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stem cell therapy autologous vs. allogeneic

According to a recent report of the European Group for Blood and Marrow Transplantation (EBMT; ref. 5) there were in total 24.168 first haematopoietic stem cell transplantations (HSCT) in 2005, 15.278 autologous (63%), 8.890 allogeneic (37%), and 3.773 additional re- or multiple transplants, reported from 597 centres in 43 participating countries. Main indications were lymphomas (13.825 (57%; 89% autologous)), leukaemias (7.404 (31%; 82% allogeneic)); solid tumours (1.655 (7%; 92% autologous)) and non-malignant disorders (1.131 (5%; 93% allogeneic)). Compared to 2004, there was a 20% increase in allogeneic HSCT; numbers of autologous HSCT remained constant. The most noticeable increase was in unrelated HSCT, which comprise 41% of all allogeneic HSCT. Unrelated HSCT were preferentially performed for leukaemias, the prenatal origin of childhood leukaemias preventing autologous HSCT. Hence, autologous HSCT is considered as challenging and controversial in childhood leukaemia, although the incidence of pre-leukemic clone is ~100 times that of the incidence of childhood leukaemia (ref. 6), indicating that a second - post-natal - trigger would be necessary for the clinical development of childhood leukaemia. The first autologous cord blood transplantation for treatment of a child with leukaemia was only reported early 2007 (ref. 7).

The mean cost for an allogeneic HSCT in The Netherlands is 70.446 €, substantially higher as compared to 40.593 € for an autologous HSCT; the mean additional cost to identify a suitable donor for allogeneic HSCT is equal to 42.000 € (ref. 8), and the disease tends to progress to advanced or high risk stage while searching for a suitable donor. These numbers indicate a clear pharmaco-economic effect in favour of autologous HSCT, whenever possible. The earlier timing might contribute to better clinical outcome because disease progression can be prevented and accumulation of e.g. chemotherapy-induced tissue toxicity can be decreased. Furthermore, chronic immunosuppression is very often required with allogeneic HSCT, reducing the quality of life even further.

Umbilical cord blood transplantation versus bone marrow or mobilised peripheral blood stem cell transplants

Risks and benefits of umbilical cord blood have become clear compared to bone marrow or mobilized peripheral blood derived stem cells (ref. 9). The collection of umbilical cord blood after birth carries no risk for the donor. Collected umbilical cord blood can be cryopreserved and stored for prolonged periods. Umbilical cord blood units are immediately available upon request and can be shipped to any transplant centre in the world with relative ease. Umbilical cord blood transplantation is associated with a lower incidence of acute Graft Versus Host Disease (GVHD), and partial HLA match between the donor and recipient is tolerable. There is also a reduced - negligible - risk of infectious disease transmission from umbilical cord blood. From a clinical perspective, no other area of stem-cell biology has so far been applied so successfully as has transplantation of umbilical cord blood stem-cells for the treatment of blood diseases, focusing on its use to reconstitute bone marrow.

Favourable results from a prospective study comparing cord blood transplantation from unrelated donors with bone marrow or peripheral blood stem-cell based transplants from related donors in adult patients with haematological malignancies were published (ref. 10), suggesting that unrelated cord blood could be a stem-cell source as safe and effective as related bone marrow or mobilized peripheral blood when used as a primary source, when applied at the same time as for patients who had a related donor, i.e. before the disease progresses to advanced or high risk stage while searching for compatible donor. However, rather than focusing on the use of umbilical cord blood stem cells for bone marrow reconstitution, particularly in the context of their greater differentiation plasticity and multipotency as compared to e.g. post-natal adult stem cells, they should be regarded as a highly valuable source for future tissue generation (vide infra).

Autologous umbilical cord blood stem cells

For acquired and genetic disorders of haematopoiesis, umbilical cord blood transplantation has been applied extensively in the allogeneic setting. Concerning the use of autologous umbilical cord blood transplantation, there is considerable less experience, as a result of the great controversy about the role of autologous umbilical cord blood collection and storage. Despite this controversy and the recent phenomenon of private umbilical cord blood storage, however, some cases have been reported in the scientific literature for the successful treatment of stage IV neuroblastoma (ref. 11), severe aplastic anemia (ref. 12) as well as for the controversial and challenging treatment of a child with leukaemia (ref. 7), clearly illustrating its significant clinical potential.

Several well documented examples clearly illustrate the significant potential of (autologous) umbilical cord blood stem cells in the emerging field of regenerative medicine. Tissue-engineered living blood vessels generated from umbilical cord progenitors represent a promising new option for the repair of congenital malformations (ref. 13). The induction of stem cells from umbilical cord blood into insulin-producing islet-like structures, which co-express insulin and C-peptide, might have a significant potential to advance human UCB derived stem-cell-based therapeutics for diabetes (ref. 14). Recently, British scientist from Newcastle University announced the world's first artificial liver created from umbilical cord blood, but still have to author a scientific article (ref. 15).

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1.1 Pubblicato su Nature –

1.2 The EBMT activity survey 2007 with focus on allogeneic HSCT for AML and novel cellular therapies

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Abstract

The 2007 report describes the current status of HSCT activity in Europe, highlights the increasing role of allogeneic HSCT in treatment of AML and gives the first quantitative information on novel cellular therapies. In 2007, there were 25563 first HSCTs, 10072 allogeneic (39%), 15491 autologous (61%) and 3606 additional transplants reported from 613 centers in 42 countries. The main indications were leukemias (8061 (32%; 89% allogeneic)); lymphomas (14627 (57%; 89% autologous)), solid tumors (1488 (6%; 96% autologous)) and nonmalignant disorders (1302 (5%; 91% allogeneic)). Peripheral blood was the main source of stem cells for autologous HSCT (98%) and the predominant source for allogeneic HSCT (71%). Among allogeneic HSCTs, the number of unrelated donor grafts equaled the number of HLA-identical sibling donor grafts for the first time (47% each). AML was the most frequent indication for allogeneic HSCT (32% of all allogeneic HSCTs), with an increase of 247 (8%). Information on novel cellular therapies was collected for the first time; there were 212 mesenchymal SCTs and 212 HSCTs for nonhematopoietic use. The indications for the latter were cardiovascular disorders (97; 46%), neurological disorders (94; 44%) and tissue repair (21; 10%). These data illustrate the expanding role of cellular therapies.

1.2..1 Keywords:

hematopoietic SCT, Europe, transplant rates, acute myeloid leukemia, mesenchymal stem cells, novel cellular therapies

Introduction

The annual European Group for Blood and Bone Marrow Transplantation (EBMT) activity report has become an established instrument to describe the current status of HSCT in Europe to observe trends and to monitor changes in technology use.[1, 2, 3] It serves as a basis for decision making at the individual patient level as well as for health care agencies in planning and providing the infrastructure for this complex medical technology. In addition to the general description of the number of transplants by indication, donor type and stem cell source, the report has focused each year on specific aspects. The increasing use of cord blood as a stem cell source, the change from BM to peripheral blood or the utilization and integration of unrelated donor transplants were the

key topics in the past.[4, 5, 6] In the 2007 report, information on the use of novel cellular therapies was integrated for the first time. The numbers of mesenchymal SCTs and the numbers of HSCT for nonhematological indications were requested.[7, 8, 9, 10] The most striking observation in the last year was the increase of allogeneic HSCTs for the treatment of AML and myelodysplastic syndromes (MDS). More detailed information is provided on the pattern of use for this indication.

Patients and methods

1.2..2 Data collection and validation

All participating teams were requested to report their data for 2007 by indication, stem cell source and donor type as listed in Table 1. Data were validated by three independent systems: through confirmation by the reporting team that received a computer printout of the entered data, by selective comparison with MED-A data sets in the EBMT ProMISE data system and by cross-checking with the National Registries. Onsite visits of selected teams were part of the quality control program (www.jacie.org).

Table 1 - Numbers of hematopoietic SCTs in Europe in 2007 by indication, donor type and stem cell source.

Full table

1.2..3 Teams

A total of 628 teams in 45 countries (38 European and 7 affiliated countries) were contacted for the 2007 report, of which 613 reported their numbers. This corresponds to a 98% return rate of active teams and includes 509 active EBMT member teams reporting to the survey. There were 15 teams known to have been performing HSCTs in 2007 that chose not to reply or failed to reply. The teams that were contacted are listed in the Appendix in alphabetical order according to country, city and EBMT center code. According to the information received, there were no blood or marrow transplants performed in Albania, Andorra, Armenia, Georgia, Liechtenstein, Malta, Moldavia, Monaco, Montenegro, San Marino and the Vatican in 2007. The non-European countries participating in the EBMT survey include Algeria, Iran, Israel, Lebanon, Saudi Arabia, South Africa and Tunisia. Their data are included in some of the analyses.

1.2..4 Definitions

1.2..4.1 Transplant numbers

The EBMT survey focused, as in previous years, on the number of patients treated for the first time with HSCT.[1] Information on additional transplants, for instance, a second, third

or fourth HSCT in a patient with a previous HSCT was collected by disease category only for those patients with a planned double allogeneic after autologous transplants; for all other situations, this information was collected generically only. The following definitions were used: 'retransplants' (autologous or allogeneic) were defined as an unplanned HSCT for rejection or relapse after a previous HSCT; 'multiple transplants' were defined as being part of a planned double or triple autologous or allogeneic transplant protocol. Information on stem cell source was collected as BM, peripheral blood or cord blood. Any transplants with a combination of stem cell source that included cord blood were reported as cord blood HSCTs. BM and peripheral blood combinations were reported as peripheral blood HSCTs. Information on reduced-intensity conditioning (RIC) was collected as a total for each team only and not for individual transplants. Definitions for RIC HSCT followed the recently published definitions.[11]

1.2..4.2 Transplant rates

Transplant rates were computed as the number of HSCTs per 10 million inhabitants as defined earlier.[12] Transplant rates refer to the number of transplants in a given country compared with its own population. The survey cannot make adjustments for patients who cross borders and receive their HSCT in a foreign country. Population data were obtained from the US census office (http://www.census.gov).

1.2..4.3 Economic factors

Economic factors considered in the analysis followed previously defined rules.[12] Countries were categorized by their Gross National Income (GNI) per capita according to the World Bank definitions into high income (Austria, Belgium, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Ireland, Italy, the Netherlands, Norway, Portugal, Slovenia, Spain, Sweden, Switzerland and the United Kingdom), middle income (Bulgaria, Croatia, Hungary, Latvia, Lithuania, Poland, Romania, Russia, Serbia, Slovakia and Turkey) and low income countries (Azerbaijan, Belarus, Bosnia and Herzegovina, Macedonia and Ukraine). The latter category refers to the World Bank definition of 'lower middle income' (http://www.worldbank.org). Furthermore, the category of high income was subdivided into a very high-income group, consisting of those countries with a GNI/capita of >40 000 per capita (Denmark, Finland, Ireland, the Netherlands, Norway, Sweden, Switzerland and the United Kingdom).

The non-European countries that traditionally participate in the EBMT activity survey (Algeria, Iran, Israel, Lebanon, Saudi Arabia, South Africa and Tunisia) are included in the overall data presentation. They were not included in the analysis on economic factors. The same applies to Iceland and Luxembourg because of some missing data over the time span.

1.2..4.4 Statistical analysis

The relation of the macroeconomic factors (GNI/capita) with transplant rates was estimated by ordinary least squares by multiple regressions to measure the coefficient of determination (r^2) or explanatory content.

Results

1.2..5 Participating teams

Of the 613 teams reporting HSCTs in 2007, 374 (61%) performed both allogeneic and autologous transplants; 225 (37%) restricted their activity to autologous transplants, 5 teams (1%) to allogeneic transplants only and 9 teams (1%) reported having performed no transplants in 2007.

A total of 216 teams (35%) reported fewer than 20 first HSCTs in 2007, 223 teams (37%) between 20 and 50 HSCTs, 121 teams (20%) between 51 and 100 HSCTs and 53 teams (8%) >100 HSCTs.

A total of 142 teams reported at least one cord blood HSCT in 2007 with 33 teams reporting >5.

1.2..6 Numbers of HSCT in 2007

1.2..6.1 First transplants in 2007

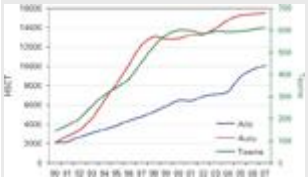
A total of 25563 first transplants, 10072 (39%) allogeneic and 15491 (61%) autologous, were carried out in 2007 (Table 1). Overall, this corresponds to a slight increase in the numbers of HSCT compared with 2006 when there were 25050 first transplants. The numbers of allogeneic HSCT increased by 4% from 9661 in 2006 to 10072 in 2007, whereas the numbers of autologous HSCT remained similar at 15389 in 2006 and 15491 in 2007.

1.2..6.2 Additional transplants in 2007

There were 1662 retransplants (810 allogeneic/852 autologous) and 1944 additional planned multiple transplants (71 allogeneic/1873 autologous). Thus, there were a total of 29169 HSCT procedures, 10953 allogeneic (38%) and 18216 autologous (62%), performed in 2007. This corresponds to an overall increase of 105 retransplants (38 allogeneic and 67 autologous) or 7% compared with 2006. A total of 522 transplants were reported as being part of a planned double autologous–allogeneic HSCT. This corresponds to a decrease of 5% when compared with 2006, where a total of 531 planned double autologous–allogeneic HSCTs were reported. The main indications for the

planned double transplant programs were, as in the previous year, multiple myeloma, non-Hodgkin's lymphoma and Hodgkin's disease. The evolution over time in the number of participating teams, numbers of allogeneic and autologous HSCTs is depicted in Figure 1.

Figure 1.



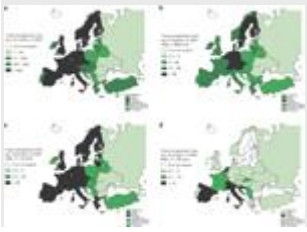
Development of the activity survey from 1990 to 2007. Numbers of participating teams (green), allogeneic (blue) and autologous (red) HSCTs.

Full figure and legend (67K)

1.2..6.3 Transplant rates in 2007

There were marked differences in transplant rates between European countries and countries affiliated with EBMT as presented in Figure 2. These differences relate to all transplants (Figure 2a) and to autologous HSCT (data not shown). The differences between Eastern and Western European countries have been reported earlier. It is interesting to note that countries with similar total transplant rates had similar transplant rates for allogeneic HSCT as well as for autologous HSCT.

Figure 2.



Transplant rates (=number of HSCTs per 10 million inhabitants) in Europe 2007 by country. (**a**) Transplant rates for all HSCTs, allogeneic and autologous. (**b**) Transplant rates for myeloid malignancies (AML and MDS), allogeneic HSCT only. (**c**) Transplant rates for AML, the first CR only, allogeneic HSCT. (**d**) Transplant rates for AML, the first CR only, autologous HSCT. HSCT, hematopoietic SCT; MDS, myelodysplastic syndromes.

Full figure and legend (287K)

1.2..7 Disease indications in 2007

The indications for HSCT in 2007 are listed in detail in Table 1. The main indications were 'lymphoproliferative disorders' with 14627 patients (57%), 1646 patients with allogeneic

HSCTs (11%), 12981 with autologous HSCTs (89%); 'leukemias' with 8061 patients (32%), 7153 patients with allogeneic HSCTs (89%), 908 with autologous (11%) HSCTs; 'solid tumors' with 1488 patients (6%), 63 with allogeneic HSCTs (4%), 1425 with autologous HSCTs (96%); and 'nonmalignant disorders' with 1302 patients (5%), 1141 with allogeneic HSCTs (91%) and 161 with autologous HSCTs (12%). The latter, autologous HSCT for nonmalignant disorders, predominantly includes patients (150) with autoimmune disorders. An additional 85 patients (0.5%), 69 with allogeneic HSCTs and 16 with autologous HSCTs, were reported as 'other indications'.

1.2..8 Stem cell source in 2007

Of the 15491 autologous first transplants, 256 (2%) were BM derived, 15234 (98%) were from peripheral blood stem cells or from combined BM and peripheral blood stem cells and one was from autologous cord blood cells (Table 1). Of the 10072 allogeneic first transplants, 23% were BM, 71% were peripheral blood and 6% were cord blood transplants. This corresponds to a stable proportion of peripheral blood as stem cell source compared with the 70% in 2006. The proportion of peripheral blood as stem cell source varied depending on donor type. It was 73% for HLA-identical sibling donor transplants, 68% for unrelated donors, 74% for HSCT from other family members and 73% for twin donors. Within allogeneic HSCT, the only disease indications with more BM than peripheral blood donors as stem cell source were BM failure syndromes (51% bone marrow) and congenital disorders (59% BM). The proportion of main indications varied as well within the three stem cell sources. Nonmalignant disease represented about a quarter of all indications for BM and cord blood but only a small fraction among the peripheral blood transplants.

1.3 Autologous Bone Marrow Stem Cells Transplant into Parkinson's Disease Patients – Safe + Improve

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1.3..1.1 Autologous Bone Marrow Stem Cells Transplant into Parkinson's Disease Patients is Safe and May Improve Their Quality of Life

Clinical study showing a minimally invasive approach was presented in The XVIII World Congress on Parkinson's Disease and Related Disorders of the World Federation of Neurology.
(PRWEB) March 11, 2010 — Eight Parkinson's Disease (PD) patients were treated with their own bone marrow stem cells (BMSC) injected via minimally invasive routes and discharged the next morning without complications.
Evaluations with UPDRS, Hoehn & Yahr scale and Schwab & England score showed encouraging improvements and the total L- dopamine dose could be decreased suggesting that stem cells may enhance endogenous dopamine synthesis. As a matter of sample, the writing test pre versus post procedure showed significant changes.

1.3..1.2 Eight Parkinson's Disease (PD) patients were treated with their own bone marrow stem cells (BMSC) injected via minimally invasive routes and discharged the next morning without complications.

"It is high time we focused our efforts in what is possible and reachable and what suffering patients demand. Not all what is researched and developed in Petri dishes or rats can automatically be used in patients, so we should stop to augment their confusion. We expect this study in PD real patients, not in animals, draws the attention of those interested in getting clinical data since, funnily enough, there are billions of dollars spent in endless animal studies but very little in clinical ones" leader investigator Dr. Luis Geffner said.

- this is a tool that may complement standard treatments and delay the progress of both the illness and the complications of the medication currently used to treat it. PD patients should be cared comprehensively; therefore, their treatment may include physical therapies as well as optimal medication and stem cells transplant, trying to improve their independence and self-care he added.

- The treating doctor's team has already transplanted 147 patients suffering from different illnesses or trauma states and many of them have been followed up 5 years showing that autologous adult BMSC neither provoke tumors, immunologic rejection, pain, infections nor arise ethical or religious controversies. That is why they stand to push these investigations forward.

- This clinical study Transplant of Autologous Bone Marrow Stem Cells into Parkinson's Disease Patients Is Safe And May Improve Their Quality Of Life was shown in Miami on December 15th, 2009 in the XVIII World Congress on Parkinson's Disease and Related Disorders organized by the World Federation of Neurology and published in December 2009 issue of Parkinson's Disease and Related Disorders journal.

For more info on stem cells and Parkinson's:
Muhammad Ali seeks ADULT STEM CELL treatment in Israel
60% PARKINSON'S PATIENTS IMPROVE AFTER REPAIR STEM CELL TREATMENT – PHYSICIANS CONFIRM RESULTS!