines for programs, facilities, and individuals performing cell transplantation and therapy or providing support services for such procedures and is responsible for accrediting transplant programmes. As a lead partner in the Joint Accreditation Committee - International Society for Cellular Therapy & EBMT (JACIE), the EBMT encourages member centres to implement a quality management programme to meet these standards aimed at promoting high-quality patient care and laboratory performance in haematopoietic SCT collection, processing and transplantation centres.

For more information, go to <http://www.jacie.org/>

Improving patient care – through permanent interactions between physicians, nurses, and supporting clinical research staff. The annual Patient & Family Day offers a forum for meeting professionals, exchanging experiences and learning from each other.

EBMT Annual Meeting

The EBMT Annual Meeting brings together over 4,500 scientists, physicians, nurses, statisticians, data managers, biologists, technicians and patients.

2014, 40th Annual Meeting in Milan, Italy

2015, 41st Annual Meeting in Istanbul, Turkey

2016, 42nd Annual Meeting in Valencia, Spain

Education

EBMT ED is the educational arm of EBMT. It offers a range of courses, events, online tools and collaboration opportunities to EBMT members and other actors interested in Blood and Marrow Transplantation and associated fields. It also produces the renowned EBMT Handbook on Haematopoietic Stem Cell Transplantation and organise the annual training course on BMT in collaboration with the European School of Haematology (ESH).

EBMT membership

EBMT members are mainly transplant centres, but also other organisations and individuals involved in the care of donors and recipients of haematopoietic stem cells or actively working within the fields of blood and marrow transplantation or haematology.

The membership currently lists 4,323 members from 563 centres across 57 countries.

18 Corporate Sponsors – in 2013 - including lead pharmaceutical and biotech companies support the day-to-day work of the EBMT. These industry partners collaborate closely with the EBMT to further the society's educational and research activities.

For further information, please visit the EBMT website (www.ebmt.org) or our Social Media accounts in Facebook, Twitter, LinkedIn and Youtube.

Haematopoietic Stem Cell Transplantation (HSCT): Key facts & figures

More than 30,000 autologous and 24,000 allogeneic transplantation procedures are performed every year worldwide. The list of diseases for which HSCT is being used is rapidly increasing. More than 75% of the autologous transplantations are performed for lymphoproliferative disorders in particular multiple myeloma and non-Hodgkin lymphoma, and a vast majority of allogeneic transplants are performed for haematologic cancers, in particular acute leukaemia's.

Table 1 summarizes the common indications for HSCT. Cord-blood transplants are being used for many of the allogeneic transplant indications whenever a suitable HLA-matched donor is unavailable or whenever time for identifying, typing, and harvesting a transplant from an unrelated donor is limited.

Autologous transplantation*	Allogeneic transplantation**
<p><i>Cancers</i></p> <ul style="list-style-type: none"> - Multiple myeloma - Non-Hodgkin's lymphoma - Hodgkin's disease - Acute myeloid leukaemia - Neuroblastoma - Ovarian cancer - Germ-cell tumours <p><i>Other diseases</i></p> <ul style="list-style-type: none"> - Autoimmune disorders - Amyloidosis 	<p><i>Cancers</i></p> <ul style="list-style-type: none"> - Acute myeloid leukaemia - Acute lymphoblastic leukaemia - Chronic myeloid leukaemia - Myelodysplastic syndromes - Myeloproliferative disorders - Non-Hodgkin's lymphoma - Hodgkin's disease - Chronic lymphocytic leukaemia - Multiple myeloma - Juvenile chronic myeloid leukaemia <p><i>Other diseases</i></p> <ul style="list-style-type: none"> - Aplastic anaemia - Paroxysmal nocturnal hemoglobinuria - Fanconi's anaemia - Blackfan–Diamond anaemia - Thalassemia major - Sickle cell anaemia - Severe combined immunodeficiency - Wiskott–Aldrich syndrome - Inborn errors of metabolism

Table 1: Diseases Commonly Treated with Haematopoietic Stem-Cell Transplantation.
(Source: NEJM 354; 17, April 27, 2006)

* More than **30,000** autologous transplantations are performed annually worldwide, two thirds for multiple myeloma or non-Hodgkin's lymphoma.

** More than **24,000** allogeneic transplantations are performed annually worldwide, more than half for acute leukaemias.

The vast majority are performed to treat lymphoid and haematologic cancers.

Figure 1 is a timeline Showing Numbers of Bone Marrow Transplantations and Advances in the Field, 1957-2006. BMT denotes bone marrow transplantation, and HLA human leukocyte antigen. Data are from the Centre for International Blood and Marrow Transplant Research.

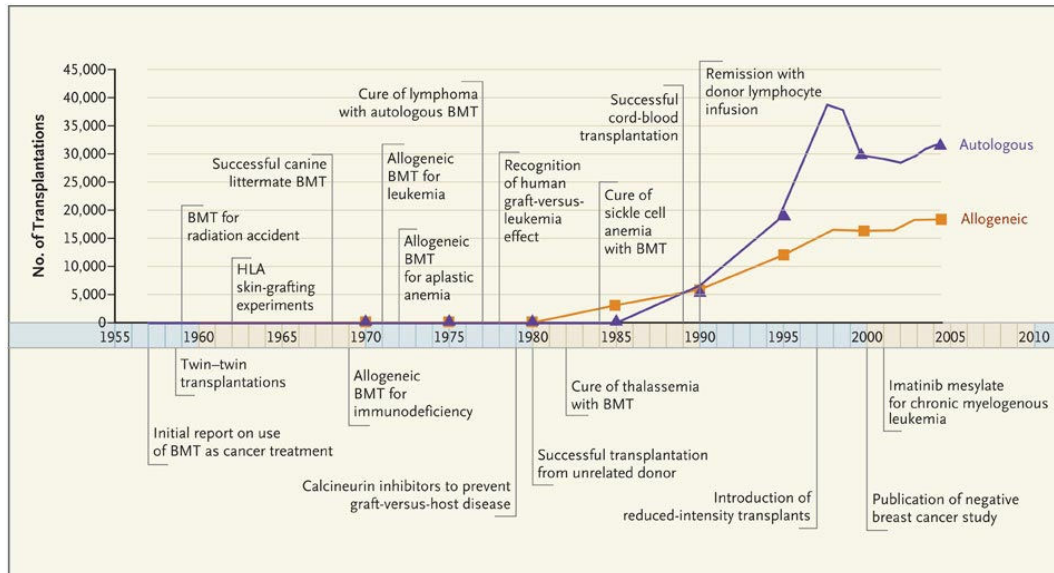


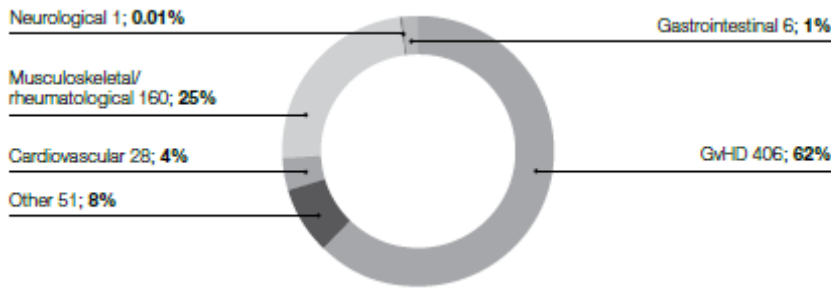
Figure 1: NEJM Timeline Showing Numbers of Bone Marrow Transplantations and Advances in the Field, 1957-2006 (Appelbaum F. N Engl J Med 2007;357:1472-1475)

In 1990, the EBMT introduced the **Activity Survey**, a novel instrument to capture comprehensive information on transplant numbers and to distribute information rapidly. All EBMT members and affiliated teams report on an annual basis their number of patients transplanted by indication, stem cell source and donor type. The Activity Survey has evolved as a mandatory self-reporting system and forms an integral part of the international quality assurance programme JACIE. The survey office is based at the University Hospital in Basel, Switzerland.

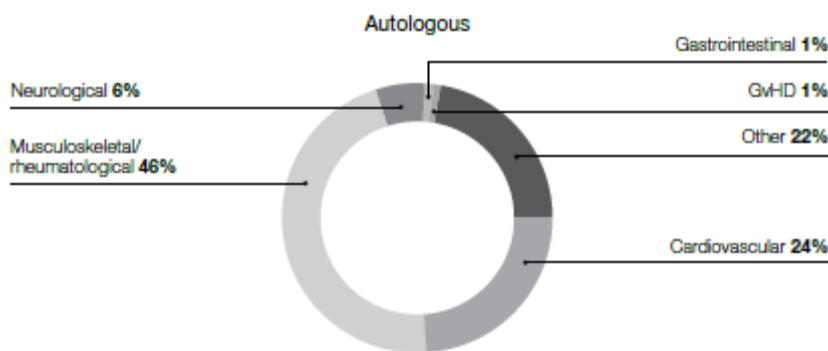
During these nearly 25 years the Activity Survey has become an instrumental tool for illustrating the current status of HSCT in Europe and for identifying trends. It provides essential data for management and planning purposes not only for health care institutions and administrative agencies in the field of stem cell transplantation, but also for the pharmaceutical industry. It is also an important source of information for patients and the general public. In the 2012 survey a record 33,678 patients and 37,818 transplants were submitted from 661 teams in 48 countries in and around Europe. There were a total of 14,165 allogeneic (42%), 19,513 autologous (58%) patients transplanted for the first time. Main indications were leukaemias; 10,641 (32%; 94 % allogeneic); lymphoid neoplasias; Non Hodgkin Lymphoma, Hodgkin Lymphoma, Plasma cell disorders; 19,336 (57%; 12% allogeneic); solid tumours; 1,630 (5%; 5% allogeneic); and non-malignant disorders; 1,953 (6%; 92% allogeneic). There were more unrelated donors than HLA identical sibling donors increased by 5.4%; proportion of peripheral blood as stem cell source was 99% for autologous and 73% for allogeneic HSCT. Cord blood was used in allogeneic transplants (6% of total).

In the last 10 years the overall number of transplants has increased by 53%. Allogeneic HSCT have doubled (7 272 to 14, 476) whilst, autologous have increased by 32% and continued to increase by about 1,100 HSCT per year since 2001.

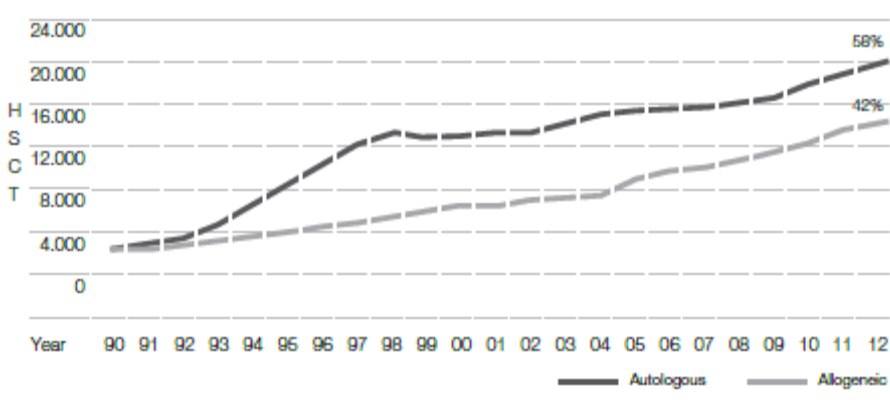
Main indications for allogeneic transplants in 2012



Main indications for autologous transplants in 2012



Increase in the numbers of allogeneic and autologous HSCT since 1990:



EBMT Data - A foundation for cutting-edge research

The **EBMT Registry** uses a central data management system to collect data on patients treated with a haematopoietic stem cell transplant (HSCT) according to indication (type of disease), donor type (allogeneic/autologous) and stem cell source (bone marrow/peripheral blood/cord blood). This megafile is comprised of data from over **380,000** transplants with over **30,000** new transplants reported each year, and is accessible to EBMT members, representing the largest transplant database available today.

From this database, studies investigating predictive factors for transplantation, outcomes of diseases, frequencies of stem cell transplantation and the outcomes of different transplantation techniques can be analysed. The information available can be used to simulate a stem cell transplant based on the experience gained over the past 30 years. The database also enables progress in stem cell transplantation over the past three decades to be tracked and is used for quality control purposes.

The EBMT has started a new Registry system with Remedy Informatics as a technology partner. This new registry aims at being a user-friendly tool with easier upload and retrieval of data and more adaptable to future changes. It will keep all the data stored up to the present using new software that will turn it into an efficient and functional tool without changing its mission of being a network of exchange of scientific data.

Disease	Patients	Transplants
Acute leukaemias: AML	55.805	61.229
Acute leukaemias: ALL	33.327	35.941
Acute leukaemias: other/unknown	1.977	2.209
Chronic leukaemias: CML	20.546	22.143
Chronic leukaemias: CLL	5.476	6.050
Chronic leukaemias: other/unknown	627	700
Lymphomas: NHL	77.743	86.255
Lymphomas: Hodgkins	26.349	30.110
Lymphomas: other/unknown	1.890	2.013
Multiple myeloma/Plasma cell disorders	79.390	107.587
Solid tumours	36.641	49.032
Myelodysplastic/myeloproliferative	22.828	25.791
Aplastic anaemias	9.243	10.205
Primary immune deficiency	3.630	4.126
Inborn errors: other / unspecified	1.775	1.993
Histiocytic	933	1.022
Autoimmune diseases	1.508	1.549
Haemoglobinopathies	4.373	4.617
Other/unknown	273	315
Total	384.334	452.887

Clinical Trials: EBMT's invaluable role

For 40 years, the EBMT has been a leader in the collection and analysis of patient transplant data in Europe, as well as an initiator of pioneering prospective clinical trials that use new ideas and techniques within the field of autologous and allogeneic haematopoietic stem cell transplantation (HSCT).

The EBMT established its Transplant Registry in 1974 to give the scientists and physicians involved in stem cell transplantation a forum within which they could share their clinical experience and to facilitate the development of clinical trials. The critical mass of data contained in the Registry has enabled the group to perform retrospective studies in the areas of prognostic factors, trends in treatment, experimental procedures, etc. These studies have informed clinical practice over the years, improving patient outcomes, and reducing morbidity.

From the date of inception, the EBMT has succeeded in bringing together the similar interests of transplant centres throughout Europe. The combination of scientific expertise and access to the wealth of data in the Registry database has provided the EBMT with an excellent scientific foundation for the development of pan-European prospective clinical trial protocols.

In the era of evidence-based medicine, it is even more important that clinical practice evolves based on the results of prospective clinical trials performed in the academic setting. Many unanswered questions in transplantation are best served by prospective clinical trials. These trials must be conducted according to the standards set down in the EU Clinical Trials Directive (2001/20/EC), national guidelines and Good Clinical Practice (2005/28/EC).

The EBMT Clinical Trials Office manages pan-European prospective clinical trials in Stem Cell Transplantation. In 2011, the EBMT Clinical Trials Office was reorganised and a new independent prospective clinical trials committee (the EBMT-CT2 Committee) was constituted. There is currently 1 prospective clinical trial recruiting patients (HCT vs CT Elderly AML trial), and 2 trials are in the advanced set-up stages (RACE and CMV). 4 studies are now under analysis (ASTIC, ASTIS, MMVAR and RICMAC)

The EU has recognised the importance of supporting academic groups to enable them to continue to run prospective clinical trials. The European Commission has reviewed the Clinical Trials Directive and in July 2012 it proposed a new Clinical Trials Regulation to improve the regulatory framework in Europe. The EBMT welcomes the changes proposed such as the coordinated approval process and the definition of a low intervention clinical trial. The Regulation is expected to be published in 2014, and should be applied in 2016.

Political and legal considerations

Blood and marrow transplantation is a cellular therapy that encompasses the collection, processing, and infusion of haematopoietic progenitor cells derived from **peripheral blood, cord blood, and bone marrow**. The field is represented by national and international organisations such as EBMT, that have the common purpose of achieving the best possible outcomes of patient care and advancing knowledge and understanding in this highly specialised and rapidly evolving medical field. Despite varying objectives and priorities, all share a common set of values and beliefs. The EBMT works in pursuit of its core value, excellence in science.

The underlying principle and bedrock belief is that patients in need of a blood or marrow transplant and their transplant donors have a right to the most appropriate, high-quality medical care.

Access to care: patients and donors should have access to appropriate transplant therapy irrespective of socioeconomic or geographic limitations. No patient should be denied life-saving therapy.

Cost of care: the cost of blood and marrow transplantation procedures for accepted indications should be appropriately reimbursed.

Patient and donor rights: right to make decisions and right to give consent based on clear information about each step of the transplantation and donation process. Right to privacy: the identity and personal records of patients and donors should be kept confidential, in accordance with national regulations.

Clinical research: the transplant community has a responsibility to foster activities that seek to improve outcomes for transplant recipients and provide a scientific basis for the standard of care. Well-designed clinical trials conducted according to good clinical practice are essential for the practice of medicine. Such research should proceed at the most rapid pace possible. Patients should have access to quality clinical trials, which often represent the most appropriate treatment strategy for life-threatening diseases.

Safety: to assure maximum safety for the patient and donor, all blood and marrow transplant personnel should be well trained and qualified to perform their respective roles in cell collection, processing and infusion. Cellular products should be of high quality and be equally available to every patient. Transplant facilities should have an active quality management programme to ensure safe and effective medical care. Facilities should participate in external review and accreditation that independently documents that standards of care are being met. Adverse events should be managed, tracked, evaluated and readily available for study to improve patient safety.

Education and awareness: the transplant community has a responsibility to inform patients, families, other health professionals and the general public about new information that might benefit or otherwise have an impact on patients or the public at large. Greater awareness by all parties concerned is beneficial for improving patient care, increasing donor interest and limiting misinformation that might impede access to care.

Quality Management: the growing emphasis on quality management and minimisation of risk in patient care is reflected in the EBMT's support since 1998 for the JACIE accreditation programme for transplant centres and its inclusion of quality management among the themes of the annual meeting.

Glossary

A

Allogeneic transplant

When the stem cells come from another person, it is called an allogeneic transplant. The donor may be a relative (allogeneic related) or a complete stranger (allogeneic unrelated). The important thing is that the donor's blood is closely matched to that of the recipient. This is more likely with a brother or sister. Relapse is less frequent than with an autologous transplant, but the procedure itself is more risky because of the graft-versus-host disease associated with this treatment.

Autologous transplant

When the stem cells come from one's own blood or bone marrow, it is called the autologous transplant. The procedure is less risky than with an allogeneic transplant but tumour recurrence seems to be the main issue. To be eligible for an autologous transplant the patient needs to be in the remission phase of the underlying disease.

B

Bone marrow

Soft, fatty tissue found inside the bones that produces blood cells (red and white blood cells, and platelets). Red blood cells carry oxygen throughout the body. White blood cells act to ward off infection. Platelets aid in blood-clotting.

Bone marrow transplants

Bone marrow transplants are performed for: *Irreversible bone marrow failure*, also called severe aplastic anaemia; *malignant diseases of the blood forming system*, including myeloid and lymphoid lineages, resulting in leukaemias and lymphomas; *inherited (genetic) diseases* such as thalassemia; *immune system disorders* such as congenital neutropenia and severe, *combined immunodeficiency syndrome*.

G

Graft-versus-Host Disease (GvHD)

GvHD is a common side effect of an allogeneic bone marrow or cord blood transplant. An allogeneic transplant uses blood-forming cells donated by a family member, unrelated donor or cord blood unit. In GvHD, the immune cells from the donated marrow or cord blood (the graft) attack the body of the transplant patient (the host). GvHD can affect many different parts of the body. The skin, eyes, stomach and intestines are affected most often. GvHD can range from mild to life-threatening.

H

Haematopoietic

From Ancient Greek: haima blood; poiesis to make, pertaining to the formation of blood cellular components. All of the cellular components of the blood are derived from haematopoietic stem cells.

Haematopoietic stem cells (HSC)

Progenitor cells (or "parent cells") of all blood and lymph node cells. They are cells at their earliest stage of development. They usually live inside the bone marrow, but are increasingly harvested from the blood instead of the marrow after mobilisation of the cells from the marrow in the blood stream. This makes donation of HSC, even in high amounts, easier and without the necessity of anaesthesia. HSC can also be obtained from the umbilical cord. Hence the more generic name, in view of the various sources of stem cells, is HSC.

HSC are actually a part of stem cells that have a remarkable potential to regenerate adult tissue following transplantation, and to become specialised human tissues, including haematopoietic, neuronal, and cardiac cells.

Haematopoietic stem cell transplantation (HSCT)

HSCT, also known as bone marrow transplantation (if the cells are harvested from the bone marrow), is a special form of therapy that involves taking cells that are normally found in the bone marrow (stem cells). But stem cells can also be taken from blood (peripheral blood SCT) or cord blood. The stem cells are given, by intravenous infusion, to the recipient, either the same person or to another person.

The source of these stem cells can be from: the patient (autologous), a relative (allogeneic), a matched unrelated donor (MUD).

Why HSCT? Many chemotherapeutic agents show a steep dose response curve, i.e. small changes in dose produce significant changes in response. But the bone marrow limits the amounts of chemotherapy and radiation that can be given. HSCT allows use of higher doses of drugs and obviates concern about marrow toxicity. This is the principle of **autologous SCT**.

In the case of **allogeneic SCT**, two mechanisms are effective. The high dose chemo/radiotherapy also called conditioning, but also the graft-versus-tumour effect. Similar to the Graft-versus-Host disease immunological reactions arise after allogeneic SCT, which kill tumor cells. This graft-versus-leukaemia effect is used in elderly patients, where maximal chemo/radiotherapy cannot be given. In such patients reduced intensity conditioning transplants are applied. These are often the only curative treatment for patients with malignant haematological diseases.

P

Prospective clinical trial

A prospective clinical trial is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes.

R

Regenerative medicine

This is the science of using the body's own cells to repair or replace damaged tissues and organs.

Retrospective study

A retrospective study is a study that uses data on events that have already happened by the time the study is initiated. The EBMT retrospective studies use the data collected in the Registry.

S

Stem cells

They are defined as the population of undifferentiated cells which have two functions: to be able to define for an indefinite period to self-renew and to generate highly specialised cells.

Treatments used to fight cancer cells in the body often also devastate healthy cells and tissues, including stem cells, and the ability to extract, purify, and then reintroduce – or transplant – stem cells to patients following cell-destroying cancer treatments can help “rescue” a patient’s compromised immune and haematologic system and speed his or her recovery.