ASBMT eNews

AMERICAN SOCIETY FOR BLOOD AND MARROW TRANSPLANTATION

March 2015

CLINICAL RESEARCH

Consecutive Transplantations Improve Young Lymphoma Patient Survival

Myeloablative autologous stem cell transplantation followed by reduced intensity allogeneic hematopoietic cell transplantation safely improved survival outcomes of children, adolescents and young adults with poor-risk refractory or recurrent Hodgkin and non-Hodgkin lymphoma, according to a study published in *Leukemia*. The multicenter prospective study included 30 patients – 16 with Hodgkin lymphoma and 14 with non-Hodgkin lymphoma – with a median age of 16 years (range 2-33 years) and median follow-up of five years (range 1.2-12 years). Patients received carmustine, etoposide and cyclophosphamide myeloablative conditioning and autologous transplantation, followed by busulfan and fludarabine reduced intensity conditioning and allogeneic transplantation from donor sources, including nine unrelated cord blood, eight unrelated donor and six matched siblings. Of the 23 patients who completed the autologous myeloablative conditioning and reduced intensity allogeneic transplantation series, transplant-related mortality was 12% and 10-year event-free survival was nearly 60% for Hodgkin patients and 70% for non-Hodgkin patients. These encouraging results should be confirmed in a larger prospective study, indicated the researchers. More...

Mismatched, UCB Transplants Acceptable Options for Lymphoma Patients

High-risk lymphoma patients who received transplantation from mismatched unrelated donors (MMUD) or umbilical cord blood (UCB) donors had comparable survival outcomes as recipients of matched unrelated donor (MUD) transplantations, reports a study appearing in *Bone Marrow Transplantation*. Transplant outcomes for nearly 1,600 adult patients with high-risk lymphoma from 2000-2010 were analyzed for the study, which included 1,176 8/8 allele HLA-A, -B, -C and DRB1 matched MUD recipients, 275 7/8 allele HLA MMUD recipients and 142 UCB recipients. Three-year nonrelapse mortality was similar for MUD (35%) and UCB (37%) recipients but higher for MMUD (44%). However, UCB recipients had lower rates of acute and chronic

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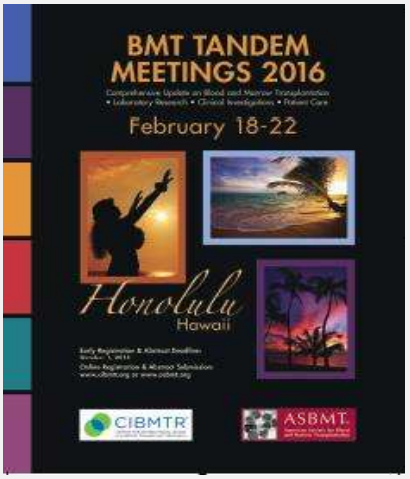

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A Word From President Effie Petersdorf, M.D.

A Bright Future

Dear Colleagues:

By now we have all returned home to our daily routines with only the fondest memories of truly exceptional BMT Tandem Meetings. If you felt like there were more colleagues at the Tandem Meetings this year, you were right: attendance surpassed 3,000, a milestone in the history of the Tandem Meetings. So many individuals worked tirelessly to create an exceptional program, from clinical and basic research and the global scene in transplantation therapies, to health care economics. Please join me in thanking our program co-chairs, Paul Veys, M.B.B.S., and Krishna Komanduri, M.D., the Scientific Planning Committee and the invited speakers for delivering outstanding presentations.

Before we address the year ahead, I would like to acknowledge the contributions our immediate-past president, Sergio Giralt, M.D., made this last year and thank him for the guidance he has given me. Dr. Giralt's unrivaled passion for who we are and the role we each play in advancing our field has been a great source of inspiration. Fortunately for ASBMT, Dr. Giralt has taken on new initiatives for the Society. We all look forward to working together toward our Preferred Future.

I also would like to thank the ASBMT committees and task forces for their exceptional productivity this past year. Suffice it to say, we are ever closer to breaking down roadblocks to patient access to transplantation. The barriers are diverse, but the economics of transplantation remains one of the most challenging. On the final day of the Tandem Meetings, Richard Maziarz, M.D., chaired the plenary session, "Health Care Economics," which highlighted current roadblocks and potential solutions.

We will continue our productive collaboration with the National Marrow Donor Program working with the Center for Medicare Services to include myelofibrosis and lymphoma as covered benefits for allogeneic hematopoietic cell transplantation. As part of the global effort to ensure adequate coverage for transplantation under the Affordable Care Act, continued dialogue with our representatives in Congress and insurance regulators will be a priority, as will working with Medicare for coverage of donor search and procurement costs. Collectively, these projects will increase access to transplantation so that every patient in need of a transplant will benefit from one.

In addition to reducing barriers to access to cellular therapy, the ASBMT Preferred Future identifies three major objectives of growth for ASBMT: 1) to be known as the clinical and translational experts in cellular therapy and transplantation biology; 2) to attract more medical professionals and scientists to the field; and 3) to establish a credentialing program in clinical stem cell transplantation.

Expertise in clinical and translational medicine relies on continued cutting-edge research in transplantation. To promote federal funding of clinical and basic research in transplantation, ASBMT and BMT CTN leaders, including Chris Bredeson, M.D., M.Sc., Mary Horowitz, M.D.,M.S., Dr. Giralt and me, have discussed the importance of funding with leadership from the National Cancer Institute and the National Heart, Lung and Blood Institute of the National Institutes of Health. Funding research will not only push clinical and basic research forward, but also will help to increase retention and bring new investigators into transplant research. Discussions in 2015 will focus on strategies for increasing clinical trials through the BMT CTN and for accessing novel therapeutics for clinical trial investigation. On ASBMT's part, continued funding of the New Investigator Awards and our training courses will attract young investigators to our field.

Education is another important objective in ASBMT's mission. The Fellows Orientation during the Tandem Meetings was chaired by Armand Keating, M.D., and reached out to

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A Word From the President (continued from page 2)

medical students and hematology/oncology fellows. The Committee on Education has made major strides developing a core curriculum and creating the Clinical Case Forum, online journal club and the "Dr. Who" session held at the Tandem Meetings to regenerate the BMT workforce. In addition, an in-depth review of possible strategies for an ASBMT-based certification in blood and marrow transplantation will culminate in a survey that will be sent to the membership this year to query interest in certification programs.

While ASBMT fostered new collaborations with the Brazilian Bone Marrow Transplantation Society in 2013-2014, we will formalize new partnerships this year with colleagues from the Asia Pacific Bone Marrow Transplant network of transplant centers and plan joint sessions for the 2016 Tandem Meetings in Hawaii. Additionally, we hope to foster new collaborations with the World Marrow Donor Association and the European Society for Blood and Marrow Transplantation, our associates across the pond. These new and continuing collaborations solidify the professional, scientific and clinical advancements in our field.

Setting and maintaining standards in transplantation has been a high priority for our Society. The Foundation for the Accreditation of Cellular Therapy (FACT) was co-founded by ASBMT and the International Society for Cellular Therapy. Our sister society is the accreditation arm for what we practice in the clinic every day. FACT standards are essential for the continued growth of the clinical practice of transplantation and play a critical role in the Process Improvement Initiatives pertaining to reimbursement. In 2015, we will continue to work closely with FACT to build our partnership. This takes on new meaning as the applications of non-hematopoietic cellular therapies expand.

The publication of ground-breaking research in our journal, *Biology of Blood and Marrow Transplantation (BBMT)*, remains the primary mode for disseminating achievements in the field. We gratefully acknowledge our editor-in-chief, Robert Korngold, Ph.D., whose dedicated efforts enabled *BBMT* to reach milestones in 2014: 719 manuscripts received for consideration and 321 accepted for publication (45.4%). 2015 is already off to a successful start with 54 manuscripts received through February. Remember that citing 2014 publications from the journal goes into its impact factor!

The practice of transplantation takes a multidisciplinary team. This is critical to tackling some of the biggest issues we face today.

I look forward to working with all of you on these important initiatives.

-Effie P.

Association News

ASBMT to Exhibit at EBMT Meeting

Visit us at booth A15 during the 2015 European Society for Blood and Marrow Transplantation (EBMT) annual meeting March 22-25 in Istanbul, Turkey.

Clinical Research Training Course Deadline Extended

The ASBMT Clinical Research Training Course for fellows-in-training and junior faculty is returning to Santa Fe, New Mexico. The application deadline has been extended until March 11 for the course that will be held July 8-13. More...

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ASSOCIATION NEWS (CONTINUED FROM PAGE 3)

New ASBMT-ISCT Training Course for Cell Therapy

The newly created ASBMT-International Society for Cellular Therapy (ISCT) Cell Therapy Training Course will be held Sept. 30-Oct. 4 in Houston, Texas. Applications opened on March 1, and the deadline is April 30.

The ISCT and ASBMT boards of directors created the course because of concerns that there is an unfulfilled need for cell therapy training covering the process of translational research to cell manufacturing and clinical trials in cellular therapy including regulatory components.

The course has four elements: 1) a proposal for a cell product by a scholar presented at the beginning of the course that will be refined in small group discussions with faculty before presentation of a final version at the end of the course; 2) visits to Good Manufacturing Process facilities producing cell products; 3) didactic lectures; and 4) round tables and informal discussions with faculty.

Tuition, travel, housing and meal expenses will be paid by ISCT, ASBMT and corporate sponsors for up to 12 scholars to attend the course. Participants will be competitively selected. Preference will be given to fellows and faculty with no more than two years of blood and marrow transplantation and cellular therapy experience following training or a faculty appointment. More...

FACT Webinar on Disaster Planning

The Foundation for the Accreditation of Cellular Therapy (FACT) recently conducted the webinar, "Planning for the Unthinkable," which focused on disaster planning. The recording is now online. This topic is of direct relevance to the ASBMT membership and often a source of questions and angst among FACT-accredited clinical centers and labs.

Transplant centers and cord blood banks are at risk for many kinds of man-made and natural disasters — fires, bomb threats, power outages, viral epidemics, floods, tornados, hurricanes and earthquakes. Some emergencies arrive with brief advance warning – others with no warning at all. The harm to patients and threat to the facility can be mitigated by thinking ahead about the unthinkable and having a plan. In this webinar, Alan Leahigh gives step-by-step guidance on preparing for, responding to and recovering from an emergency.

Expert Review in Hepatic Veno-Occlusive Disease: Emerging Preventive and Therapeutic Strategies

Veno-occlusive disease (VOD), also known as sinusoidal obstruction syndrome, is a devastating complication that develops within three to four weeks after hematopoietic cell transplantation (HCT). Damage to sinusoidal endothelial cells and hepatocytes may lead to venous occlusion, prominent sinusoidal obstruction and subsequent hepatocellular necrosis and fibrosis. Clinical symptoms include rapid weight gain, ascites, painful hepatomegaly and jaundice. Severity ranges from mild, reversible disease to a severe syndrome that often leads to multiorgan failure (MOF) and death. Day-100 mortality rates greater than 80% have been reported in severe VOD. Defibrotide therapy was shown to significantly improve severe VOD patient outcomes with a favorable toxicity profile. In the United States, defibrotide is not approved but has been made available for U.S. patients with VOD through an expanded access treatment investigational new drug protocol. An interim analysis showed improvements in survival rates compared to previously published data. Among 425 HCT patients, 100-day complete remission was 35% and 100-day survival was 55%. Among 284 patients with severe VOD, 29% had a complete remission and 48% were alive on day 100. This ongoing trial is currently enrolling post-HCT or post-chemotherapy patients with a diagnosis of VOD by Baltimore criteria with or without MOF. For more information, please view the prIME Oncology Expert Review in Hepatic VOD.

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BMT Tandem Meetings

BBMT Editorial and New Investigator Award Winners

Three medical scientists received new investigator editorial awards for their articles published in 2014 in *Biology of Blood and Marrow Transplantation (BBMT)*. Selection of the winning articles was by the *BBMT* editorial board and the ASBMT Publications Committee.

The Ernest McCulloch & James Till and George Santos Awards are supported jointly by grants from STEMCELL Technologies Inc. and STEMSOFT Software Inc. **Jessica C. Shand, M.D.,** University of Rochester Medical Center, is the recipient of the Ernest McCulloch & James Till Award for best basic science article by a new investigator: "Minor Antigen Distribution Predicts Site-Specific Graft-versus-Tumor Activity of Adoptively Transferred, Minor Antigen-Specific CD8 T Cells."

Alex F. Herrera, M.D., Dana-Farber Cancer Institute, is the recipient of the George Santos Award for best clinical science article by a new investigator: "A Phase II Study of Bortezomib Plus Prednisone for Initial Therapy of Chronic Graft-versus-Host Disease."

The ASBMT/BBMT Karl Blume Award was established last year by ASBMT in memory of Karl Blume, M.D. **Marie Bleakley, M.D., Ph.D.,** Fred Hutchinson Cancer Research Center, is recipient of the Karl Blume Award for best clinical science article by a new investigator: "Engineering Human Peripheral Blood Stem Cell Grafts that are Depleted of Naïve T Cells and Retain Functional Pathogen-Specific Memory T Cells."

In addition, seven new investigator awards were given this year to the following fellows and junior faculty:

- The ASBMT/Gabrielle's Angel Awards, sponsored by ASBMT and Gabrielle's Angel Foundation for Cancer Research: **Pavan Bachireddy, M.D.,** Dana Farber Cancer Institute, "Dissecting Clinical Response and Resistance to Donor Lymphocyte Infusion by Molecular Profiling of In-Situ Tumor and T Cells"; **Hema Dave, M.D., M.P.H.,** Children's Research Institute, "Generation of BK Virus-Specific T Cells from Naïve Umbilical Cord Blood Cells"; and **Yusuke Shono, M.D., Ph.D.,** Memorial Sloan-Kettering Cancer Institute, **"**Strategies to Overcome Transplantation Barriers and Treat Hematologic Malignancies Enabled by a Novel Small Molecule Compound Promoting c-ReIlNF-KB Inhibition."
- The Robert A. Good Award, sponsored by ASBMT and Otsuka America Pharmaceutical, Inc.: **Vedran Radojcic, M.D.,** University of Michigan, "Mapping Notch Signaling During Priming of Alloantigen-Specific T Cells in Graft-versus-Host Disease."
- The ASBMT/Millennium Award, sponsored by ASBMT and Millennium: The Takeda Oncology Company: **Dominik Schneidawind, M.D.,** Stanford University School of Medicine, "Mechanism of Tolerogenic Invariant Natural Killer T Cells for Protection from Lethal GVHD."
- The ASBMT Awards, sponsored by ASBMT: **Maite Alvarez-Rodriguez, Ph.D.,** Stanford University School of Medicine, "Infusion of NK-Committed Progenitors Accelerates Immune Reconstitution and Improves Outcome of Allogeneic Hematopoietic Stem Cell Transplantation" and **Antonio Pierini, M.D.,** Stanford University School of Medicine, "Regulatory T Cells for Tolerance Induction and B Cell Reconstitution in Children with Immunodeficiencies and Hemoglobinopathies."

The awards were presented by ASBMT President Sergio A. Giralt, M.D., during the 2015 BMT Tandem Meetings in San Diego, California.

BMT Tandem Meetings

Registration for the 2015 BMT Tandem Meetings in San Diego was more than 3,100 – continuing our streak of record-breaking attendance – with 613 submitted abstracts from 28 different countries.

Planning is already underway for the 2016 BMT Tandem Meetings Feb. 18-22 in Honolulu, Hawaii. Check www.asbmt.org later in the year for more information and details.

ASSOCIATION NEWS (CONTINUED FROM PAGE 4)

New Practitioner in the HCT Field?
Attend a training course designed for practitioners in their first years of practice focused on therapeutic management of hematopoietic cell transplantation patients.

The course will be held March 28-29 in conjunction with the Hematology/Oncology Pharmacy Association 11th Annual Conference in Austin, Texas.

Pharmacists: This activity is eligible for Accreditation Council for Pharmacy Education credit; see the final continuing pharmacy education activity announcement for specific details.

Nurses: The National Marrow Donor Program is accredited as a provider of continuing nursing education (CNE) by the American Nurses Credentialing Center's Commission on Accreditation. This activity has been approved for up to eight hours of CNE credit. Nurses should claim only the credit commensurate with the extent of their participation in the activity. Find out more and register for the course at Fundamentals of HCT Course Registration.

LLS and NMDP/Be The Match-Sponsored Webinar to Focus on AML
Registration is open for the free webinar, "Acute Myeloid Leukemia (AML): Treatment Options, including BMT, Care and Support," sponsored jointly by the National Marrow Donor Program (NMDP)/Be The Match and The Leukemia & Lymphoma Society (LLS). Speakers Gail J. Roboz, M.D., and Sergio A. Giralt, M.D., will address the risks and benefits of treatment options for patients with AML; how cytogenetics can help to inform clinicians' treatment decisions; and the impact of timely referral for blood and marrow transplantation on outcomes for patients with AML.

The free webinar will be held March 31 from 11 a.m.-12:15 p.m. (CST). It is intended for hematology/oncology and BMT social workers at all levels of experience and licensure, transplant center coordinators and other allied health professionals.

Continuing education credit is available. See full webinar details for more information. Register and view program description and event details. Encourage colleagues to attend, too.

CLINICAL RESEARCH (CONTINUED FROM PAGE 1)

graft-versus-host disease. MMUD recipients had the lowest incidence of three-year relapse (25%), while the results were nearly the same for UCB and MUD recipients (30% vs. 33%). Three-year overall survival was similar for all three groups but highest among MUD recipients (43%), followed by UCB (41%) and MMUD (37%). The researchers concluded that MMUD and UCB both can extend the curative potential to transplant recipients who do not have a matched sibling or unrelated donor source. More...

Auto-HCT for Severe Autoimmune Disorders Does Not Affect Pregnancy, Childbirth
Autologous hematopoietic cell transplantation (HCT) for severe and refractory autoimmune diseases does not appear to affect pregnancy or the ability of women to deliver a healthy baby, according to a study published in *Bone Marrow Transplantation*. Using databases from the European Blood and Marrow Transplantation and University of Sao Paulo, Ribeirao Preto, Brazil, researchers discovered 324 female patients, ages 18-50, who underwent autologous HCT for autoimmune diseases between 1994 and 2011. Of these patients, 22 pregnancies were reported among 15 women, who received autologous HCT for multiple sclerosis, systemic sclerosis, rheumatoid arthritis, juvenile idiopathic arthritis or Takayasu disease. Most of the pregnancies – 20 – were conceived naturally, 15 resulted in healthy births, with no reports of congenital or developmental issues or other diseases, and seven pregnancies failed. There were no pregnancy- or postpartum-related mortalities among the women, but two women experienced autoimmune disease flare-ups during their second pregnancies. More...

Translational Science Studies

HDAC Inhibition Reduces Inflammation and Enhances Tregs Post-Allogeneic HCT

According to results of a new study appearing in *Blood*, the histone deacetylase (HDAC) inhibitor, vorinostat, reduced peripheral blood mononuclear cell (PBMC) inflammatory responses and enhanced regulatory T cells (Tregs) after allogeneic hematopoietic cell transplantation (HCT). Oral vorinostat was administered to 50 allogeneic HCT patients as graft-versus-host disease prophylaxis from 10 days prior to HCT until 100 days after HCT. Compared to a control group (25 patients) that did not receive vorinostat, histone acetylation in PBMCs increased in vorinostat recipients. This reduced proinflammatory cytokine levels both in plasma and from PBMCs. In addition, ex vivo responses of PBMCs to proinflammatory TLR-4 stimuli decreased, but the number or response of conventional T cells to nonspecific stimuli was not affected. However, the number of Tregs grew, revealing greater demethylation of the Foxp3 T regulatory-specific demethylation region. Vorinostat also increased expression of CD45RA and CD31 on Tregs, which demonstrated greater suppression on a per cell basis. Consistent with preclinical findings, HDAC inhibition also improved signal transducer and activator of transcription 3 acetylation and induced indoleamine-2, 3-dioxygenase. More...

Modified T Memory Cells Can Survive More Than a Decade

A study published in *Science Translational Medicine* reports that genetically modified T memory stem cells can survive in humans for up to 12 years. Researchers studied patients infused with either gene-corrected hematopoietic stem cells or mature lymphocytes, using high-throughput sequencing of retroviral vector integration sites to track more than 1,700 T cell clones in patients. Comparing healthy donors and bone marrow transplant recipients, researchers investigated long-term in vivo T cell composition, particularly the impact of age, conditioning regimen, disease background, cell source, long-term reconstitution and ex vivo gene correction processing on T memory cells. This study enabled researchers to better understand long-term in vivo clonal relationships among different T cell subtypes and to discover that T memory cells can safely function for an extended period of time, which may have useful therapeutic applications in the future. More...

Altered UCB T Cells Improve Survival Chances for ALL Patients

Researchers have developed a new way to increase the quantity of umbilical cord blood (UCB) T cells into clinically relevant numbers of cytokine-expressing cells that can be used to treat patients with high-risk, relapsed or refractory acute lymphoblastic leukemia (ALL). According to a study appearing in *Leukemia*, researchers cultured UCB T cells with interleukin (IL)-12 and IL-15, which caused more than a 150-fold increase in the number of cells with a unique central- and effector-memory phenotype. The UCB T cells were also modified to express 1928Z – a CD19-specific chimeric antigen receptor (CAR) – and secrete IL-12. These modified cells retained a central- and effector-memory phenotype and had better antitumor effects in vitro. When the adapted cells were transplanted into $CD19^{+}$tumor-bearing SCID-Beige mice, survival improved. Researchers concluded that CAR-modified UCB T cells could improve the graft-versus-leukemia effect after UCB transplantation, increasing the likelihood of disease-free survival for B-cell ALL transplant patients. More...

Calendar of Events

•March

European School of Haematology
World Cord Blood Congress
March 5-8
Monaco

National Comprehensive Cancer Network
20th Annual Conference: Advancing the Standard of Cancer Care
March 12-14
Hollywood, Florida

Association of Community Cancer Centers
41st Annual Meeting
March 16-18
Arlington, Virginia

ASBMT Pharmacy Special Interest Group & National Marrow Donor Program/Be The Match
Fundamentals of HCT Training Course
March 28-29
Austin, Texas

•April

American Association for Cancer Research
Annual Meeting
April 18-22
Philadelphia, Pennsylvania

Oncology Nursing Society
40th Annual Congress
April 23-26
Orlando, Florida

Meredith A. Cowden Foundation/The Case Comprehensive Cancer Center/ The Seidman Cancer Center of University Hospitals of Cleveland/Cleveland Clinic's Taussig Cancer Institute
2015 National GVHD Health Symposium
April 24
Independence, Ohio

•April

The Myelodysplastic Syndromes Foundation
13th Annual International Symposium on Myelodysplastic Syndromes
April 29-May 2
Washington, D.C.

•May

American Society of Transplant Surgeons
American Transplant Congress
May 2-6
Philadelphia, Pennsylvania

International Society for Biological and Environmental Repositories
Annual Meeting
May 5-9
Phoenix, Arizona

American Society of Pediatric Hematology/Oncology
28th Annual Meeting
May 6-9
Phoenix, Arizona

American Association of Immunologists
Annual Meeting
May 8-12
New Orleans, Louisiana

American Society of Gene and Cell Therapy
18th Annual Meeting
May 13-16
New Orleans, Louisiana

Regenerative Medicine Workshop
May 13-16
Hilton Head Island, South Carolina

International Society for Cellular Therapy
Annual Meeting
May 27-30
Las Vegas, Nevada

•May

American Society of Clinical Oncology
Annual Meeting
May 29-June 2
Chicago, Illinois

•June

European Hematology Association
20th Congress
June 11-14
Vienna, Austria

Federation of Clinical Immunology Societies
Annual Meeting
June 24-27
San Diego California

International Society for Stem Cell Research
Annual Meeting
June 24-27
Stockholm, Sweden

Worldwide Innovative Networking
2015 WIN Symposium
June 29-30
Paris, France

•July

Society for Cryobiology
CRYO 2015 – 52nd Annual Meeting
July 26-29
Ostrava, Czech Republic

•2016

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

•2017

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

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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.