ASBMT eNews

American Society For Blood and Marrow Transplantation

September 2014

Clinical Research

Young, Related Male With NIMA Best Option as Haplotype Mismatched Donor

Patients who receive a haplotype-mismatched donor transplant from a young, related male with noninherited maternal antigens (NIMA) are more likely to have better survival outcomes, according to a recent study published in *Blood*. Researchers examined data from more than 1,200 transplant recipients to determine if donor gender, age, relationship and NIMA impact graft-versus-host disease (GVHD), survival and nonrelapse mortality. They discovered that patients who received transplants from male donors and donors under the age of 30 had less nonrelapse mortality and better chances of survival. Father donors were linked to more successful patient outcomes than mother donors, including less nonrelated mortality and acute GVHD and better survival; better nonrelapse mortality and survival were associated with older sister donors than with mother donors, but older sister donor transplant outcomes were inferior to those for father donor recipients; and when children were donors to their parents, there was less acute GVHD than if a sibling was the donor. NIMA-mismatched sibling donors were associated with the lowest occurrence of acute GVHD in patients compared with acute GVHD outcomes for parental donor and noninherited paternal antigen-mismatched sibling donor recipients. Researchers concluded that transplantations from young, male, NIMA-mismatched donors are a better choice than transplantations from older mothers and noninherited paternal antigen-mismatched donors. More...

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Association News

ASBMT and Twitter

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ASBMT and You Tube

View select sessions from the 2013 BMT Tandem Meetings. Subscribe to the ASBMT You Tube Channel.

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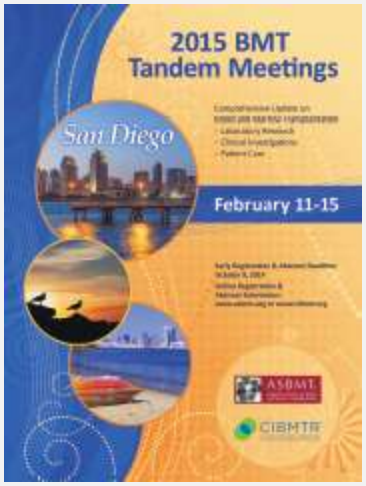

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A Word From President Sergio Giralt, MD

A "Marriage of Convenience" or "The Whole is Greater Than the Sum of Its Parts"

Dear Colleagues:

Last month's **Transplant Trivia** was "When was the ASBMT founded?" The exact date was Aug. 31, 1994. For those of you looking for extra credit points, see if you can identify the founding fathers and mothers in this picture (courtesy of Dr. Keith Sullivan):

The founders of our Society recognized that it was essential to have an organization that would voice our needs and concerns in the new field of blood and marrow transplantation, particularly when it came to federal regulations, clinical and laboratory guidelines, stem cell collection and processing regulations, U.S. Food and Drug Administration mandates and third party payors.

These individuals sacrificed an enormous amount of time and effort (and took on a significant personal financial risk) to ensure that providers wouldn't be burdened by unnecessary regulations while still advocating high standards for quality through a rigorous "peer-review" process (a.k.a. the Foundation for the Accreditation of Cellular Therapy) and to provide a journal that would help disseminate the best research in our field (*Biology of Blood and Marrow Transplantation*).

So, the next time the Society asks you to answer a survey, serve on a task force or volunteer for a committee, think of what these colleagues did for us and feel free to say, "yes." Likewise, whenever you see one of our founding members, please don't be shy; thank them for their service and ask what you can do to help the Society meet its goals.

This year also marks another important landmark in blood and marrow transplant history. On July 1, 2004, the Center for International Blood and Marrow Transplant Research (CIBMTR) was formed through the affiliation of the research programs of the International Bone Marrow Transplant Registry (IBMTR), the Autologous Blood and Marrow Transplant Registry at the Medical College of Wisconsin and the National Marrow Donor Program/Be the Match (NMDP). I think it is appropriate to congratulate all of our colleagues at the CIBMTR on this 10th anniversary.

I was the chair-elect of the IBMTR Advisory Committee at the time of the affiliation and one of the first co-chairs of the CIBMTR. I remember the doubts many had regarding this new association. What was viewed by some as a "marriage of convenience" between NMDP's financial and information technology resources and an extensive biorepository and IBMTR's statistical expertise and extensive experience managing an observational database has truly become larger than "the sum of the parts."

The most palpable example is CIBMTR's portfolio of research projects that culminate in

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A WORD FROM THE PRESIDENT (CONTINUED FROM PAGE 2)

peer-reviewed publications. The following table compares the number of CIBMTR publications since its inception in 2003-2004 to the combined number of publications from IBMTR and NMDP in prior years. Many of these published studies were led by junior investigators partnering with more senior investigators to test hypotheses using registry data.

	1993-1997	1998-2002	2003-2007	2008-2012
# of Peer-Reviewed Publications	34	66	119	235
# of Authors	177	295	357	775
# of Institutions	98	158	211	339

NMDP started and continues to maintain the world's largest blood and marrow transplant donor/recipient sample bank, facilitating research that has demonstrated the importance of molecular mismatches, KIR mismatching and single nucleotide polymorphisms for transplant outcomes, among others. These are just a few examples of what these organizations have done with the "people's money," providing not only an enormous return on investment, but the foundation for better outcomes for the stem cell transplant recipients of tomorrow.

I invite all of you to visit the CIBMTR website and take a look at all that is happening; look at the publications over the last five years, as well as what the Working Committees are up to and where you can contribute. As always, I also encourage you to get involved with CIBMTR activities by joining a working group or actively participating in an ongoing study. Active participation of the ASBMT community in CIBMTR working groups will keep this research enterprise alive and on the cutting edge of transplant research to help us provide better care for our patients.

Now for last month's answer to **For the Boards**. True or False? Allogeneic hematopoietic progenitor cell transplantation is the treatment of choice for patients with primary refractory acute myelogenous leukemia (AML).

The answer is **TRUE**. Although no large randomized trials are likely to be performed in this setting, a number of large retrospective analyses all support the use of allogeneic hematopoietic cell transplantation (HCT) as the treatment of choice for primary refractory acute leukemia. Primary refractory acute leukemia, or primary induction failure (PIF) as it is also called, has been defined as "failure to achieve a morphological complete remission after one or two cycles of induction chemotherapy."[1] Craddock et al. analyzed data from the European Group for Blood and Marrow Transplantation on 168 patients with PIF AML. The five-year overall survival for the group was 22%. In multivariate analysis, fewer than three courses of induction chemotherapy and a lower percentage of bone marrow blasts at transplant were associated with better outcomes.[2] Duval et al., using CIBTMR data, also showed that patients with PIF could achieve long-term disease control with allogeneic HCT, and as with other retrospective analysis, the percentage of bone marrow and peripheral blood blasts predicted outcomes.[3] More recently, Chen et al. showed in a retrospective analysis that patients who underwent allogeneic HCT within four weeks of reinduction did as well as those that waited longer, underscoring the importance of early referrals.[4]

Now for this month's **Transplant Trivia** question: Who funds the Blood and Marrow Transplant Clinical Trials Network? And **For**

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A WORD FROM THE PRESIDENT (CONTINUED FROM PAGE 3)

the Boards: True or False? With current molecular classification, no patient with inv 16 AML should be considered for allogeneic HCT as consolidation of a first remission.

On a final note, the Executive Committee has been working hard with Executive Administration, Inc., (our association management company) to recruit the replacement for Thomas Joseph, who recently resigned as our executive director. On behalf of the entire Society, I want to thank Robert Krawisz and Andrea King for keeping the wheels of the Society running on time and the Society officers on task.

As always, I look forward to hearing your comments or questions at giralts@mskcc.org.

-Sergio

(Reference information can be found on page 5.)

ASSOCIATION NEWS (CONTINUED FROM PAGE 1)

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 membership in 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...

Corporate Council Meeting

The eighth annual Corporate Council Meeting will take place Sept. 21-22 at the Royal Palms Resort in Phoenix, Arizona. Fifteen representatives from our pharmaceutical membership will be given the opportunity to meet face-to-face with past and current ASBMT leadership in an informal, collegial environment. Invited speakers will talk on a range of subjects, from the relationship between academia and the corporate world, to cord blood expansion, microtransplantation, chronic graft-versus-host disease and more.

Gabrielle's Angels to Fund Three New Investigator Awards

Gabrielle's Angel Foundation for Cancer Research will support awards in the amount of $60,000 each to three new investigators over the course of 2015-2016. The mission of Gabrielle's Angel Foundation for Cancer Research is to encourage the development of more effective therapies for patients with leukemia, lymphoma and related cancers. The Foundation funds innovative clinical or basic science research that will lead to novel therapeutic approaches that could replace or be used in combination with existing effective therapies. Such therapeutic approaches could include alternative or complementary medicine.

Caring for Pediatric HCT Survivors Webinar

The National Marrow Donor Program/Be The Match is offering a live webinar on pediatric late effects and the latest guidelines for providing hematopoietic stem cell follow-up care. "Pediatric Survivors After HCT: Long-Term Screening and Preventive Practices" will be held Thursday, Oct. 9 from 4 p.m. – 5 p.m. (CDT). Learn more and register.

BMT Tandem Meetings

Registration is Now Open for 2015 BMT Tandem Meetings in San Diego
Online registration and housing is now open for the 2015 BMT Tandem Meetings, which will be held Feb. 11-15 in San Diego, California. Links to meeting registration, housing reservations, the preliminary program, abstract submission and parallel conferences can be found in one convenient location. More...

Abstract Submission Deadline is Oct. 9 for BMT Tandem Meetings
The abstract submission site for the BMT Tandem Meetings in San Diego is open through Oct. 9. Invitations for oral presentations will be offered to more than 100 authors whose abstracts receive the highest scores from the review committees. Many others will be accepted for poster presentation. More...

October Deadlines for New Investigator Awards, Travel Grants
New Investigator Awards of $60,000 each, to be presented at the 2015 BMT Tandem Meetings, are being supported by Gabrielle's Angel Foundation for Cancer Research, Millennium Pharmaceuticals, Inc., Otsuka American Pharmaceutical, Inc., and ASBMT. The deadline for New Investigator Award applications is Oct. 1. In addition, approximately 10 grants of $1,000 each will be awarded to introduce young clinicians and investigators to the field of hematopoietic cell transplantation. Applicants must be enrolled in an accredited hematology and/or oncology training program in the U.S. or Canada and recommended by their program director, as well as an ASBMT member. The deadline for travel grant applications is Oct. 31. More...

Carl June to Present E. Donnall Thomas Lecture
Carl H. June, MD, of the Abramson Cancer Center, will present the 18th annual E. Donnall Thomas Lecture at the 2015 BMT Tandem Meetings, which will be held Feb. 11-15 in San Diego. His presentation will be on Friday, Feb. 13.

ASBMT Awards
During the 2015 BMT Tandem Meetings, ASBMT will present the annual Lifetime Achievement Award to Daniel Weisdorf, MD, and the Public Service Award to University of Miami President Donna E. Shalala, PhD.

A Word From the President (continued from page 4)

1. Cheson BD, Cassileth PA, Head DR, et al. Report of the National Cancer Institute-sponsored workshop on definitions of diagnosis and response in acute myeloid leukemia. *J Clin Oncol*. 1990;8(12):813–819.

2. Craddock C, Labopin M, Pillai S, et al. Factors predicting outcome after unrelated donor stem cell transplantation in primary refractory acute myeloid leukaemia. *Leukemia*. 2011;25(5):808–813.

3. Duval M, Klein JP, He W, et al. Hematopoietic stem-cell transplantation for acute leukemia in relapse or primary induction failure. *J Clin Oncol*. 2010;28(23):3730-3738.

4. Chen GL, Liu H, Zhang Y, et al. Early versus late preemptive allogeneic hematopoietic cell transplantation for relapsed or refractory acute myeloid leukemia. *Biol Blood Marrow Transplant*. 2014;20(9):1369-1374.

CLINICAL RESEARCH (CONTINUED FROM PAGE 1)

Transplantation on Newborns and Infection-Free Infants Improves SCID Survival

Infants have a better chance of surviving severe combined immunodeficiency (SCID) when they receive a hematopoietic cell transplant before the age of 3.5 months and prior to the onset of related infections, reports a study appearing in the *New England Journal of Medicine.* Researchers studied data from 240 infants with SCID who underwent transplants and discovered that transplants from matched sibling donors were more likely to result in survival five years post-transplantation, autonomy from immunoglobulin substitution, and $CD3^+$ T-cell and IgA recovery than transplantation from other donors. However, the donor type did not adversely affect infants who had better survival rates when transplantation was performed before the age of 3.5 months (94%) and among older infants without prior infection (90%) or infection that had been resolved (82%). Infants with active infection who received a matched sibling donor transplant had better survival outcomes when haploidentical T-cell-depleted transplantation was performed without pretransplantation conditioning. Patients who received reduced-intensity or myeloablative conditioning before transplantation were more likely to have a $CD3^+$ T-cell count higher than 1,000 per cubic millimeter, no need for immunoglobulin substitution and IgA recovery, but conditioning did not affect recoveries of $CD4^+$ T-cells or phytohemagglutinin-induced T-cell proliferations. The genetic subtype of SCID also affected the quality of $CD3^+$ T-cell recovery but not survival. These study results led researchers to conclude that matched sibling donor transplantation recipients have higher survival rates when diagnosis is made before the onset of active infection, and asymptomatic infants are likely to survive regardless of the donor source. More...

Therapy for AML Relapse After HCT Benefits Survival Odds

A new study from *Bone Marrow Transplantation* suggests that acute myeloid leukemia (AML) patients who are able to undergo intensive therapy for relapse after allogeneic hematopoietic cell transplantation (HCT) increase their likelihood of short-term survival. Nearly 350 AML patients who received either a matched related donor or umbilical cord blood transplantation were included in the study. Relapse after transplantation occurred in 72 of the 222 umbilical cord blood recipients and 32 of the 126 patients who received related donor transplants. Three patients experienced complete remission when immune suppression was discontinued and no further therapy was administered. In addition, complete remission was achieved by 25% of the 52 patients who received either systemic chemotherapy, a second allogeneic HCT or donor lymphocyte infusion with or without chemotherapy. Among all of the patients, survival one year after relapse was 22%. The probability of survival was higher among patients who received intensive therapy for relapse but lower for patients with peripheral blood blasts above the median, active infection and medical complications unrelated to infection. More...

TRANSLATIONAL SCIENCE STUDIES

Prenatal Therapy for Congenital Stem Cell Disorders Improves Engraftment

Mice that were injected in utero with an antibody against the murine c-Kit receptor (ACK2) to treat congenital hematopoietic disorders experienced a decrease in fetal host hematopoietic stem cells, which, in turn, improved engraftment after neonatal congenic hematopoietic cell transplantation. The study, published in *Blood*, found that there was minimal toxicity following the low-dose ACK2 therapy, which cleared from the serum before transplantation was performed on the first day of life. Compared to controls, the ACK2-treated mice had higher chimerism levels. To confirm the findings, researchers treated some of the mice with ACK2 after birth, but the increase in engraftment was lower than that observed prenatally, suggesting that fetal ACK2 treatment may be effective at achieving clinically appropriate levels of engraftment to treat congenital stem cell disorders. More...

GVHD Risk Linked to ILC Recovery and Treatment-Related Tissue Damage

Recovery of innate lymphoid cells (ILCs) together with treatment-related tissue damage play a role in the development of graft-versus-host disease, suggests results of a study from *Blood*. Researchers performed a longitudinal study on 51 acute leukemia patients to determine the effects of induction chemotherapy, conditioning radiochemotherapy and allogeneic hematopoietic cell transplantation (HCT) on the composition, phenotype and recovery of circulating ILCs. The researchers discovered that reconstitution of ILC1, ILC2 and NCR^-ILC3 was slower than that of neutrophils and monocytes and that NCR^+ILC3 cells were present after induction chemotherapy and HCT. Circulating patient ILCs before transplantation and donor ILCs after transplantation expressed activation, proliferation and gut and skin tissue homing markers that correlated with a decreased risk for therapy-induced mucositis and acute graft-versus-host disease (GVHD). Researchers concluded that chemotherapy and radiotherapy diminish ILCs from the blood and that ILCs with potential for tissue homing before HCT reduce the risk for GVHD. More...

HLA-Matched Donor and Recipient Exomes Have Nucleotide Sequence Variation

A study published in *Blood* reports that researchers have discovered nucleotide sequence variation in the exomes of human leukocyte antigen (HLA)-matched donors and recipients. Researchers used whole exome sequencing on stem cell transplant donor and recipient pairs to determine the potential for antigenic variation at the molecular level and discovered that a small sample of the pairs exhibited a high frequency of sequence variation between the donor and recipient exomes independent of HLA matching. In addition, nonsynonymous, nonconservative single nucleotide polymorphisms occurred twice as often in HLA-matched unrelated donor-recipient pairs than related pairs and were distributed across the entire exome rather than in individual chromosomes. More...

Calendar of Events

•September

International Chronic Myeloid Leukemia Foundation/European School of Haematology
16th Annual John Goldman Conference on Chronic Myeloid Leukemia: Biology & Therapy
September 4-7
Philadelphia, Pennsylvania

World Congress of the International Society of Hematology
September 4-7
Beijing, China

3rd World Congress on Controversies in Hematology
September 11-13
Istanbul, Turkey

American Association of Tissue Banks
Annual Meeting
September 16-20
San Diego, California

European Society for Medical Oncology
39th Congress
September 26-30
Madrid, Spain

•October

European Association of Tissue Banks
22nd Annual Congress
October 1-3
Lund, Sweden

International Federation of Biomedical Laboratory Science
31st World Congress
October 3-7
Taipei, Taiwan

Association of Community Cancer Centers
31st National Oncology Conference
October 8-11
San Diego, California

•October

American Society for Histocompatibility & Immunogenetics
40th Annual Meeting
October 20-24
Denver, Colorado

European School of Haematology
6th International Conference on Myeloproliferative Neoplasms
October 23-25
Estoril, Portugal

European Society of Gene and Cell Therapy/Netherlands Society of Gene and Cell Therapy
22nd Annual Congress
October 23-26
The Hague, The Netherlands

1st Regional Bone Marrow Transplant Conference for NPs/PAs and Fellows
October 25-26
Boston, Massachusetts

American Association of Blood Banks
Annual Meeting
October 25-28
Philadelphia, Pennsylvania

Histiocyte Society
30th Annual Meeting
October 28-30
Toronto, Canada

•November

National Marrow Donor Program/Be The Match
Council Meeting
November 6-8
Minneapolis, Minnesota

European School of Haematology
2nd International Conference on Multiple Myeloma
November 7-9
Athens, Greece

•November

Worldwide Network for Blood and Marrow Transplantation/World Health Organization
Workshop
November 14-15
Cape Town, South Africa

European School of Haematology
International Conference on New Concepts in B Cell Malignancies: From Molecular Pathogenesis to Personalized Treatment
November 14-16
Athens, Greece

•December

3rd Annual Bone Marrow Transplant Winter Workshop
December 5
San Francisco, California

American Society of Hematology
56th Annual Meeting and Exposition
December 6-9
San Francisco, California

•January

BioLeaders Forum
January 26-28
Washington, D.C.

•February

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

•2016

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

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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.