Are Peripheral Blood Stem Cell transplants fulfilling the expectations?

By Claudio Anasetti, MD
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Introduction
Many studies of allogeneic marrow transplantation show that higher doses of marrow cells correlate with more robust hematopoietic engraftment and lower mortality from infections. Peripheral blood stem cells (PBSC) collected after mobilization with granulocyte colony stimulating factor (G-CSF) contain more CD34-positive (CD34) progenitors and total cells than bone marrow. These observations led to the hypothesis that transplantation of PBSC would lead to lower mortality compared to transplantation of marrow. Additionally, PBSC grafts also have more T cells, predicting a more powerful anti-leukemia effect. However, the higher T cell content may also lead to increased incidence and severity of acute and chronic graft-versus-host disease (GVHD). This concern is especially serious when the donor and recipient are unrelated.

Cell Dose Effect
Marrow cell dose was long recognized as a limiting factor for engraftment and survival. Among patients receiving HLA-identical sibling transplants for aplastic anemia, infusion of < 3 x 10^6 cells per kilogram (kg) was associated with increased risks of graft failure and death.1 The authors of that report suggested: “The greatest possible amount of donor marrow, perhaps supplemented by stem cells derived from the peripheral blood, should be obtained.” Subsequent studies supported this concept. Improved survival was associated with transplantation of higher marrow cell doses in patients with acute myeloid leukemia (AML) in first remission.2 The number of hematopoietic precursor cells in T-replete marrow grafts was associated with better survival after transplantation from HLA-identical siblings.3 A higher number of CD34 cells, a population that includes hematopoietic progenitors, was associated with improved survival after T cell depleted,4 or T-replete marrow grafts from HLA-identical siblings.5 Cell dose was limiting with transplantation of HLA incompatible unrelated cord blood,6,7 and with transplantation of HLA incompatible related donor marrow.8 Engraftment across the HLA barrier was achieved with the use of T-depleted PBSC containing a large dose of CD34 cells.8 Studies of unrelated donor transplants showed similar results. Among patients with acute leukemia receiving T-replete marrow from unrelated donors, transplantation of nucleated cell doses > 3.65 x 10^8/kg was associated with faster neutrophil and platelet engraftment, decreased incidence of severe GVHD, fewer non-leukemic deaths and better leukemia-free survival.8,11 Similar findings were reported in children receiving unrelated donor transplants for chronic myeloid leukemia (CML)12 or Hurler’s syndrome.13 Thus, the new center is expected to greatly expand research activities during the next five years to increase scientific knowledge regarding blood and marrow transplantation through:

- Retrospective studies of the world’s largest blood and marrow transplant databases and tissue sample repositories
- Prospective, multi-center trial design and implementation to explore new strategies to increase the safety and success of transplantation
- Research in immunobiology
- Transplant-focused biostatistics expertise to assist researchers in accessing, analyzing and presenting scientific studies
- Research to improve access to health care services

Scientific and administrative oversight of the Center is modeled on the Working and Advisory Committee structure of the IBMTR/ABMTR. The Center retains the longstanding IBMTR/ABMTR commitment to fostering collaboration and facilitating research efforts of the transplant community. Future issues of this newsletter will come from the CIBMTR and will further inform you on the Center’s organizational structure and activities.
Perspectives

By Olle Ringdén, MD, PhD
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Last year was another prosperous year for the IBMTR. There were 19 papers published and another 8 submitted for publication. The 2004 Tandem BMT Meeting in Orlando raised a lot of interest with more abstracts submitted (314) and participants (>1500) than to previous meetings. Although the IBMTR/ABMTR continues to maintain fiscal balance, increasing research and education activities have led to increasing needs for personnel and other resources. Ideas to raise funds were discussed and new ideas are most welcome.

During the past year, the IBMTR and the National Marrow Donor Program (NMDP) reached consensus that a formal collaboration between the two organizations will take advantage of complimentary strengths for a productive research program. NMDP brings sophisticated information technology and contracting expertise and a high quality clinical database and IBMTR, its statistical center of experienced data analysis staff, including MD and PhD support, to the collaboration. Hopefully, this combination will have a synergistic effect on research productivity.

The research activity of the IBMTR is a continuous process, among other things comparing stem cell transplantation (SCT) with alternative therapies for various disorders. The role of allotransplant in CML needs to be evaluated in the imatinib era as well as in MDS. What is the optimal timing for such transplants? PBSC transplants are increasingly used, but may result in increased risks of chronic GVHD. A recent IBMTR study suggests that PBSC may not be a good choice (compared to bone marrow) in children and adolescents. A previous study from the IBMTR/EBMT showed that PBSC was favorable compared to bone marrow in patients with advanced leukemia. The role of PBSC for various transplant recipients must be fully evaluated. The IBMTR database can play an important role in this assessment. Transplants using reduced intensity conditioning (RIC) are increasingly used, not only in elderly patients ineligible for conventional myeloablative conditioning, but also in younger patients. There is a lot of enthusiasm about RIC, but a lack of comparative trials. The IBMTR will play a major role in monitoring the outcome of such transplants and determining whether less toxic regimens will result in a better quality of life and survival for patients with various disorders, such as leukemia, lymphomas, and myeloma. Defining the role of unrelated donor transplants will be an important collaborative task for the IBMTR and the NMDP. Allotransplants for solid tumors such as renal carcinoma, breast cancer, and colon carcinoma will be evaluated in the near future. Mesenchymal stem cells have immune modulatory effects and may enhance engraftment and suppress GVHD. Prospective studies are under way in the US and in Europe. Report Forms for such transplants should be developed and provided by the IBMTR, so that this treatment modality can also be evaluated.

A large proportion of prior IBMTR studies have been proposed and conducted by productive veterans in the field of SCT. However, for the future of the IBMTR, it is important to encourage and welcome young investigators in this important international collaboration. It is also necessary that we utilize our statistical resources in an optimal way. Increased communication between investigators and the Statistical Center via telephone conferences and websites are effective ways to maintain the progress.

An External Review Committee, which met in Milwaukee last year, suggested that the IBMTR/ABMTR should continue to do what it is good at—outcomes research. However, IBMTR contributions should be increased in the evaluation of rare diseases, late effects of SCT and the immunology of immune reconstitution after SCT. It was also recommended to simplify data reporting and to establish a tissue bank of DNA and RNA, among other things. The latter would enable the evaluation of cytokine polymorphisms and HLA antigens of importance for SCT.

Several scientific, financial and administrative challenges lie ahead for the IBMTR. However, with the collaboration of Mary Horowitz and her enthusiastic staff at the Statistical Center and academic and industrial support worldwide, it is expected that these will be solved in an expert way. We look forward to future Tandem BMT Meetings, at Keystone in 2005 and in Hawaii in 2006, where these and other issues will be discussed. I look forward to these productive years.

Continued on page 3
Perspectives

By Richard E. Champlin, MD

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Reece and colleagues reported on autologous stem cell transplants for myeloma related to age less than or greater than 60 years (Bone Marrow Transplant 32:1135, 2003). Manuscripts have been submitted reporting that pretransplant consolidation chemotherapy decreases leukemia relapse after autologous blood and bone marrow transplants for AML in first remission (Talman et al) and describing the results of cord blood transplantation in children (Rubinstein et al) and adults (Laughlin et al).

ABMTR committees continue to address critical issues involved with the indications and optimal use of autologous stem cell transplantation, including its role vs. allogeneic transplant options or standard dose treatment. There continues to be a major role for observational studies employing the large datasets of the ABMTR, IBMTR and collaborating cooperative group organizations. We continue to work productively with colleagues in the European Bone Marrow Transplant Group and National Marrow Donor Program. The ABMTR is also active as the coordinating body for the U.S. Blood and Marrow Clinical Trials Network, facilitating the conduct of prospective clinical trials addressing fundamental issues of hematopoietic transplantation. The ABMTR/IBMTRR fills a major unmet need to collect research data on patients receiving hematopoietic transplants throughout the world and leading the development of both observational research and prospective clinical trials necessary to address the critical issues in this field. Under Dr. Horowitz’s leadership, the ABMTR and IBMTR have emerged as a central organization leading research in hematopoietic transplantation.

This is an exciting time in the field of hematopoietic transplantation. Advances in molecular and cell biology, hematopoiesis and stem cells, transplant and tumor immunology and genetic therapies all come together in innovative translational applications in hematopoietic transplantation. It is a major challenge for ABMTR and IBMTR to stay abreast of the important advances and lead the further development of the field. The use of autologous and allogeneic stem cell transplants is rapidly evolving from a supportive care modality allowing administration of high dose chemotherapy to becoming the platform for innovative applications involving tumor vaccines, immunotherapy and use of engineered stem cells and lymphoid populations to improve the specificity and efficacy of transplant based therapies.

ABMTR and IBMTR are dynamic organizations dependent on the quality of its staff and participating investigators from transplant centers. The organization involves a large and diverse group of investigators and provides enormous opportunities for junior and established investigators to lead and participate in cutting edge clinical research. I encourage physicians and scientists from all participating centers to become active in ABMTR/IBMTR. Individuals are encouraged to contact the Working Committee chairs or any of the ABMTR/IBMTR leadership and become involved in the research projects. We encourage proposals for new analyses or projects to be sent to the appropriate committee chair. The annual Tandem meetings provide a great opportunity to become involved. I look forward to seeing you there.

Continued on page 2

Results of Randomized Trials of PBSC versus Marrow from HLA-Identical Siblings

Engraftment: Eight randomized trials compared transplantation of mobilized PBSC and marrow from HLA-identical sibling donors. Each of these trials enrolled 30 to 350 patients. Neutrophil engraftment occurred significantly earlier with PBSC in seven trials, and platelet engraftment occurred significantly earlier with PBSC in all trials.

Acute GVHD: The risks of acute grades II-IV GVHD were similar in seven trials, while the European Blood and Marrow Transplant (EBMT) study noted a 13% greater incidence of grade II-IV GVHD and a 12% greater incidence of grade III-IV GVHD with PBSC.

Continued on page 4
Continued from page 3

following differences among the trials may explain the discrepant results:

1. All trials used cyclosporine and methotrexate for GVHD prevention. However, the EBMT study omitted the Day 11 methotrexate from the regimen while the next two largest trials in the U.S. and Canada included Day 11 methotrexate. In prior studies of marrow transplantation, the omission of Day 11 methotrexate increased the risk of GVHD.

2. The EBMT trial employed G-CSF posttransplant while the U.S. and Canadian trials did not. There is no obvious relationship between posttransplant G-CSF and GVHD.

3. The EBMT trial was the largest and therefore had the most statistical power to detect a difference.

Chronic GVHD: All trials suggested that PBSC transplantation was associated with more chronic GVHD, and three trials found a statistically significant increase in chronic GVHD. The Day 11 dose of methotrexate was omitted in the three trials where PBSC led to a statistically significant increase in incidence of chronic GVHD. While this observation does not directly explain a higher incidence of chronic GVHD, patients with acute GVHD are more likely to develop chronic GVHD and patients who do not receive the Day 11 dose of methotrexate are more likely to develop acute GVHD.

Survival and Relapse: The second and third largest trials, involving 228 and 172 patients in Canada and the U.S., respectively, showed significantly better survival or disease-free survival with PBSC. In the U.S. study, the survival difference of 13% at 2 years was greatest among patients with advanced hematologic malignancies. Both reduced transplant-related mortality and reduced relapse contributed. This study enrolled more patients with advanced hematologic malignancies than the others. The U.S. trial failed to detect improved survival with PBSC in patients with early stage disease, perhaps because of the relatively small sample size or perhaps because both transplant-related mortality and relapse are lower in this group regardless of graft source. The Canadian trial enrolled patients with early leukemia, and found a significant survival advantage with PBSC of 10% at 2 years, primarily due to reduced non-relapse mortality. The EBMT trial enrolled almost exclusively patients with early leukemia, and showed no differences in disease-free survival or overall survival.

Differences between the EBMT and Canadian trials were discussed above. One possible interpretation is that the administration of postgrafting methotrexate, using full dose and schedule, may be critical to prevent acute and chronic GVHD after PBSC transplantation and to realize the potential for PBSC to improve patient survival by 10-13% at 2 years.

Results of Phase II Studies of PBSC from Unrelated Donors

European Studies: Initial reports demonstrated the feasibility and potential safety of G-CSF-mobilized PBSC transplants from unrelated donors. In matched-cohort studies by Ringden and Rembarger, PBSC achieved faster neutrophil and platelet engraftment compared to marrow transplantation, with no difference in acute GVHD, relapse, treatment-related mortality, or survival. Elmaagacli and colleagues proposed that for patients with CML in chronic phase, HLA-matched unrelated PBSC transplants decreased relapse and improved survival when compared with bone marrow.

Preliminary NMDP Phase II Data in Unrelated Donor PBSC Transplants: A prospective study was conducted by the NMDP to test the feasibility of harvesting PBSC from volunteer donors and the safety of transplanting those PBSC to patients with hematological disorders. Donors were treated daily with G-CSF 10 mcg/kg and PBSC were harvested on Days 5 and 6. Cells collected on Day 5 were stored at 2-8°C. The two-day collection was transported to 2-8°C and infused fresh into the recipient. An interim analysis evaluated results of 222 transplants facilitated by 55 apheresis centers and 57 transplant centers over the first year of study. PBSC were obtained in a one-day (n=47) or two-day (n=175) collection. The median blood volume processed was 12 liters per day, and 24 liters per total collection. Transplant regimens varied according to institutional protocols. The incidence of engraftment was 96%, acute GVHD grades II-IV 47%, acute GVHD grades III-IV 33%, extensive chronic GVHD 36%, non-relapse mortality 18% at 100 days and 41% at one year, relapse 26%, survival 35% and disease-free survival 32% at one year. Outcomes of PBSC and marrow transplants conducted at the same institutions over the same period were compared. Multivariate analyses were used to adjust for differences in patient age, gender, cytomegalovirus serology, performance status, diagnosis and stage, interval from diagnosis to transplant, donor age, HLA matching, transplant center, year of transplant, conditioning and immunosuppressive regimens. PBSC were associated with faster neutrophil and platelet engraftment, similar risk of GVHD grades II-IV, increased GVHD grades III-IV, and similar rates of relapse, survival and disease-free survival.

Models were controlled for transplant center and year, recipient age, gender, diagnosis, Karnofsky score and CMV, donor age, HLA matching, conditioning and immunosuppressive regimens.

Within the initial 100 days after transplantation, PBSC was associated with a lower hazard of death (relative risk [RR] 0.6, 95% CI 0.4-0.8, p=0.003); after the 100 days there was no association (RR 1.2, 95% CI 0.8-1.7, p=0.39). When reduced-intensity transplants, defined by the use of whole body irradiation at a dose below 800 cGy or the use of mycophenolate mofetil, were excluded from the analysis, PBSC was associated with a small but not statistically significant survival advantage at 100 days (RR=0.7, p=0.10) and similar overall survival (RR=0.95, p=0.73). A multivariable analysis restricted to PBSC recipients found that the highest quintile of CD34 cell doses (i.e. > 10⁷ per kg) was associated with an increased risk of chronic GVHD but had no association with survival.

We conclude that harvest and transplantation of PBSC from volunteer donors are feasible and, within the constraints of this initial study, appear at least as safe and effective as marrow grafts. Since this study was not randomized and the groups of patients who received PBSC and marrow differed for many variables, we cannot conclude with certainty that PBSC is better, worse, or the same as marrow. Although the benefits and risks of PBSC transplants from unrelated donors are not proven, the utilization of unrelated donor PBSC in the U.S. is increasing: use of PBSC now exceeds the use of marrow for unrelated donor transplantation. The continued rise in utilization of PBSC in the absence of definitive data demonstrating any long-term advantages over marrow and concern about possible increased risks of chronic GVHD, supports the rationale for the timely conduct of a prospective randomized trial of PBSC versus marrow in unrelated donor transplantation. A prospective, randomized, multicenter clinical trial of unrelated donor transplantation sponsored by the U.S. Blood and Marrow Clinical Trials Network and the NMDP was recently activated and will test the hypothesis that transplantation of PBSC leads to similar patient survival compared to transplantation of marrow.
IBMTR/ABMTR Data Management Updates

By Mark Reitz

This column is dedicated to announcing new tools and forms available to help those who submit data to the IBMTR/ABMTR Statistical Center. In addition, there is a list of the most Frequently Asked Questions (FAQ) received at the Statistical Center.

A New IBMTR/ABMTR Mentoring Committee is available

Make sure you visit www.datamanager.blogspot.com to find an international group of Clinical Research Associates who are willing to help others in their field. The mentoring committee is a great resource for all involved in the ever-changing world of clinical research. It allows you to correspond with someone doing the same job as you.

There are many useful internal and external links, including:
- A list of Mentors willing to help you with your questions.
- Pre-Registration Forms.
- List of helpful abbreviations for Data Managers.
- Links to: EBMT, NMDP, BMT-infonet, CTCAE(3.0), HIPAA, HLA Typing, Social Security Death Index, Internet Drug Index, Medical Calculator and more...

During the past year the IBMTR/ABMTR has released a new version of virtually all Report Forms, as Series 2002, including:
- Core Insert
- Follow-up Core Insert
- Five new Graft Inserts
- Donor Cellular Infusion (DCI) Insert
- AlloDCI Graft Insert
- Twelve new DCI Supplement Inserts

You can view and download the new forms online at http://www.ibmtr.org/. Click on the menu far left side “Data Collection”. Click on “Report Forms”.

Some StemSoft Centers print out their forms and mail them to us. For accuracy and efficiency reasons, the IBMTR/ABMTR prefers that all data is submitted electronically rather than paper. Please contact Mark Reitz at reitzm@mcw.edu or 414-456-8137 with any questions.

During the past year the IBMTR/ABMTR has released a new version of the following registration form:

Pre-registration Form

You can view and download the new form online at http://www.ibmtr.org/. Click on the menu far left side “Data Collection”. Click on “Registration Form”. Next, click on “Research Centers”. Finally, click on “Registration Forms”.

In addition, the IBMTR/ABMTR and StemSoft have worked together, and are pleased to announce the release of TED on the Web. This allows online data entry for all Registration Forms. Please visit http://www.ibmtr.org/dataportal/dataportal.html for more information.

Also, recently released: The Instructions for Completing the Series 2002-Core Insert, Follow-up Core Insert and DCI Insert. Please visit http://www.ibmtr.org/dataportal/dci_manual.html and on the Manual for Clinical Research Professionals link to gain access to this manual that describes how to complete the 002-Core Insert.

This manual is divided into three sections:
Section 1 lists general reporting rules that apply not only to completing Research Report Forms, but also apply to the Registration process.
Section 2 lists each question from the 002-Core Insert.
Section 3 contains information on electronic reporting and some helpful appendices, including a table that shows the relationship between questions found in 002-Core, 002-CoreFU and 002-DCI Inserts. The information contained in this document is subject to change without notice. Please check back at least every few months to make sure you have the most up-to-date instructions and direct your questions, suggestions or comments about this Manual to Diane Knutson at dknutson@mcw.edu.

Frequently Asked Questions:

Q: Why does every patient need to be Registered?
Which form do I use to register a patient?

A: Research Teams

Most Pre-Register all patients ≤ 2 weeks prior to start of high dose conditioning (including day 1 of conditioning) using the IBMTR/ABMTR Pre-Registration Form. This is to insure the IBMTR/ABMTR database is representative of the BMT population.

The Pre-Registration Form is adapted from the TED-01 form but includes several additional data fields to allow rational selection of patients for comprehensive data reporting. The Pre-Registration Form information is entered in a randomization program that weighs cases based on the needs for current and future studies while ensuring adequate representation of all transplant types and indications. Comprehensive data via the Report Form may be requested for 100% of all registered patients with rare diseases or utilizing new therapies. Diseases that are more common are randomized for Report Form completion to insure a statistically significant representation. All cases require a TED and TED follow-up (TEDFU) yearly whether or not a Report Form was due.

A: Registering Teams

Must Register all patients using the Transplant Essential Data Form (TED-01) at 100 days post transplant and TED follow-up (TEDFU) yearly to insure the IBMTR/ABMTR database is representative of BMT population. Note that Registering Teams do not submit Pre-Registration Forms.

Q: Does each transplant receive a different IUBMID number?

A: No, every patient receives only one IUBMID number, regardless if they receive an Allo transplant, Auto transplant, Subsequent Transplant or DCI. Do not assign a new IUBMID number for subsequent transplants/infusions for any reason.

IUBMID numbers are assigned by your institution, should be unique and by itself, should suffice to identify the patient and should not be liable to change. IUBMID numbers cannot be assigned using patient identifiers such as name, social security number, medical record number, etc., and should only be six digits long.

Q: What does the IBMTR/ABMTR Report Form consist of?

A: A Day-100 Report Form consists of a Core Insert, Graft Insert and Disease Insert. It is possible that a Report Form is requested for a patient in which a Disease Insert does not yet exist. In those instances, complete the 2002 Core Insert and Graft Insert only. When the Disease Insert has been released, you will receive a request to complete one at that time.

Q: What is the difference between multiple infusions, subsequent transplants and DCI’s?

A: Any infusion given within 14 days of the first infusion for an HSCT will be counted as one single transplant with multiple infusions. If a Report Form is required, you will complete one Core Insert and one Disease Insert, but you must complete separate Graft Inserts for different tissues or separately answer Graft Insert questions pertaining to the handling of the graft and quantity of cells infused for each day of infusion for the same tissue.

Typically, engraftment has occurred by day 14. If not, intervention is generally taken and should be reflected as a separate HSCT, unless it is an autologous rescue.

DCI’s were given the cut off of 28 days. Any infusions less than 28 days from the first are considered multiple infusions for a single DCI.

Anything after must be reported separately.

Anytime conditioning is used, that HSCT must be reported separately, regardless of how much time has lapsed.

Please refer to Appendix A of “The Instructions for Completing the Series 2002-Core Insert, Follow-up Core Insert and DCI Insert” for detailed timelines for reporting data.
Both related and unrelated donor transplantation remain treatment options for chronic myelogenous leukemia (CML), though the numbers of transplantations for early stage CML dropped after introduction of imatinib mesylate as a nontransplant therapy. Three-year probability of survival after HLA-identical sibling transplantation for chronic phase CML done within the first year of diagnosis is 71 ± 1%; if transplantation is done more than one year after diagnosis, the probability is 59 ± 2%. Corresponding probabilities with unrelated donors are 55 ± 2%, and 52 ± 2%.

Among 5,307 allotransplants performed between 1996 and 2001 for acute myelogenous leukemia (AML), reported to the IBMTR, recipients of HLA-identical sibling transplants in first remission had a 3-year survival probability of 61 ± 1%; patients in ≥2nd remission had a 3-year survival probability of 48 ± 2%. Three-year survival probabilities after unrelated donor transplantations were lower than after HLA-identical sibling transplantation, 41 ± 2% and 42 ± 2% in 1st and ≥2nd remissions, respectively. Age at transplantation is also associated with survival with younger patients having higher survival probabilities.

From 1996 to 2001, 231 and 1,609 autotransplants for AML were performed in patients ≤20 years old and >20 years old, respectively, and were registered with ABMTR. Three-year survival probabilities for patients transplanted in first remission were 62 ± 5% in those ≤20 and 48 ± 2% among those older than 20. Corresponding survival probabilities after transplantation in second remission were 48 ± 8% and 37 ± 4%. There are few autotransplants performed for AML in relapse and outcome is poor.
Many patients with acute lymphoblastic leukemia (ALL) are cured with conventional chemotherapy. For patients failing chemotherapy, i.e. in relapse or \( \geq 2 \)nd remission, or patients in first remission at high risk for failing chemotherapy (older age, high leucocyte count at diagnosis, Philadelphia or other chromosome abnormalities), transplantation is a viable option. Three-year probability of survival after HLA-identical sibling transplantation for ALL in first remission is 62 ± 2% for patients \( \leq 20 \) years of age and 48 ± 2% for older patients. Survival probabilities are 6 to 10% lower after transplantation in second remission. The 3-year survival probabilities after unrelated donor transplantation in first remission are 46 ± 3% and 42 ± 3%, for patients \( \leq 20 \) years old and > 20 years old, respectively; survival probabilities are 6 to 10% lower if transplantation is performed in second or subsequent remissions.

Between 1996 and 2001, 368 autologous transplants were performed for ALL and registered with the ABMTR. Three-year survival probabilities were 51 ± 4%, 44 ± 7% and 10 ± 6% for patients in 1st remission, \( \geq 2 \)nd remissions, and not in remission, respectively.

Transplantation for CLL has generally been reserved for patients with advanced disease for whom other therapy has failed. Patients selected for allotransplantation, in particular, have many poor prognostic characteristics. Among 325 patients receiving autotransplants for CLL between 1996 and 2001 and registered with ABMTR, the 3-year survival probability was 83 ± 4%. Among 271 patients who underwent myeloablative HLA-identical sibling transplantation between 1996 and 2001 and were registered with the IBMTR, the 3-year survival probability was 50 ± 3%.


myelodysplastic syndromes. Survival of patients differs by the type of donor, recipient age and FAB classification. Among patients < 20 years of age, 3-year survival probabilities are 78 ± 6% after HLA-identical sibling transplants for refractory anemia (RA) or refractory anemia with ringed sideroblasts (RAS) and 60 ± 6% after HLA-identical sibling transplants for refractory anemia with excess blasts (RAEB), RAEB in transformation (RAEB-T) or chronic myelomonocytic leukemia (CMML), 46 ± 8% after unrelated donor transplants for RA or RARS and 45 ± 5% after unrelated transplants for RAEB, RAEB-T or CMML. Among patients older than 20 years of age, 3-year survival probabilities are 52 ± 7% after HLA-identical sibling transplants for RA or RARS, 38 ± 2% after HLA-identical sibling transplants for RAEB, RAEB-T or CMML, 36 ± 6% after unrelated donor transplants for RA or RARS and 33 ± 3% after unrelated donor transplants for RAEB, RAEB-T or CMML.

Allogeneic transplantation can cure some patients with myelodysplastic syndromes. Survival of patients differs by the type of donor, recipient age and FAB classification. Among patients < 20 years of age, 3-year survival probabilities are 78 ± 6% after HLA-identical sibling transplants for refractory anemia (RA) or refractory anemia with ringed sideroblasts (RAS) and 60 ± 6% after HLA-identical sibling transplants for refractory anemia with excess blasts (RAEB), RAEB in transformation (RAEB-T) or chronic myelomonocytic leukemia (CMML), 46 ± 8% after unrelated donor transplants for RA or RARS and 45 ± 5% after unrelated transplants for RAEB, RAEB-T or CMML. Among patients older than 20 years of age, 3-year survival probabilities are 52 ± 7% after HLA-identical sibling transplants for RA or RARS, 38 ± 2% after HLA-identical sibling transplants for RAEB, RAEB-T or CMML, 36 ± 6% after unrelated donor transplants for RA or RARS and 33 ± 3% after unrelated donor transplants for RAEB, RAEB-T or CMML.

Combination chemotherapy is the standard treatment for most patients with Hodgkin Disease. In the 20 to 30% of patients who fail conventional therapy, autologous transplantation is an effective salvage therapy. A total of 3,526 patients with Hodgkin disease underwent autologous transplantation in 1996-2001 and were registered with the ABMTR. Patients transplanted in first remission had a 3-year survival probability of 82 ± 3%; those transplanted in ≥ 2nd remission had a probability of 77 ± 2%. Although survival rates are lower, there is still a substantial salvage rate for patients who never achieved remission with conventional therapy (58 ± 2%) and for those transplanted in relapse (65 ± 1%).

In a unanimous vote, the directors of the Accreditation Council for CME approved revised “Standards for Commercial Support” that have been sent to member organizations for approval. A major concern with an initial draft was the stipulation precluding physicians from teaching if they had a conflict of interest. The new revision includes no such prohibition, but does require that everyone who is in a position to control CME content must disclose all relevant financial relationships with any commercial interest. Anyone who refuses to disclose cannot participate in the development of the CME program and is disqualified from being a planning committee member, a teacher, or an author.

ACCME Board of Directors drafts new CME standards
Non-Hodgkin lymphoma (NHL) is the most common indication for hematopoietic stem cell transplantation. Most of these transplants use autologous peripheral blood or bone marrow cells. Among 1,705 patients with follicular lymphoma who received autologous transplantation between 1996 and 2001 and were registered with the ABMTR, 3-year survival probabilities were 85 ± 4% for patients transplanted in first remission, 70 ± 3% for patients transplanted in ≥2nd remission, 69 ± 2% for patients transplanted in relapse, and 67 ± 3% for patients who never achieved remission with conventional chemotherapy. The major cause of treatment failure after autotransplantation for NHL is recurrent lymphoma. An alternative approach is allogeneic transplantation. Using standard myeloablative conditioning, the 3-year survival probability of patients with follicular lymphoma who underwent HLA identical sibling transplantation between 1996 and 2001 and were registered with the IBMTR was approximately 60%. Most deaths were transplant-related.

Between 1996 and 2001, 3,518 patients with diffuse large cell lymphoma who underwent autologous transplantation were registered with the ABMTR. The 3-year survival probability of patients by disease stage are as follows: 66 ± 3% for patients in first remission, 54 ± 3% for patients in ≥2nd remission, 41 ± 2% for patients in relapse and 49 ± 2% for patients who never achieved remission. Only 333 patients receiving HLA identical sibling transplants for diffuse large cell lymphoma between 1996 and 2001 were registered with the IBMTR. Three-year survival probabilities for these patients ranged from 23 to 33%, with little difference by disease stage, though numbers were small and all patients had some high-risk features.

Hematopoietic stem cell transplantation is now considered standard therapy for multiple myeloma, a disease incurable with conventional chemotherapy. The 3-year survival probability of patients transplanted within 18 months of diagnosis is 63 ± 1% compared to 54 ± 2% for patients transplanted later. The 3-year survival probability after standard myeloablative HLA identical transplantation is 52 ± 2% for patients transplanted within 18 months of diagnosis and 43 ± 4% for patients transplanted later. Early transplant-related mortality is high after allotransplantation.
Publications List – 2003


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newsletter

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