CLINICAL RESEARCH

Positive Outcomes for MDS Patients After CD34-Selected HCT

Advanced myelodysplastic syndrome (MDS) patients had encouraging long-term overall and relapse-free survival outcomes after CD34-selected allogeneic hematopoietic cell transplantation (HCT), according to a study appearing in Biology of Blood and Marrow Transplantation. In addition, these patients had a low occurrence of acute and chronic graft-versus-host disease (GVHD) and did not have an elevated risk of relapse. Researchers analyzed the outcomes of 102 adults with advanced MDS who received peripheral blood grafts depleted of donor T cells via CD34 selection. They discovered that the cumulative incidences of grades 2-4 acute GVHD were 9.8% at day 100 and 15.7% at day 180, and chronic GVHD was 3.9% one year after transplantation. The cumulative incidences of relapse also were low: 11.8% at one year and 15.7% at two years. Nearly six years after transplantation, 48 patients were alive, and researchers learned that the rates of overall survival had been 56.9% two years post-HCT and 49.3% five years after transplantation, while the rates for relapse-free survival at two and five years were 52% and 47.6%, respectively. In addition, nonrelapse mortality was 7.8% 100 days after HCT, 22.5% one year post-HCT and 33.4% five years following HCT. More...

Adverse Post-HCT Outcome Predictors Identified for Cytogenetically Normal AML

Age, presence of FLT3 internal tandem duplications (FLT3-ITD) and more than one round of chemotherapy were found to be the best predictors of adverse outcomes after allogeneic hematopoietic cell transplantations (HCT) performed on adult cytogenetically normal acute myeloid leukemia patients in first complete remission, reports a study published in Blood. Researchers from the European Group of Blood and Marrow

Continues on page 7
A Word From President Effie Petersdorf, M.D.

Good Will to All

Dear Colleagues:

There is really no comparable specialty that has fostered so much international collaboration as what we have collectively accomplished in transplantation. To describe what we do as “multidisciplinary” only captures a fraction of what happens day to day.

Reflect for a moment on two vital statistics of which we should be extremely proud:

1. There are more than 25 million volunteer donors worldwide – a true humanitarian response to the needs of patients past, present and future. How did 25 million heroes come about? Through individual efforts of donors, family members, patients and professionals involved in donor recruitment (Petersdorf EW. The World Marrow Donor Association: 20 years of international collaboration for the support of unrelated donor and cord blood hematopoietic cell transplantation. Bone Marrow Transplant. 2010;45(5):807-810). They are colleagues, neighbors, fathers, mothers, brothers and sisters. This activity has been propelled by the realization that no single country can be self-sufficient in providing unrelated donors and other products to patients. There is still more work to be done. To increase the chances that a suitable donor is available for any patient in need of a transplant, continued recruitment of donors from under-represented regions, including Africa, the Eastern Mediterranean and Southeast Asia, require our continued efforts.

2. Collectively, we recently achieved a milestone with the performance of the one millionth transplant (Gratwohl A, Pasquini MC, Aljurf M, et al. One million haemopoietic stem-cell transplants: A retrospective observational study. Lancet Haeme. 2015;2(3):e91-100). This was accomplished by sharing experiences and data across transplant centers, donor centers, transplant registries and donor registries that enable us to improve ways to perform transplantation and support our patients through, what is for most of them, an intense physical and emotional experience. ASBMT’s collaboration with the Worldwide Network for Blood and Marrow Transplantation reflects our common interests and goals in fostering the growth of transplant programs and in optimizing patient care no matter where the patient lives.

The global effort to deliver high-quality patient care is also reflected by a continued need to increase the educational efforts of ASBMT with international sister societies, identify ways to promote and improve the dissemination of new research findings, and collaborate on international clinical trials. ASBMT has developed a relationship with the Brazilian Society of Bone Marrow Transplantation, and recent discussions have been ongoing with the Asia Pacific Bone Marrow Transplantation Society (APBMT).

To promote our collaboration with colleagues in the Asia-Pacific rim, our president-elect, Chris Bredeson, M.D., recently travelled with ASBMT staff to Okinawa, Japan, to present at the 20th Congress of the APBMT. His presentation addressed ASBMT’s use of partnerships to meet challenges associated with hematopoietic cell transplantation.

This theme of partnership carried over to discussions about ways ASBMT and APBMT can further our missions to foster education and training in hematopoietic cell transplantation. Increasing participation in the ASBMT Clinical Case Forum, encouraging hematology-oncology fellows and junior faculty to apply for the ASBMT Clinical Research Training Course, developing future international exchanges of

Continues on page 3
transplant physicians to sister institutions as observers and conducting research are some of the activities the societies will explore together. As we look forward to the future, ASBMT will continue to foster international collaborations with sister societies.

Wishing you peace and happiness this season,

-Effie P.

ASSOCIATION NEWS

Online Voting for Officers, Directors

We are pleased to announce that online voting for the annual election of ASBMT officers and directors has begun. The candidates on the nominating slate represent a wide range of experience and expertise in, as well as passion for, the blood and marrow transplantation field.

As in past years, we are choosing a vice president, treasurer and three directors (community or clinical practice, laboratory science and director-at-large). Members qualified to vote in the election are being sent instructions via email beginning Dec. 1; the ballot deadline is Jan. 6. Please take a few moments to participate in the online election and help choose the leaders who will direct the future of the Society.

One additional nomination this year is for the office of president-elect. This fall, Ginna Laport, M.D., ASBMT vice president, advised us that she was taking a leave from academic medicine for industry work. As a result, she stepped down as ASBMT vice president.

Under ASBMT bylaws, the incoming ASBMT vice president automatically elevates to president-elect at the ASBMT Annual Business Meeting held at the BMT Tandem Meetings. Thus, the election of a vice president is essentially the election of a president two years hence. This permits the vice president the opportunity to fully familiarize him or herself with the work of the board of directors and the breadth of issues faced by the Society.

With the vice presidency vacancy during 2015, this meant that ASBMT needed to identify a new candidate for the office of president-elect. The ideal candidate would be someone with recent experience on the board and a good understanding of the issues facing the profession and the ASBMT. After thorough discussion, the Nominating Committee unanimously recommended Krishna Komanduri, M.D., for the office of president-elect. Thus, this year’s election has the regular slate of candidates for each vacancy plus the addition of the president-elect election.

The slate of officers being nominated for 2016 will be:

A. Office of President-Elect
   • Krishna Komanduri, M.D.

B. Office of Vice President
   • Ronald E. Gress, M.D.
   • John DiPersio, M.D., Ph.D.

C. Community or Clinical Practice Director
   • Markus Mapara, M.D., Ph.D.
   • Joseph McGuirk, D.O.

D. Laboratory Science Director
   • Joachim Deeg, M.D.
   • Sophie Paczesny, M.D., Ph.D.

E. Director-at-Large
   • James Gajewski, M.D.
   • Mark Juckett, M.D.

Continues on page 4
ASSOCIATION NEWS (CONTINUED FROM PAGE 3)

Visit ASBMT at 2015 ASH - Booth #1808
ASBMT will be hosting an exhibit booth at the 2015 American Society for Hematology Annual Meeting Dec. 6-9 in Orlando, Florida. Staff will be available in booth #1808 to recruit new members and answer questions from current members. Located in the nonprofit section of the exhibit hall, other organizations such as the Center for International Blood and Marrow Transplant Research, the National Marrow Donor Program and the Foundation for the Accreditation of Cellular Therapy, will be located nearby to provide information about careers in hematopoietic cell transplantation, emphasizing the growth of the field, its opportunities and the resources that are available to young clinicians and investigators.

Free ASBMT Membership for Trainees
Postdoctoral fellows and physicians, pharmacists, nurses and other advanced practice professionals in training for blood and marrow transplantation are eligible for free ASBMT membership. From June through October, annual dues will be waived for new trainees who apply for membership to the Society. The program is made possible through a grant from Otsuka America Pharmaceuticals, Inc. Please email a completed membership application and letter from your program director that verifies your in-training status to membership@asbmt.org. For more information, click here.

Online BMT Journal Club Meeting Dec. 10
The BMT Online Journal Club (BMTOJC) for trainees has been meeting for one year thanks to the efforts of Andreas Klein, M.D., and Miguel Perales, M.D.

The next installment of the BMTOJC will be Thursday, Dec. 10, at 8 p.m. (EST)/ 5 p.m. (PST). This live event will feature expert discussion with Mohamed Sorror, M.D., an associate member at Fred Hutchinson Cancer Research Center.


Please RSVP to join the Google Hangout video chat or to let us know you’ll be watching. The Twitter conversation can be joined at any time: #BMTOJC, follow at @bmtojc.

Visit www.bmtojc.net for more information about the club, including updates, links and archived videos.

Fourth Annual BMT Winter Workshop Dec. 4
On the eve of the American Society of Hematology Annual Meeting, leaders in blood and marrow transplantation (BMT) will review their latest findings in a dynamic workshop, the BMT Winter Workshop.

Created by co-chairs Marcel van den Brink, M.D., Ph.D., head of the Division of the Hematologic Oncology at Memorial Sloan Kettering Cancer Center, and Edmund K. Waller, M.D., Ph.D., director of Emory University’s Bone Marrow and Stem Cell Transplant Center, the annual workshop has provided a catalytic forum that has helped facilitate the application of new technologies to old and new BMT challenges since its inception in 2012. The program features fast-paced talks by 18 experts addressing recent unpublished data on high-impact clinical and pre-clinical studies, with this year’s topics including microbiota,

Continues on page 5
ASSOCIATION NEWS (CONTINUED FROM PAGE 3)

chimeric antigen receptors and T-cell receptor sequencing.

The fourth annual BMT Winter Workshop, hosted by Moffitt Cancer Center under the direction of Claudio Anasetti, M.D., senior member and chair of Blood and Marrow Transplantation, Moffitt Cancer Center, will be held Friday, Dec. 4, at Rosen College of Hospitality Management, University of Central Florida, within miles of the Orlando convention center. The workshop will begin at 3 p.m., followed immediately by a reception from 6:30 p.m.–8:30 p.m. Shuttle service will be available between the Orlando convention center and Rosen College. For more information or to register for the workshop, click here or contact Marsha.Moyer@Moffitt.org or Janet.Young@Moffitt.org.

---

BMT TANDEM MEETINGS

Recordings from Tandem 2015

Thanks to support from Celgene Corporation, professional recordings are now available for most plenary and concurrent scientific sessions, as well as peripheral conferences, from the 2015 BMT Tandem Meetings in San Diego, California. Slides and audio recordings are free for registered meeting attendees and files are $25 each for nonattendees. Meeting attendees will need their registration ID number – if you lost yours, please contact bmttandemregistration@conferencedirect.com. Click here to access the recordings.

Registration for BMT Tandem Meetings

Register for the 2016 BMT Tandem Meetings, which will be held Feb. 18-22 in Honolulu, Hawaii, by clicking here.

Opportunities for Trainees

Check the preliminary program for information about the many opportunities available to trainees at the 2016 BMT Tandem Meetings Feb. 18-22 in Honolulu, Hawaii.

---

TRANSLATIONAL SCIENCE STUDIES

Study Examines Roles of Molecules During GVHD of the Liver

A new study published in Biology of Blood and Marrow Transplantation reports that mucosal vascular addressin cell adhesion molecule 1 (MAdCAM-1) was aberrantly expressed in mice with hepatic graft-versus-host disease (GVHD) and in patients with GVHD of the liver but that the β7-MAdCAM-1 axis appeared to be insignificant to donor T cell recruitment to the liver in experimental GVHD. To determine how integrin-β7 and CC chemokine receptor 9 (CCR9) influence hepatic GVHD development after bone marrow transplantation, researchers used CCR9Δ− and integrin-β7Δ− donor T cells and MAdCAM-1Δ− recipients in acute GVHD models. They demonstrated that T cell homing that changed after bone marrow transplantation because of integrin-β7 deficiency on T cells or its ligand MAdCAM-1 contributed to the pathophysiology of experimental GVHD. However, a lack of CCR9 on donor T cells altered tissue homing without affecting GVHD survival. In addition, donor T cells depended on MAdCAM-1 expression to infiltrate the gut. The researchers concluded that homing and/or retention of donor T cells relies on divergent molecular pathways, depending on the GVHD target tissue. More...

Continues on page 6
Researchers have discovered that protease activated receptor 1 (PAR1) and endothelial protein C receptor (EPCR) are involved in controlling nitric oxide production to maintain and recruit EPCR-positive (EPCR⁺) long-term repopulating hematopoietic stem cells (LT-HSCs) in bone marrow. The study, appearing in Nature Medicine, reports that signaling cascades typically connected to coagulation control retention of EPCR⁺ LT-HSCs in bone marrow and their recruitment to the blood through two pathways facilitated by PAR1. Thrombin-PAR1 signaling stimulates nitric oxide production, followed by EPCR shedding controlled by tumor necrosis factor-α-converting enzyme, improved CXCL12-CXCR4-induced motility, and rapid stem and progenitor cell mobilization. However, researchers learned that bone marrow blood vessels provide a microenvironment enriched with activated protein C that maintain EPCR⁺ LT-HSCs by limiting nitric oxide production. This reduced Cdc42 activity and improved integrin VLA4 affinity and adhesion. Nitric oxide production inhibited by aPC-EPCR-PAR1 signaling reduced progenitor cell egress from bone marrow, increased retention of low nitric oxide EPCR⁺ LT-HSCs in bone marrow and protected mice from chemotherapy-induced hematological failure and death. Researchers concluded that these study findings may be applicable to stem cell transplantation in a clinical setting. More...

Bone Marrow and Blood Defects Caused by Deletion of a del(5q) MDS Gene

A study appearing in The Journal of Experimental Medicine reports that hematopoiesis is affected by the loss of TRAF-interacting protein with forkhead-associated domain B (TIFAB), a haploinsufficient gene in del(5q) myelodysplastic syndrome (MDS), causing progressive bone marrow and blood defects. To study this further, mice were transplanted with TIFAB knockout (KO) hematopoietic stem/progenitor cells (HPSCs). Some of the mice developed bone marrow failure with neutrophil dysplasia and cytopenia, while competitive transplants resulted in wild-type cells that outperformed TIFAB KO HSPCs. Analyzing the gene expression of TIFAB KO HSPCs, researchers identified dysregulation of immune-related signatures, as well as hypersensitivity to TLR4 stimulation. Among their other findings, TIFAB formed a complex with TRAF6 and reduced TRAF6 protein stability. However, loss of TIFAB increased TRAF6 protein and the dynamic range of TLR4 signaling, which contributed to ineffective hematopoiesis. When both TIFAB and miR-146a were deleted, TRAF6 expression and hematopoietic dysfunction both increased. In addition, when TIFAB was re-expressed in del(5q) MDS/acute myeloid leukemia cells, TLR4 signaling weakened and viability decreased. Researchers concluded that these study findings emphasize the importance of efficient regulation of innate immune/TRAF6 signaling within HSPCs by TIFAB and its role with miR-146a in the pathogenesis of hematopoietic malignancies. More...
Transplantation conducted a retrospective registry analysis of 702 patients to evaluate criteria, including different combinations of NPM1 mutations (NPM1\textsuperscript{mut}) and FLT3-ITD, that could allow them to predict relapse, nonrelapse mortality, leukemia-free survival and overall survival outcomes. Patients were divided into four genotype groups, according to the presence or absence of NPM1\textsuperscript{mut} and FLT3-ITD at diagnosis. Patients without either genotype were assessed for CCAAT/enhancer binding protein α (CEBPα) gene mutations. Combining NPM1/FLT3-ITD profiles and risk factors that researchers identified, prognostic risk classifications of overall survival two years after transplantation were calculated at 81% for patients with NPM1\textsuperscript{mut}/FLT3\textsuperscript{wt}, 75% for NPM1\textsuperscript{wt}/FLT3\textsuperscript{wt}, 66% for NPM1\textsuperscript{mut}/FLT3-ITD and 54% for NPM1\textsuperscript{wt}/FLT3-ITD. In addition, analysis of CEBPα in patients with NPM1\textsuperscript{wt}/FLT3\textsuperscript{wt} indicated 100% survival two years post-transplant, both in patients with a CEBPα mutation and a triple negative genotype. When the number of risk factors were taken into account to predict two-year overall and leukemia-free survival, patients with at least two risk factors had an overall survival of 53% compared to 77% for patients with one risk factor and 88% for patients without any risk factors. NPM1 mutational status, transplant protocols and development of graft-versus-host disease did not play roles in predicting outcomes. More...

Upfront Unrelated HCT for Pediatric Idiopathic Severe Aplastic Anemia

According to a study from the *British Journal of Haematology*, outcomes for upfront-unrelated donor hematopoietic cell transplantation (HCT) in children with idiopathic severe aplastic anemia (SAA) who did not receive prior immunosuppressive therapy (IST) were similar to results for matched-sibling/family donor (MSD) HCT recipients but better than outcomes for recipients of just IST or unrelated donor HCT after IST failure. For the study, researchers compared upfront-unrelated donor HCT recipients to matched historical controls who had received first-line therapy with either MSD HCT (87 patients) or IST (58 patients) or second-line therapy with an unrelated donor HCT after failed IST (24 patients). They discovered that two-year overall survival was 96% for the upfront cohort, 91% for the MSD group, 94% for the IST group and 74% for the unrelated donor HCT post-IST failure group. However, while two-year event-free survival was similar for the upfront and MSD groups at 92% and 87%, respectively, the outcomes were lower for the patients who received IST or unrelated donor HCT after unsuccessful IST at 40% and 74%, respectively. These results led researchers to conclude that using matched unrelated donor HCT is a promising first-line therapy for idiopathic SAA patients without a matched sibling donor. More...
## Calendar of Events

**December**
- Moffitt Cancer Center
  4th Annual BMT Winter Workshop
  December 4
  Orlando, Florida
- American Society of Hematology
  57th Annual Meeting and Exposition
  December 5-8
  Orlando, Florida
- European Society for Medical Oncology
  Asia Congress
  December 18-21
  Singapore

**January**
- Bioleaders Forum
  January 25-27
  Washington, D.C.

**February**
- BMT Tandem Meetings
  Combined ASBMT and CIBMTR Annual Meetings
  February 18-22
  Honolulu, Hawaii

**March**
- Association of Community Cancer Centers
  42nd Annual Meeting
  March 2-4
  Washington, D.C.
- European School of Haematology
  International Conference on Aging and Hematological Malignancies: Biology and Therapy
  March 11-13
  Athens, Greece
- Regenerative Medicine Workshop
  March 16-19
  Hilton Head Island, South Carolina
- National Comprehensive Cancer Network
  21st Annual Conference: Advancing the Standard of Cancer Care
  March 31-April 2
  Hollywood, Florida
- European Society for Blood and Marrow Transplantation
  42nd Annual Meeting
  April 3-6
  Valencia, Spain
- International Society for Biological and Environmental Repositories
  Annual Meeting
  April 5-8
  Berlin, Germany
- European School of Haematology
  5th International Conference on Myelodysplastic Syndromes
  April 14-16
  Estoril, Portugal
- American Association for Cancer Research
  Annual Meeting
  April 16-20
  New Orleans, Louisiana
- British Society for Haematology
  Annual Scientific Meeting
  April 18-21
  Glasgow, Scotland
- Oncology Nursing Society
  41st Annual Congress
  April 28-May 1
  San Antonio, Texas

**April**
- American Society of Gene and Cell Therapy
  19th Annual Meeting
  May 4-7
  Washington, D.C.
- The American Society of Pediatric Hematology/Oncology
  29th Annual Meeting
  May 11-14
  Minneapolis, Minnesota
- European School of Haematology
  20th Training Course on Haemopoietic Stem Cell Transplantation
  May 11-14
  Budapest, Hungary
- The American Society of Immunologists
  Annual Meeting
  May 13-17
  Seattle, Washington
- World Cord Blood Congress
  May 18-19
  London, England
- International Society for Cellular Therapy
  Annual Meeting
  May 25-28
  Singapore

**2017**
- BMT Tandem Meetings
  Combined ASBMT and CIBMTR Annual Meetings
  February 22-26
  Orlando, Florida

**2018**
- BMT Tandem Meetings
  Combined ASBMT and CIBMTR Annual Meetings
  February 21-25
  Salt Lake City, Utah