ASBMT eNews

AMERICAN SOCIETY FOR BLOOD AND MARROW TRANSPLANTATION

May 2013

CLINICAL RESEARCH

Clinical Trial Demonstrates Safety of T-Rapa Cell-Based Therapy

The results of a phase 2 multicenter clinical trial on rapamycin-resistant donor $CD4^+$ T helper 2 (Th2)/T helper 1 (Th1) (T-Rapa) cells following allogeneic-matched sibling donor hematopoietic cell transplantation (HCT) for refractory hematologic malignancy treatment were published in a recent issue of *Blood*. Two weeks after transplantation, patients received an infusion of T-Rapa cell products to facilitate engraftment and permit a graft-versus-tumor effect, while minimizing graft-versus-host disease (GVHD). Following the infusion, researchers discovered that mixed donor/host chimerism changed and that there was preferential immune reconstitution with donor $CD4^+$ Th2 and Th1 cells relative to regulatory T cells and $CD8^+$ T cells. The probability of acute GVHD was 20% 100 days after transplantation and 40% 180 days post-HCT. In addition, there were no transplant-related mortalities, and nearly half (45%) of patients were still in complete remission anywhere from 42 to 84 months after transplantation. The researchers indicated that this is a safe low-intensity transplant method and warrants further comparison to standard transplant regimens. More...

Chemotherapy and HCT May Benefit MPN Patients with LT

Researchers evaluated clinical outcomes of 75 patients with leukemic transformation (LT), a complication of Philadelphia-negative myeloproliferative neoplasms (MPNs), reports a study appearing in *Blood*. The patients included in the study had a reasonable fitness level and were treated with curative intent and offered induction chemotherapy. Patients who responded to therapy and had a suitable donor were considered for allogeneic hematopoietic cell transplantation (HCT). More than half of the patients (52%) were treated with

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ASSOCIATION NEWS

ASBMT and Twitter

ASBMT is pleased to announce a new member benefit – Twitter. Connect with fellow ASBMT members and discuss the latest breaking news and information relevant to BMT. Follow us on Twitter @ASBMT.

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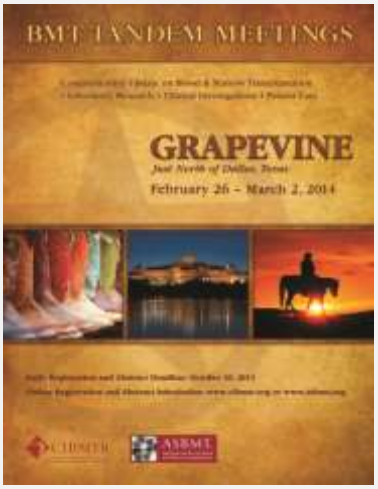

ASBMT
American Society for Blood and Marrow Transplantation

A Word From President Fred LeMaistre, MD

System Capacity

I think one of the best examples of potential pitfalls in building a great team is the Miami Heat. At the time of this writing, they had just eclipsed the NBA record for consecutive wins at 23 and are apparently on their way to winning their second NBA Championship in a row. Most observers thought this might be their third in a row since they added Chris Bosh and LeBron James to complement Dwayne Wade in 2010. With three such superstars, how could they lose? In fact they started off 9-8 that season. While they did make it to the championship series, their season ended with three losses in a row to the Dallas Mavericks. A lesson learned might be that a great team is not made of superstars playing for themselves but players who complement each other and understand how to execute their role on the court.

Last fall, the National Marrow Donor Program (NMDP) completed a three-year program called the System Capacity Initiative (SCI). The goal of the SCI was to address system capacity challenges with the future growth of HCT. Critical barriers to growth of HCT involve human resources, structural constraints and patient access (Majhail NS, Murphy EA, Denzen EM, et al. The National Marrow Donor Program's symposium on hematopoietic cell transplantation in 2020: A health care resource and infrastructure assessment. *Biol Blood Marrow Transpl*. 2012; 18:172-182). The most sobering aspect to the SCI findings is that we face projected shortages in virtually all positions on our transplant teams: physicians, advanced practice professionals, nurses and pharmacists. While all of these positions on the transplant team are critical to achieving successful patient outcomes, we have slightly more information about physician shortages. Some estimates suggest that we may need to double the number of HCT physicians by 2020 to keep pace with projected needs (Gajewski JL, LeMaistre CF, Silver S, et al. Impending challenges in the hematopoietic stem cell transplantation physician workforce. *Biol Blood Marrow Transpl*. 2009; 15:1493-1501).

The challenges associated with addressing these shortages are well-detailed in a report from the SCI and are beyond the scope of this newsletter (Majhail NS, Murphy EA, Denzen EM, et al. The National Marrow Donor Program's symposium on hematopoietic cell transplantation in 2020: A health care resource and infrastructure assessment. *Biol Blood Marrow Transpl*. 2012; 18:172-182). Common themes applicable to all groups are issues associated with recruitment, retention, work hours, compensation and workforce diversity. The ASBMT Board of Directors not only committed to addressing these issues in partnership with NMDP at the BMT Tandem Meetings in Salt Lake City but also embraced the challenge in a way that bodes well for our future. We are engaging the relevant standing committees of the ASBMT along with the NP/PA, Nursing, Pharmacy and Administrative Special Interest Groups (SIGs) to develop and implement solutions.

An important theme for us will be to define best practice as well as to critically evaluate and share best models of care. We clearly need to better define the role and scope of practice for the NP/PA and pharmacist on the HCT team in addition to the role of the nurse in the best care delivery models. For obvious reasons, our administrators are key partners in helping us define key processes as well as advocating for the staffing and skill mix that is necessary for best care. To extend the basketball metaphor slightly, we need to

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A Word From the President (continued from page 2)

understand how we can better win with the team we have on the court by maximizing their strengths and coordinating their efforts with other team members. For many of us, the opportunity to practice as part of a dedicated multi-disciplinary team has been one of the great attractions to a career in HCT. It is my belief that the value we place on the team approach to care for the transplant patient will allow us to successfully navigate the challenges of caring for more patients. We will need to work together to define and refine each of our roles in the process of patient care.

-Fred

Association News (Continued from page 1)

New Online Membership Directory and Seminars

ASBMT is pleased to announce two new benefits for members only: the online Membership Directory and the online Seminars. Both are "free of charge" to all ASBMT members within the Member Login section. Members will need their ID and password to access these new benefits. More...

New Tools for Your Practice: ASBMT Practice Improvement Modules

Do you need to earn maintenance of certification credit? Are you looking for ways to improve your clinical practice? Recently, the ASBMT Committee on Education introduced two Practice Improvement Modules (PIMs) for use "free of charge" to all ASBMT members within the Member Login section. Members will need their ID and password to access the PIMs. Focusing on the management of patients post transplantation, one PIM is on Chronic Graft-Versus-Host Disease and the other is on Infection Control.

Both PIMs are web-based self-evaluation tools that guide care providers through chart abstractions, while supporting practice-based learning and improvement via links to educational materials and resources. The interactive personal summary report guides reflection on detailed performance data, selecting areas for improvement and creating an improvement plan with goals and strategies.

The Chronic Graft-Versus-Host Disease module is based on the NIH Consensus Development Project (Filipovich AH, Weisdorf D, Pavletic S, Socie G, et al. *Biol Blood Marrow Transpl.* 2005; 11:945-955) and includes five measures for the management of disease. Six measures are included in the Infection Control module that is based on the Guidelines for Preventing Infectious Complications (Tomblyn M, Chiller T, Einsele H, Gress R, et al. *Biol Blood Marrow Transpl.* 2009; 15:1143-1238).

Although the PIMS are designed for use by both adult and pediatric practitioners, maintenance of certification credit is currently available only through the American Board of Internal Medicine. However, all physicians who complete a PIM earn 20 Category 1 CME credits. More...

HCT Resources

The National Marrow Donor Program (NMDP), in conjunction with the ASBMT, pursues issues related to transplant coverage, benefits and reimbursement on behalf of its network centers. More...

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BMT Tandem Meetings

Registration Will Open Soon for 2014 BMT Tandem Meetings in Texas
Online registration and housing will open soon for the 2014 BMT Tandem Meetings Feb. 26 – March 2 in Grapevine, just north of Dallas. Links to meeting registration, housing reservations, preliminary program, abstract submission and parallel conferences will all be found in one convenient location. *Continue checking the website for further updates…*

Abstract Submission Deadline is Oct. 10 for BMT Tandem Meetings
The abstract submission process for the BMT Tandem Meetings in Grapevine, Texas, will open soon and will remain open through Oct. 10. Invitations for oral presentations will be offered to 90 authors whose abstracts receive the highest scores from the review committees. Many others will be accepted for poster presentation. *Continue checking the website for further updates…*

Clinical Research (Contnued from page 1)

curative intent and had a two-year overall survival of 26% compared to only 3% survival for those who were not treated with curative intent. Of the curative intent group, 46% of patients achieved complete remission or complete remission with incomplete recovery and 31% of patients reverted to a chronic MPN phase. In addition, 17 patients received HCT. Transplant patients who responded to induction therapy had better two-year survival outcomes (47%) than patients who responded to induction therapy but did not receive a transplant (15%), leading researchers to conclude that induction chemotherapy followed by HCT may control long-term disease in certain patients with LT complication from MPN. More...

AML Patients with NPM1 and Low Ratio FLT3 Mutations Have Better Outcomes
More than 300 patients with intermediate-risk cytogenetics acute myeloid leukemia (AML) were included in a study to analyze the effect of FLT3 internal tandem duplication (ITD)/FLT3 wild-type (FLT3wt) ratio depending on NPM1 mutation (NPM1mut). All patients had received intensive chemotherapy. According to the study published in *Blood*, the NPM1mut patients in FLT3wt and low ratio (<0.5) subgroups had similar overall survival, relapse risk and leukemia-free survival, while the high ratio (>0.5) patients had a worse outcome. The NPM1wt patients in FLT3-ITD subgroups had a higher risk of relapse and shorter overall survival compared to the FLT3wt patients. Patients in all subgroups – other than NPM1mut patients without FLT3-ITD ratio or with low ratio FLT3-ITD – who received allogeneic stem cell transplantation in the first complete remission were less likely to relapse. These study results suggest that the effect of the FLT3 burden is modulated by the NPM1 mutation, especially in patients with a low ratio. More...

Association News (Continued from page 3)

BBMT Website

The new www.bbmt.org website was recently launched. ASBMT members and individual subscribers receive online access to full articles with their print subscription. All that is needed to gain access is an ASBMT member number. Authors and reviewers can access the online submission system via a separate login. For more details, please visit the website.

ASBMT Special Interest Group Listserv

ASBMT is pleased to announce a new member benefit for all Special Interest Groups (SIG) – a Listserv. For more information, please send an email to mail@asbmt.org.

Translational Science Studies

Anti-Third-Party CD8 Central Memory T Cells Eliminate Remaining Lymphoma Cells

According to a study appearing in *Blood*, researchers demonstrated that donor anti-third-party CD8 T cells with central memory phenotype (Tcm) on mice display graft-versus-leukemia reactivity through a T-cell receptor-independent method. Approximately 30% to 40% of the mice who received Tcm therapy after autologous bone marrow transplantation experienced long-term tumor-free survival. In addition, an infusion of donor Tcm into mice in an allogeneic model eliminated the remaining lymphoma cells and resulted in 100% long-term survival without graft-versus-host disease. These findings suggest that patients with B-cell malignancies may benefit from Tcm therapy and allogeneic T-cell-depleted bone marrow transplantation when they cannot tolerate intensive myeloablative conditioning. More...

Low-Dose IL-2 Therapy Studied

To determine how daily low-dose interleukin-2 (IL-2) therapy causes selective expansion of functional $CD4^+Foxp3^+$ regulatory T cells (T_{regs}) and improves chronic graft-versus-host disease (GVHD), researchers studied this treatment's immunologic effects on homeostasis of $CD4^+$ T cell subsets after transplantation. According to the study published in *Science Translational Medicine*, chronic GVHD is distinguished by constitutive phosphorylation of signal transducer and activator of transcription 5 (Stat5) in conventional $CD4^+$ T cells (T_{cons}) associated with elevated amounts of IL-7 and IL-15 and relative functional deficiency of IL-2. Using IL-2 therapy increased Stat5 phosphorylation in Tregs and decreased phosphorylated Stat5 in T_{cons}. In addition, IL-2 therapy caused such changes in T_{reg} homeostasis as increased proliferation, increased thymic export and enhanced resistance to apoptosis, while low-dose IL-2 had little effect on T_{cons}. More...

Targeting Notch Receptors and Ligands Controls GVHD

This study appearing in *The Journal of Clinical Investigation* demonstrates that γ-secretase inhibitors can block all Notch signals in alloreative T cells, leading to severe on-target intestinal toxicity. Researchers used newly developed humanized antibodies and conditional genetic models to show that Notch 1/Notch 2 receptors and the Notch ligands Delta-like 1/4 mediate all effects of Notch signaling in T cells during graft-versus-host disease (GVHD) and that Notch 1 and Delta-like 4 are dominant in this process. While Notch 1 inhibition controlled GVHD but resulted in treatment-limiting toxicity, Delta-like 1/4 inhibition blocked GVHD without limiting adverse effects and preserved anticancer activity. Researchers concluded that targeting individual Notch receptors or ligands has the potential to be an effective therapeutic strategy for controlling GVHD after allogeneic bone marrow transplantation. More...

Calendar of Events

•May

American Association of Immunologists
Annual Meeting
May 3-7
Honolulu, Hawaii

12th International Symposium on Myelodysplastic Syndrome
May 8-11
Berlin, Germany

CIMT Annual Meeting
May 14-16
Mainz, Germany

American Society of Gene & Cell Therapy
16th Annual Meeting
May 15-18
Salt Lake City, Utah

American Society of Transplant Surgeons/American Society of Transplantation
American Transplant Congress
May 18-22
Seattle, Washington

The New York Academy of Sciences/Rutgers University
The Bone Marrow Niche, Stem Cells, and Leukemia: Impact of Drugs, Chemical, and the Environment Conference
May 29-31
New York, New York

American Society of Clinical Oncology
Annual Meeting
May 31-June 5
Chicago, Illinois

•June

International Society for Stem Cell Research
11th Annual Meeting
June 12-15
Boston, Massachusetts

Federation of Clinical Immunology Societies
Annual Meeting
June 27-30
Boston, Massachusetts

•July

CRYO 2013
50th Annual Meeting
July 28-31
Bethesda, Maryland

•August

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

•September

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

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

•October

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

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

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

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

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

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

• 2014

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

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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.