ASBMT eNews

American Society For Blood and Marrow Transplantation

March 2012

Clinical Research

Study Examines Relapse After Reduced Intensity Conditioning Transplantation for Acute Myeloid Leukemia

Researchers reviewed data on 263 relapsed acute myeloid leukemia patients who had previously received reduced intensity conditioning (RIC) allogeneic hematopoietic stem cell transplantation (HCST) to determine overall survival risk factors and a prognostic score. According to the study published in *Blood*, complete remission (CR) was reinduced in 32% of the patients, and researchers discovered that remission duration following transplantation was the only predictive factor for this response. The two-year overall survival from relapse was approximately 14%. Remission for more than five months after HSCT, bone marrow blasts less than 27% and absence of acute graft-versus-host disease were among the variables that predicted for better survival. Long-term survival was most likely to occur in patients who were able to achieve a CR by cytoreductive therapy, followed by either donor lymphocyte infusion or second HSCT for consolidation. More...

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Basic Science Studies

Alloantibody Secretion Partial Cause of Chronic GVHD

Researchers have discovered that alloantibody secretion is partially to blame for chronic graft-versus-host disease (cGHVD), according to a study appearing in *Blood*. CGVHD manifestations were found in several target organs, including those with mucosal surfaces. In fact, the lung and liver had fibrosis which was linked to $CD4^+$ T cells and $B220^+$ B-cell infiltration and alloantibody deposits. In addition, a lower incidence of bronchiolitis obliterans (BO) and cGVHD was found in bone marrow donated from mice unable to secrete IgG alloantibody. Lymphotoxin-receptor-immunoglobulin fusion protein was used to block germinal center formation, which, in turn, suppressed cGVHD and BO, leading researchers to conclude that this could be useful in preventing and treating cGVHD. More...

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A Word from President Elizabeth Shpall, MD

The Future of Cord Blood Transplantation

At our Tandem meetings last month, Professor Eliane Gluckman received the well-deserved ASBMT Lifetime Achievement Award for her transformative contributions to the field of umbilical cord blood (CB) transplantation. Eliane has been a great friend, a role model and a mentor to many of us in ASBMT. She led the team that bravely performed the first CB transplant in 1988. With her expertise and leadership, this source of stem cells has become widely used and has allowed many patients who were lacking acceptable donors to be transplanted. However, new regulations are currently making CB banking and transplantation more challenging.

On Oct. 20, 2011, the Food and Drug Administration's (FDA) regulations for unrelated CB Bank licensure went into effect. From that date forward, unrelated CB units for patients transplanted in the United States were required to be 1) licensed under an FDA-approved Biologics License application (BLA); 2) provided under an FDA-approved Investigational New Drug (IND) application sponsored by a CB bank, the acquiring transplant center or a registry such as the National Marrow Donor Program (NMDP); or 3) for an FDA-approved treatment IND. Additionally, U.S. transplant centers are now required to obtain consent from every patient who receives an unlicensed CB unit under the sponsored IND or their own treatment IND. If none of those options are available, transplant centers can procure a CB unit as an "urgent medical need" under a single-use compassionate IND with specific approval from the FDA.

This new law created substantial anxiety among the clinicians and bankers involved in CB transplantation. Patients with sickle cell anemia or rare metabolic diseases commonly transplanted with stem cells derived from other sources were initially excluded by the FDA from accessing CB without a specific treatment IND. In addition, many transplant centers with diverse patient populations procure a high percentage of their CB units from outside the United States. Would these international banks be able to develop a BLA or IND mechanism allowing them to send their units to the United States? Would our patients who often need a CB transplant quickly for high-risk disease in short-lived remission be denied this life-saving therapy because of the regulatory burden? Would these regulations slow (or, even worse, arrest) the substantial progress that has been made steadily since the first CB transplant was performed in 1988?

I am gratified to report that with the hard work of banks, the NMDP, HRSA, CIBMTR and the FDA, the initial barriers for implementing these regulations were less than anticipated. Thanks to the NMDP, which was extremely pro-active in getting CB banks to be part of its IND, the transition so far has enabled banks to distribute CB units for patients in need. There are now more than 64 banks outside the United States and 21 banks inside the United States that are releasing units under the NMDP IND. Additionally, last-minute negotiations with the FDA resulted in relaxation of the language for clinical use enabling continued distribution of CB units for sickle cell anemia and metabolic diseases under licensure or IND, which the transplant community is hoping will be continued. While the process is certainly more cumbersome than it was in the past, it appears that access to CB units for patients who need them has not been substantially compromised.

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A WORD FROM THE PRESIDENT (CONTINUED FROM PAGE 2)

What remains, however, are the significant financial and regulatory burdens that have been placed on the U.S. CB banks. Much of this is due to the fact that, in spite of the obvious differences with a cellular product, CB is being regulated as a drug. With this major expenditure of money, time and substantial effort on the part of the institutional CB banking staff, it still remains to be seen whether the units are really safer or better. Many banks have spent hundreds of thousands to millions of dollars creating GMP-compliant facilities and procedures which may have little or no impact on the quality of the CB unit. For some banks, more money is now being spent on the regulations than on the actual collection and storage of the units. Many in the field argue that licensure is making CB banking more complicated and expensive without a perceptible improvement in quality. When these costs are passed on to the patients, it will make CB a much more expensive source of hematopoietic support compared to alternative products from adult donors.

Historically, FACT-NETCORD accreditation and quality institutional management have produced an outstanding record of CB safety and quality. In this light, with health care reform looming and medical care resources shrinking, FDA-mandated licensure of CB as well as other hematopoietic cells should be re-evaluated. Available data suggest that we are expending tremendous resources to fix something that was not broken. At a minimum, the FDA should commit to agency-supported data acquisition to justify this costly new mandate. Banks should report the cost of the BLA process to a central registry to assist in this analysis. Strong consideration should be given to creating new regulations specifically designed for cellular therapies, including transplantation. In this way, the full potential of these promising and emerging modalities to improve the lives of patients with serious and life-threatening diseases may be realized.

-Elizabeth

CLINICAL RESEARCH (CONTINUED FROM PAGE 1)

Trial Shows Further Proof that Dasatinib is Potent Chronic Myeloid Leukemia Treatment

A phase 3 trial comparing dasatinib to imatinib confirms that dasatinib is an excellent first-line treatment for newly diagnosed chronic phase chronic myeloid leukemia (CML). The trial results appearing in *Blood* show that after 24 months of once daily use, 86% of patients included in the randomized dasatinib-treated group achieved complete cytogenetic response compared to 82% of patients in the imatinib-treated group. In addition, major molecular response was 64% vs. 46% and BCR-ABL reduction to < 0.0032% (4.5 log reduction) was 17% vs. 8%. In addition, transformation to accelerated- / blast-phase CML was 2.3% in dasatinib-treated patients and 5% in imatinib-treated patients. More...

ASSOCIATION NEWS

BMT Tandem Meetings

Registration for the 2012 BMT Tandem Meetings in San Diego was 2,544 – the second largest meeting ever. In addition, 553 submitted abstracts from 31 different countries were received.

BMT Tandem Meetings Abstracts

All accepted abstracts for the 2012 BMT Tandem Meetings were published in the February issue of *Biology of Blood and Marrow Transplantation* (Vol. 18, No. 2, Supplement 2). Abstracts are also available online at http://www.abstracts2view.com/bmt/.

Audio and Slide Recordings

Order your copy of audio and slide recordings from the 2012 BMT Tandem Meetings by completing and submitting this **form**.

Six Abstracts Chosen as Best at Tandem Meetings

Of the 553 abstracts submitted for the 2012 BMT Tandem Meetings, six of the abstracts were selected for awards by the abstract review committees. More...

Two New Investigators Win BBMT Editorial Awards

Two medical scientists are the recipients of editorial awards for new investigators for their articles published this past year in *Biology of Blood and Marrow Transplantation.* More...

Clinical Research Training Course

The ASBMT Clinical Research Training Course for fellows-in-training and junior faculty will be held in Park City, Utah, in 2012. Applications are being accepted through March 1 for the course that will be held July 11-16. More...

5th Edition Cellular Therapy Standards Published

The 5th edition of the *FACT-JACIE International Standards for Cellular Therapy Product Collection, Processing, and Administration,* with its accompanying Accreditation Manual and online FACTWeb compliance application, is available on the FACT website. The Standards and the Accreditation Manual are both available for download and/or purchase online; the compliance application (formally known as inspection checklists) is in the new online FACTWeb accreditation portal; and ancillary documents, including guides and crosswalks, are posted in the FACTWeb user area.

The 5th edition becomes effective on May 31. All accredited cellular therapy programs must be in compliance with the Standards by that date. To assist with the transition, a comprehensive outline of changes is available at FACTWeb > Cellular Therapy Document Library > Checklists and Amendments. While this outline does not address every change, it does highlight the major revisions to the Standards and provides explanations and references.

Cellular therapy programs are encouraged to contact the FACT office with any questions regarding the 5th edition Standards.

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ASSOCIATION NEWS (CONTINUED FROM PAGE 4)

New President of FACT

Helen Heslop, MD, is the new president of the FACT Board of Directors. Dr. Heslop began serving on the FACT Board of Directors in 2001 and has since chaired several committees and participated in many strategic initiatives.

Dr. Heslop's leadership will enable FACT to remain current and relevant in the rapidly evolving field of cellular therapy. Dr. Heslop was the 2008-2009 ASBMT president.

BASIC SCIENCE STUDIES (CONTINUED FROM PAGE 1)

Toll-Like Receptor 3 Signaling Changes Tumor-Supporting Cells into Tumor Destroyers

Researchers injected polyI:C into mice implanted with a Lewis lung carcinoma tumor and discovered that the tumor regressed by changing tumor-supporting macrophages (Mfs) into tumor suppressors. When Mfs entered the tumor, inflammatory cytokines were generated and M1 polarization quickened. Following the injection, tumor necrosis factor-alpha increased within one hour in both the tumor and serum. This was subsequently followed by tumor hemorrhagic necrosis and growth suppression. Among other findings in the study appearing in *Proceedings of the National Academy of Science*, Mfs sustained cytotoxic activity and M1 polarization-supporting genes were up-regulated in the tumor-infiltrating Mfs. The tumor responses were eliminated in Toll-like receptor 3/Toll-IL-1 receptor domain-containing adaptor molecule 1- (TICAM-1) negative mice leading researchers to conclude that TICAM-1 pathway is significant to mature myeloid dendritic cells for cross-priming and natural killer cell activation to induce tumor immunity, as well as to giving tumor-supporting Mfs tumor-destroying properties. More...

NKT Cells and Tregs Affect Bone Marrow and Organ Transplantation Tolerance

Natural killer (NK) T-cell production plays a positive role in bone marrow and organ graft tolerance by promoting changes in negative co-stimulatory receptor expressions and anti-inflammatory cytokines by Tregs and other T-cell subsets in an IL-4-dependent manner. Researchers of a study published in *Blood* induced tolerance and chimerism in a bone marrow and heart transplantation model by conditioning with fractionated irradiation of the lymphoid tissues and anti-T-cell antibodies. Host invariant NKT-cell production of IL-4-enhanced host $CD4^+$ $CD25^+$ Treg production of IL-10, which was necessary for the graft acceptance and chimerism. NKT cell production of IL-4 also improved up-regulation of PD-1 on host Tregs, $CD4^+$ $CD25^+$ conventional T cells and $CD8^+$ T cells. More...

Calendar of Events

•March

Association of Community Cancer Centers
38th Annual Meeting
March 12-14
Baltimore, Maryland

Regenerative Medicine: Harvesting Biology for Regeneration
16th Annual Hilton Head Workshop
March 14-17
Hilton Head Island, South Carolina

National Comprehensive Cancer Network
Clinical Practice Guidelines & Quality Cancer Care
March 14-18
Hollywood, Florida

American Association of Tissue Banks
16th Annual Spring Meeting
March 24-27
San Juan, Puerto Rico

American Association for Cancer Research
Annual Meeting
March 31-April 4
Chicago, Illinois

• April

European Group for Blood and Marrow Transplantation
38th Annual Meeting
April 1-4
Geneva, Switzerland

American Society of Apheresis
Annual Meeting
April 11-14
Atlanta, Georgia

•May

7th International Symposium on Neuroprotection and Neurorepair
May 2-5
Potsdam, Germany

Oncology Nursing Society
37th Annual Congress
May 3-6
New Orleans, Louisiana

The American Association of Immunologists
Immunology 2012
May 4-8
Boston, Massachusetts

American Society of Pediatric Hematology Oncology
25th Annual Meeting
May 9-12
New Orleans, Louisiana

American Society of Gene & Cell Therapy
15th Annual Meeting
May 16-19
Philadelphia, Pennsylvania

•June

American Society of Clinical Oncology
Annual Meeting
June 1-5
Chicago, Illinois

American Transplant Congress
American Society of Transplant Surgeons/American Society of Transplantation
June 2-6
Boston, Massachusetts

CRYO 2012
Society for Cryobiology, 49th Annual Meeting
June 3-6
Rosario, Argentina

•June (cont.)

International Society for Cellular Therapy
18th Annual Meeting
June 5-8
Seattle, Washington

Foundation for the Accreditation of Cellular Therapy
Cord Blood Inspection and Accreditation Workshop
June 10
San Francisco, California

International Society for Stem Cell Research
10th Annual Meeting
June 13-16
Yokohama, Japan

Federation of Clinical Immunology Societies
Annual Meeting
June 21-24
Vancouver, British Columbia, Canada

•July

2012 Pan Pacific Lymphoma Conference
July 17-20
Maui, Hawaii

•August

The 30th World Congress of Biomedical Laboratory Sciences
August 18-22
Berlin, Germany

Society for Hematology and Stem Cells
41st Annual Scientific Meeting
August 23-26
Amsterdam, Netherlands

• 2013

BMT Tandem Meetings
Combined ASBMT and CIBMTR Annual Meetings
February 13-17
Salt Lake City, Utah

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Do you have news, responses or opinions to share with us?
Please e-mail the association office at enews@asbmt.org.