ASBMT eNews

American Society For Blood and Marrow Transplantation

August 2013

Clinical Research

Outcomes for High- and Standard-Risk AML Pediatric Patients Similar After Allo-HCT in First Remission

High-risk acute myeloid leukemia (AML) patients have comparable outcomes to standard-risk patients after myeloablative allogeneic hematopoietic cell transplantation (allo-HCT) in first remission, according to a study published in *Biology of Blood and Marrow Transplantation*. Researchers reviewed the transplantation outcomes of 36 high-risk children and young adults with AML to 14 standard-risk AML patients. High-risk patients had FLT3-ITD mutations, 11q23 *MLL* rearrangements, chromosome 5 or 7 abnormalities, induction failure, and/or persistent disease. Most of the patients in both groups were treated with cyclophosphamide and total body irradiation conditioning. In addition, patients received cyclosporine-based graft-versus-host disease prophylaxis. The outcomes for high-risk patients were similar to those for standard-risk patients: overall survival was 72% vs. 78%, leukemia-free survival was 69% vs. 79%, relapse was 11% vs. 7%, and treatment-related mortality was 17% vs. 14%. More...

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Banked Third-Party Virus-Specific T Cells May Be Effective Post-Transplantation Viral Infection Treatment

Banked third-party virus-specific T cell (VST) lines may be an effective and safe way to quickly treat patients with severe, refractory Epstein-Barr Virus (EBV), cytomegalovirus or adenovirus following a hematopoietic stem cell

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Association News

ASBMT and YouTube

View select sessions from the 2013 BMT Tandem Meetings. **Subscribe to the ASBMT YouTube Channel**.

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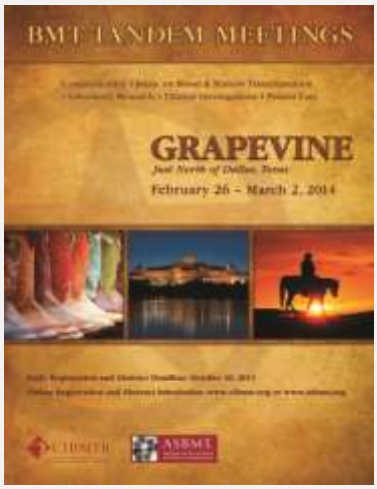

ASBMT
American Society for Blood and Marrow Transplantation

A Word From President Fred LeMaistre, MD

Is It Bragging If It's FACT?

Which achievements in our field have most contributed to improved patient care? Responses to this question would likely range from improvements in preparative regimens or supportive care to alternative cell sources or patient selection. How many of you would list the Foundation for the Accreditation of Cellular Therapy (FACT)? As the three of us have had the honor of serving as president of both ASBMT and FACT, we would like to share some reasons justifying its inclusion.

Many of our colleagues in other disciplines are scrambling to define quality in their respective fields. Almost two decades ago, the ASBMT and International Society for Cellular Therapy exhibited bold leadership by supporting a commitment to the development of standards and an accreditation process for hematopoietic cell therapy through the formation of FACT. Despite scarce resources, these young professional societies' efforts to support programs in improving quality became a priority.

From its inception, the elements that have differentiated FACT are that the process is voluntary and has always addressed the continuum of laboratory and clinical practice in transplantation. Standards development, inspection and accreditation decisions are performed by experts qualified by experience and training. These experts are so committed to their colleagues and the patients they serve that they volunteer their time. An additional differentiator is the international scope of FACT through its partnership for standards and accreditation first with JACIE for cell therapy and then with the International NetCord Foundation for cord blood banking. These partnerships are critical in assuring that donor cells collected, transported internationally and transplanted meet the highest standards of quality. What may be less appreciated is that such standardization and harmonization establish a platform for rapid improvement in patient care.

A number of measures suggest that we are meeting our commitment:

- More than 90% of facilities in North America are accredited by FACT.

- FACT is now accrediting facilities in Central and South America, Australia, New Zealand and Asia.

- FACT accreditation is required for all cancer cooperative research groups to participate in trials involving transplant.

- Payors require FACT accreditation for participation in "Center of Excellence" networks.

- FACT accreditation is a factor considered for the *U.S. News and World Report* ranking of the top U.S. cancer centers.

These accomplishments have only occurred through commitment to our patients by our facilities, the membership of ASBMT and ISCT, and the volunteers of FACT.

The field of hematopoietic cell therapy has always been defined by leadership, innovation and focus on the well-being of our patients. We can take great pride in knowing that we are also leaders in assuring quality outcomes for our patients.

C. Fred LeMaistre, MD –
Current ASBMT President

Elizabeth Shpall, MD –
Immediate-Past President

Helen Heslop, MD –
2008-2009 ASBMT President

CLINICAL RESEARCH (CONTINUED FROM PAGE 1)

transplant without having to create a separate line for each patient, according to a study appearing in *Blood.* Researchers prepared a bank of 32 virus-specific lines from HLA individuals who possessed common polymorphisms and immunity to EBV, cytomegalovirus or adenovirus. Within 24 hours, researchers were able to identify a line for most of the patients enrolled in the study, and eighteen lines were used to treat 50 patients. Six weeks after infusion, the cumulative rates of complete or partial responses were 74% for the entire group, 73.9% for cytomegalovirus patients, 77.8% for the adenovirus group, and 66.7% for EBV patients without any adverse reactions from the infusion. Only four patients experienced a recurrence or progression, and two patients developed graft-versus-host disease. More...

Study Demonstrates Promising Responses to Ibrutinib

A phase 1b-2 multicenter study was conducted on 85 patients to determine the safety, efficacy, pharmacokinetics and pharmacodynamics of ibrutinib to treat relapsed or refractory chronic lymphocytic leukemia or small lymphocytic lymphoma. Patients received a daily oral dose of either 420 or 840 mg of ibrutinib. The results of the study published in the *New England Journal of Medicine* indicate that the overall response rate was 71% for both groups. In addition, another 20% of the patients who received 420 mg of ibrutinib and 15% of the patients who were treated with 840 mg experienced a partial response with lymphocytosis. Grade 1 or 2 toxic effects, including brief diarrhea, fatigue and upper respiratory tract infection, were most common among patients. More than two years after treatment, the estimated progression-free survival rate was 75% and the overall survival rate was 83%. More...

ASSOCIATION NEWS (CONTINUED FROM PAGE 1)

Free ASBMT Membership for Trainees

Postdoctoral fellows and physicians-in-training for blood and marrow transplantation are eligible for free membership to the American Society for Blood and Marrow Transplantation. Through October, annual dues are waived for new trainees who apply for membership to the Society. This program is made possible through a grant from Otsuka America Pharmaceuticals, Inc. More...

Oct. 1 Deadline for New Investigator Awards

Supported by Amgen, Celgene, Genentech, Otsuka and ASBMT, new investigator awards of $60,000 each will be presented at the 2013 BMT Tandem Meetings. The deadline for applications is Oct. 1. More...

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ASSOCIATION NEWS (CONTINUED FROM PAGE 4)

2013 Guidelines: *Recommended Timing for Transplant Consultation*

Studies have shown that for many diseases, hematopoietic cell transplant (HCT) performed early in the disease process is associated with lower risks of transplant-related mortality and disease recurrence. If allogeneic transplant is an option, appropriate planning and early donor identification, including high-resolution HLA typing of patients and potential family donors, is critical for optimal outcomes. To provide quick access to the latest recommendations on timing of referral for autologous or allogeneic transplant, the updated **2013 Guidelines: *Recommended Timing for Transplant Consultation*** is now available.

These newly updated guidelines include disease categories for patients at risk for disease progression who should be referred for HCT consultation. Developed by the American Society for Blood and Marrow Transplantation and the National Marrow Donor Program®/Be The Match®, the recommendations are based on current clinical practice, medical literature and evidence-based reviews. The guidelines are also available in a mobile app and online. For more information please contact the ASBMT office at mail@asbmt.org.

BMT TANDEM MEETINGS

Registration Open for 2014 BMT Tandem Meetings in Grapevine, Texas

Online registration and housing is now open for the 2014 BMT Tandem Meetings, which will be held Feb. 26 - March 2 in Grapevine, Texas, just north of Dallas. Links to meeting registration, housing reservations, the preliminary program, abstract submission and parallel conferences can all be found in one convenient location. More...

Abstract Submission Deadline is Oct. 10 for BMT Tandem Meetings

The Abstracts submissions process for the BMT Tandem Meetings to be held in Grapevine, Texas, just north of Dallas, is now open through Oct. 10. Invitations for oral presentations will be offered to 90 authors whose abstracts receive the highest scores from the review committees. Many others will be accepted for poster presentation. More...

TRANSLATIONAL SCIENCE STUDIES

NOTCH Signaling Plays Key Role in Aplastic Anemia

To determine what causes severe aplastic anemia to progress in patients, researchers used a mouse model to prove that intracellular $NOTCH1^{IC}$ and T-BET expression increased in spleen and bone marrow-infiltrating T cells when aplastic anemia was active. However, when NOTCH1 was deleted or y-secretase inhibitors (GSIs) were administered in vivo, the condition improved, preventing fatal bone marrow failure in the mice. Examining peripheral T cells from patients with aplastic anemia, researchers discovered that $NOTCH1^{IC}$ was elevated and bound to the *TBX21* promoter. This indicates that NOTCH1 regulates the gene encoding T-BET, according to the study published in *The Journal of Experimental Medicine*. When patient cells were treated with GSIs in vitro, there were decreases in $NOTCH1^{IC}$ levels, NOTCH1 detectable at the *TBX21* promoter, and T-BET expression. These results suggest that NOTCH1 signaling responds to GSI treatment during active disease, identify NOTCH signaling as a major cause of Th1-mediated pathogenesis in aplastic anemia, and indicate a potential new treatment. More...

Genetic and Epigenetic Alterations Linked to ALL

Researchers analyzed 137 B-lineage and 30 T-lineage pediatric acute lymphoblastic leukemia (ALL) cases for genetic and epigenetic changes by performing microarray analysis of DNA copy number alterations and gene expression, and genome-wide cytosine methylation profiling. They discovered that different genetic subtypes of ALL have distinct DNA methylation signatures that correlate with gene expression profiles. In addition, the same epigenetic signature was identified in all of the cases and was associated with gene expression in 65% of the genes. This suggests that a core set of epigenetically deregulated genes play an important role in starting or maintaining lymphoid transformation, according to the study appearing in *The Journal of Clinical Investigation*. The researchers also identified abnormal methylation in several genes targeted by recurring DNA copy number alterations in ALL. The study results led researchers to conclude that there are subtype- and disease-specific alterations in cytosine methylation in ALL that influence transcriptional activity and most likely play a significant role in the development and progression of ALL. More...

Success of Methotrexate Treatment for ALL Related to Genetic Variations

Genetic variations influence how children respond to high doses of methotrexate (MTX) used to treat acute lymphoblastic leukemia (ALL), reports a study published in *Blood.* Researchers genotyped 499 MTX-treated pediatric ALL patients from the ALL-BFM (Berlin-Frankfurt-Munster) 2000 trial to determine MTX pharmacokinetics, toxicities and outcomes related to genotypes. The researchers examined eight single nucleotide polymorphisms in five candidate genes of the MTX/folate pathway and discovered a link between the SLCO1B1 rs4149056 variant and MTX kinetics. A multiple regression model revealed that the MTX area under the concentration time curve $(AUC)_{0\text{-}48h}$ increased by 26% per SLCO1B1 rs4149056 C allele and predicted overall toxic adverse events during MTX treatment. In addition, the thymidylate synthase rs34743033 tandem repeat polymorphism predicted stomatitis. Multiple Cox regression analyses showed an association of minimal residual disease and methylenetetrahydrofolate reductase rs1801131 with event-free survival. More...

Calendar of Events

•August

Society for Hematology and Stem Cells
42nd Annual Meeting
August 22-25
Vienna, Austria

•September

ESH-iCMLf
Chronic Myeloid Leukemia: Biology and Therapy
September 26-29
Estoril, Portugal

European Society for Medical Oncology
European Cancer Conference
September 27-October 1
Amsterdam, Netherlands

•October

American Association of Tissue Banks
Annual Meeting
October 2-6
National Harbor, Maryland

2nd International Congress on Controversies in Stem Cell and Cellular Therapies
October 10-13
Berlin, Germany

American Association of Blood Banks
Annual Meeting
October 12-15
Denver, Colorado

•October (cont.)

National Marrow Donor Program/Be The Match
2013 Council Meeting
October 17-19
Minneapolis, Minnesota

Histiocyte Society
Annual Meeting
October 21-23
Washington, D.C.

European School of Hematology/Eurocord-Ed/Eurocord World Cord Blood Congress IV and Innovative Therapies for Sickle Cell Disease
October 24-27
Monaco

European Society of Gene and Cell Therapy
Congress 2013
October 25-28
Madrid, Spain

•November

Meredith A. Cowden Foundation
4th Annual Graft vs. Host Disease National Symposium
November 1
Cleveland, Ohio

American Society for Histocompatibility & Immunogenetics
39th Annual Meeting
November 17-21
Chicago, Illinois

•November (cont.)

European Association of Tissue Banks
22nd Annual Congress
November 20-22
Brussels, Belgium

•December

American Society of Hematology
Annual Meeting
December 7-10
New Orleans, Louisiana

• 2014

BMT Tandem Meetings
Combined ASBMT and CIBMTR Annual Meetings
February 26-March 2
Dallas, Texas

• 2015

BMT Tandem Meetings
Combined ASBMT and CIBMTR Annual Meetings
February 11-15
San Diego, California

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The editor for ASBMT eNews is Georgia B. Vogelsang, MD, MBA.
ASBMT eNews services provided by Lori O'Keefe.

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