ASBMT eNews

American Society For Blood and Marrow Transplantation

October 2015

Clinical Research

GVHD and Reduced-Intensity Conditioning Linked to Lower Relapse for Some Lymphomas

Follicular and mantle cell lymphoma patients who developed graft-versus-host disease (GVHD) after reduced-intensity transplantation were less likely to relapse, yet GVHD still negatively affected patient outcomes. In this study, published in *Biology of Blood and Marrow Transplantation*, researchers analyzed the impact of GVHD on the relapse rates of 2,611 adult patients with a diagnosis of Hodgkin lymphoma, diffuse large B cell lymphoma, follicular lymphoma, peripheral T cell lymphoma or mantle cell lymphoma. Human leukocyte antigen- identical sibling or unrelated donor hematopoietic cell transplantation (HCT) was performed using a reduced-intensity conditioning regimen for 62.8% of the patients. Of the remaining 970 patients who received myeloablative conditioning, neither acute GVHD (aGVHD) nor chronic GVHD (cGVHD) affected relapse. However, all of the reduced-intensity conditioning recipients with follicular lymphoma or mantle cell lymphoma had a lower occurrence of relapse if they had cGVHD, and patients with these two types of lymphoma who developed both aGVHD and cGVHD had the lowest rates of relapse. Whether or not patients were chemoresistant did not impact the influence of GVHD on lessening relapse. Researchers also discovered that both aGVHD and cGVHD negatively affected follicular lymphoma patient treatment-related mortality and overall survival but did not impact treatment-related mortality, overall survival nor progression-free survival for mantle cell lymphoma patients. Researchers concluded that reduced-intensity allogeneic HCT is a promising treatment for follicular and mantle cell lymphoma patients. More...

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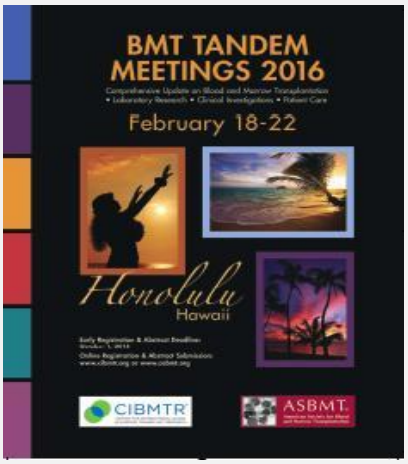

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A Word From President Effie Petersdorf, M.D.

Transplantation for Myelofibrosis and Sickle Cell Disease

Dear Colleagues:

The Centers for Medicare and Medicaid Services (CMS) provide health care for more than 53 million Americans, the vast majority of whom are older than 65 years of age. Health care providers are reimbursed for delivery of medically necessary services, but few of the diseases that are treated and cured by hematopoietic cell transplantation (HCT) are actually covered under CMS policy. Myelodysplastic syndromes (MDS), for example, afflict primarily older adults and are eminently treatable with (and curable by) allogeneic HCT. However, transplantation for MDS was not covered until the ASBMT, the National Marrow Donor Program (NMDP) and the Center for International Blood and Marrow Transplant Research partnered in 2009 to request that CMS arrive at a clear statement regarding coverage for MDS that would apply to all beneficiaries. The success of this request led to a dramatic increase in the use of allogeneic HCT to cure patients of MDS.

This positive experience served as the platform for ASBMT and NMDP to initiate a series of requests to CMS in January 2015 regarding several diagnoses, beginning with coverage of transplantation for myelofibrosis and sickle cell disease. We are well into the process, and an important part of these requests to CMS are disease-specific reviews that provide evidence of the efficacy of transplantation in each patient population. To meet this need, ASBMT assembled expert working groups to present reviews on the role of transplantation in the treatment of myelofibrosis and sickle cell disease. The products of these two groups will be published soon in *Biology of Blood and Marrow Transplantation*. These reviews serve the primary purpose of informing the community of the necessity of therapy for patients with these diseases but are also outstanding evaluations of the state-of-the-art for transplantation.

The writing committee for myelofibrosis, chaired by Joachim Deeg, M.D., reviewed indications for myeloproliferative neoplasms, with a focus on primary myelofibrosis. The availability of janus kinase inhibitors provides many patients with substantial symptomatic relief and improved quality of life, but currently, the only known curative therapy remains transplantation. Decision analyses demonstrate the importance of close monitoring of disease risk and earlier referral to transplantation for patients who have high-risk features of their underlying disease. As myelofibrosis is, by nature, a disease of older individuals, the concept of age restriction for transplantation takes on different meaning than in other diseases, including sickle cell disease. The myelofibrosis writing committee notes that the success of transplantation for patients ages 60 years and older has progressively increased and is appropriate therapy for otherwise fit patients.

The sickle cell disease writing committee, led by Mark Walters, M.D., has similarly addressed the role of allogeneic transplantation for this disease in a paper that will be published later this year. Unlike myelofibrosis, sickle cell disease afflicts patients from birth, and some patients under 2 years of age have received curative HCT therapy. An important roadblock to the availability of transplantation for patients with sickle cell disease is the lack of suitable human leukocyte antigen (HLA)-matched donors, due in part to the extreme diversity of HLA in patients affected by sickle cell disease. Beyond donor availability, additional challenges include the need to strike a balance between the long-term risks of the end-organ involvement of the disease and the short-term risk of toxicity related to the transplant procedure itself, especially the long-term sequelae of impaired growth and maturation in young patients. The worldwide data are clear, however, that young

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PRESIDENT'S MESSAGE (CONTINUED FROM PAGE 2)

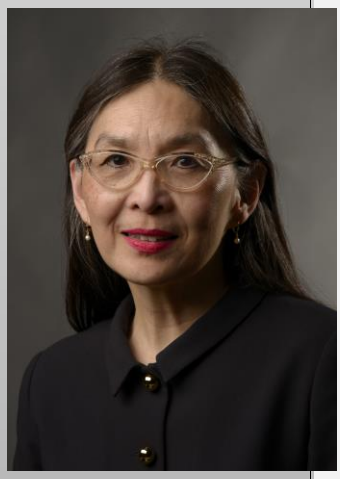
symptomatic patients with sickle cell disease who have HLA-matched sibling donors benefit from transplantation when the transplant is performed at an early age, preferably preschool age.

A much more challenging population of sickle cell disease patients are adults who carry increased morbidity from lifelong organ damage caused by the disease. The writing committee concluded that transplantation is very likely to confer a survival advantage over the long term in adults with sickle cell disease, and given the curative potential, allogeneic transplantation also should be considered in these patients.

ASBMT and NMDP eagerly await the decision by CMS for coverage of myelofibrosis and sickle cell disease. We have an opportunity to respond to their decision in an upcoming comment period that is anticipated to open in late October. We encourage providers to participate in this important dialogue with CMS.

Looking toward the future, ASBMT and NMDP will similarly explore improved Medicare coverage for patients suffering from lymphoma and myeloma. Therefore, please participate in any way that you can.

-Effie P.



LEGISLATION AND REGULATION

Specialty Designation Status

Jim Gajewski, M.D., with the assistance of Paul Rudolf, M.D., formerly of the Centers for Medicare and Medicaid Services (CMS), crafted a letter on behalf of the ASBMT recommending that physicians involved with "hematopoietic cell transplantation and cellular therapy" (HCTCT) be considered a separate specialty by the CMS.

HCTCT as a specialty designation would allow patients and referring physicians to identify physicians who are best qualified to provide the complex patient management and care decisions required for successful transplantation and improved patient outcomes. It would also allow health care insurers to ensure that their provider networks appropriately include access to high-quality transplant care by incorporating HCTCT physicians into their networks.

In addition, insurers could better align HCTCT reimbursement with the unique care provided by these physicians rather than defaulting to the reimbursement models designed to pay for oncology care. Such differentiation is particularly critical as Medicare and other payers explore alternative payment models for infusion-focused oncology care that would not be appropriate for the transplant-related services.

Initiatives to CMS for Coverage Determination

In response to a request by the ASBMT and the National Marrow Donor Program, the Centers for Medicare and Medicaid Services (CMS) indicated a willingness earlier this year to review myelofibrosis and sickle cell disease as covered indications for transplantation. ASBMT developed two writing work groups to review published literature substantiating hematopoietic cell transplantation as therapy for myelofibrosis and sickle cell disease. These groups were also charged with developing detailed, focused information for the CMS. For more details, please see the president's message from Effie Petersdorf, M.D., beginning on page 2.

Association News

ISOPP Symposium Announcement
The International Society of Oncology Pharmacy Practitioners (ISOPP) presents the XV International Symposium on Oncology Pharmacy Practice (ISOPP 2016), taking place April 17-20 at the Sheraton Santiago Hotel in Santiago, Chile. Meet international peers, exchange ideas and experiences, learn from a comprehensive program, and promote and advocate for your research and ideas. Submit your abstract by Monday, Nov. 16, and register online by the early bird registration deadline of Monday, Jan. 18. For more information on ISOPP 2016 and to sign up for the e-newsletter, visit www.isopp2016.org or contact symposia@isopp.org.

Free ASBMT Membership for Trainees
Postdoctoral fellows, physicians-in-training and any allied health professionals training for blood and marrow transplantation are eligible for *free* membership to the American Society for Blood and Marrow Transplantation. Through October, annual dues will be 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...

Last Chance for Conference Registration
Online registration for the second ASBMT Regional Conference for NPs, PAs and Fellows will close on Oct. 20 at midnight (EDT). This conference is designed to support clinicians by integrating and inspiring new knowledge and research findings into the evaluation and treatment of blood and marrow transplantation patients. The goal of this meeting is to inform and discuss current and future trends in the field and provide attendees with practice tools that can be used upon returning to work. Attendees can earn up to 13.5 continuing medical education credits/continuing education units at the course. More...

BMT Tandem Meetings

Travel Grants Available for Fellows
ASBMT is pleased to announce that approximately 15 travel grants worth $500 each will be awarded to U.S.-/Canada-based fellows and two travel grants worth $750 each will be awarded to international fellows to attend the 2016 BMT Tandem Meetings Feb. 18-22 in Honolulu, Hawaii. Travel grant winners will also receive the early registration rate for the meeting.

The grants will be awarded on a competitive basis to ASBMT in-training members who have submitted an abstract for presentation at the meeting, and consideration will be given to those who can show no other financial support from their institution. Applications must be accompanied by letters of support from the applicant's training program director and an ASBMT member. If the training program director is an ASBMT member, one letter is acceptable. Applicants who have won a travel grant within the last three years will not be considered. More...

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BMT TANDEM MEETINGS (CONTINUED FROM PAGE 4)

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 held in San Diego. Slides and audio recordings are free for registered meeting attendees and $25 per file for non-attendees. Meeting attendees will need their registration identification number**.** If you lost yours, please contact bmttandemregistration@conferencedirect.com. Click here to access the recordings.

CLINICAL RESEARCH (CONTINUED FROM PAGE 1)

Transplantation Options for Acute Leukemia

A new study in *Leukemia* reports that transplantation with unmanipulated haploidentical stem cells or unrelated cord blood are both valid options for acute leukemia patients when a human leukocyte antigen-matched donor is unavailable. Approximately two years after transplantation, researchers compared outcomes of 918 de novo acute myeloid leukemia (AML) and 528 acute lymphoblastic leukemia (ALL) patients who received either unmanipulated haploidentical stem cell or unrelated cord blood transplantation (UCBT). They discovered that UCBT recipients were more likely to experience delayed engraftment and higher graft failure but less likely to have chronic graft-versus-host disease, regardless of whether they had AML or ALL. In addition, AML and ALL patients had similar results for relapse, nonrelapse mortality and leukemia-free survival outcomes, despite the type of transplant they received. More...

Reduced-Intensity Conditioning Better for Female Puberty Outcomes

A reduced-intensity conditioning regimen for stem cell transplantation had more favorable puberty-associated outcome for girls than a myeloablative regimen, yet neither conditioning regimen had significant adverse effects – if any – on boys' puberty, according to a study appearing in *British Journal of Haematology*. Researchers retrospectively analyzed gonadal function outcomes of 91 pediatric patients who received a transplant utilizing either a myeloablative regimen of busulfan and cyclophosphamide (BuCy) or reduced-intensity conditioning with fludarabine and melphalan (FluMel). After BuCy, spontaneous puberty occurred in 56% of girls and 89% of boys and 61% of the girls required hormone replacement therapy. The FluMel group had more positive outcomes with 90% of females and all of the males entering puberty spontaneously. However, follicle-stimulating hormone (FSH) levels took longer to increase after the onset of puberty for girls in the FluMel group than those in the BuCy group. Neither conditioning regimen impacted FSH elevation in boys. Researchers concluded that ovarian function appears to be better preserved with a reduced-intensity regimen. More...

TRANSLATIONAL SCIENCE STUDIES

Prenatal and Postnatal Transplants Cure Sickle Cell Disease and Thalassemia

In utero hematopoietic cell transplantation (HCT), combined with postnatal nonmyeloablative allogeneic bone marrow transplantation, cured mice of sickle cell disease (SCD) and thalassemia (Thal), according to results of a study published in *Blood*. Using murine models, researchers discovered that prenatal HCT induced donor-specific tolerance of sickle cell and β-Thal but that allogeneic engraftment levels were low. However, after the postnatal transplant, chimerism levels increased and hemoglobin replacement from healthy donors was almost complete. High chimerism levels corrected the phenotype in the murine models, curing mice of SCD and Thal without undergoing toxic conditioning currently used with postnatal transplant regimens. More...

MDSCs Play Key Role in Preventing GVHD

Myeloid-derived suppressor cells (MDSCs) prevented graft-versus-host disease (GVHD) in mice by skewing allogeneic T cells toward type 2 T cells upregulating T helper 2 (Th2)-specific cytokines, reports a study appearing in *Blood*. Analyzing murine allogeneic bone marrow transplantation models, researchers discovered that transplanted MDSCs prevented GVHD-related mortality and reduced progression of GVHD severity, while maintaining antitumor cytotoxicity of alloantigen-specific T cells. MDSCs expanded in vivo, invaded lymphatic and GVHD target organs, and did not require major histocompatibility complex class 1 expression for suppression. In addition, MDSCs were needed during T-cell priming to prevent GVHD, but allogeneic T-cell numbers and homing in lymphoid and GVHD target organs were not affected. When allogeneic STAT6-deficient T cells were transplanted into mice, GVHD was not prevented, confirming that Type 2 T-cell induction is crucial to inhibiting GVHD. These study results led researchers to conclude that MDSC-induced Th2 induction might be used to treat GVHD. More...

microRNA Cluster Causes GVHD and can be Blocked to Eliminate GVHD

A study published in *Blood* found that T cells required the microRNA (miR)-17-92 cluster to induce graft-versus-host disease (GVHD), but using antagomir to block miR-17-92 eliminated GVHD. Major histocompatibility complex-matched, -mismatched and haploidentical murine models of allogeneic bone marrow transplantation were used in this study to demonstrate that miRNA-17-92 expression on donor T cells is necessary to induce GVHD but does not impact the graft-versus-leukemia (GVL) effect. Researchers discovered that miRNA-17-92 promoted CD4 T-cell activation, proliferation and survival and T helper 1 differentiation, while preventing differentiation of T helper 2 and induced regulatory T cells. In addition, study results indicate that miR-17-92 promoted CD8 T cell migration to GVHD target organs but had little influence on CD8 T-cell proliferation, survival or cytolytic function, which could play a role in GVL preservation mediated by T cells deficient in miR-17-92. Researchers also discovered that giving antagomir to mice with GVHD prolonged survival and preserved the GVL effect by blocking either miR-17 or miR-19b, which inhibited alloreactive T-cell expansion and interferon-γ production. More...

Calendar of Events

•October

European Association of Tissue Banks
24th Congress
October 1-3
Split, Croatia

International Chronic Myeloid Foundation/European School of Haematology
17th Annual John Goldman Conference on CML: Biology and Therapy
October 1-4
Estoril, Portugal

National Comprehensive Cancer Network
10th Annual Congress: Hematologic Malignancies
October 16-17
San Francisco, California

The New York Academy of Sciences
10th Cooley's Anemia Symposium
October 18-22
Chicago, IL

Association of Community Cancer Centers
32nd National Oncology Conference
October 21-24
Portland, Oregon

2nd Annual ASBMT Regional Conference
October 23-25
Clearwater Beach, Florida

AABB
Annual Meeting
October 24-27
Anaheim, California

•November

Society for Immunotherapy of Cancer
Annual Meeting
November 4-8
National Harbor, Maryland

National Marrow Donor Program/ Be The Match
Council Meeting
November 5-7
Minneapolis, Minnesota

European Society for Medical Oncology
Summit Americas
November 6-8
Miami, Florida

European Society for Medical Oncology
Symposium on Immuno-Oncology
November 20-21
Lausanne, Switzerland

•December

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.

National Comprehensive Cancer Network
21st Annual Conference: Advancing the Standard of Cancer Care
March 31-April 2
Hollywood, Florida

•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

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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.