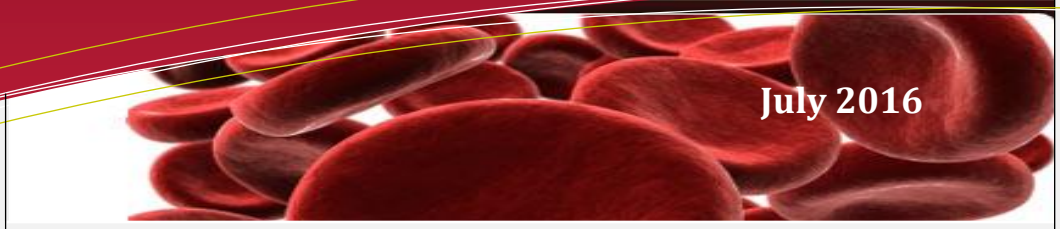
ASBMT eNews

AMERICAN SOCIETY FOR BLOOD AND MARROW TRANSPLANTATION



CLINICAL RESEARCH

Conditioning Intensity Affects Outcomes of MDS Patients With MID

The presence of minimal identifiable disease (MID) before hematopoietic cell transplantation (HCT), combined with the type of conditioning intensity, appears to make a difference in patient outcomes, according to a study appearing in a recent issue of *Biology of Blood and Marrow Transplantation*. Researchers reviewed outcomes of 289 myelodysplastic syndrome patients whose MID markers were determined prior to HCT using multiparameter flow cytometry (MFC) or cytogenetics on bone marrow aspirates. Among the patients included in the study, 154 patients had MID and 65 did not. Outcomes differed for low- and high-intensity recipients, but low-intensity conditioning recipients whose cytogenetic results indicated MID had higher overall mortality than patients who had high-intensity conditioning, even if MFC showed presence of MID. However, patients who did not have MID, according to both MFC and cytogenetics, had similar mortality outcomes, despite the conditioning intensity. According to the study, relapse was the biggest factor associated with mortality for MID-positive patients who received low-intensity conditioning. The researchers concluded that MID should be considered when choosing conditioning intensity. More...

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ASSOCIATION NEWS

ASBMT and Twitter

Connect with fellow ASBMT members and discuss the latest breaking news and information relevant to transplant. Follow ASBMT on Twitter @ASBMT – join the conversation: #bmtsm; #BMTTandem17.

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SEE ALSO

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American Society for Blood and Marrow Transplantation

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A Word From President Christopher Bredeson, M.D.

Greetings:

This month, I am detouring from my usual introduction based on Canadiana. Instead, I will share with you two of my loves: fiction set in the First World War (for Canada, it was waged from 1914-1918) and poetry (oh, how the eyes roll!).

What brings these to mind were insights, or rather reminders, discovered in Helen Simonson's new novel, *The Summer Before the War*.

In the book, a young surgeon, having dealt with the carnage from the most recent bombardment, is resting against the doorframe of the makeshift surgical area. Two nurses walk past and wish him a good night as they disappear into the dark, dank cold of a February night in France. His reflection begins, "They had surprised him, the nurses, with their quiet endurance."

His observations, though set in the context of the British class system, formality and sexual mores of the early 20th century, reminded me of the challenging work our BMT nurses encounter at bedsides for those long periods between attendings' visits. There, besides hands-on-care, the best of our nurses act as educators, buffers, confessors and providers of courage to patients in their most human and vulnerable state.

"How much harder it must be to have the veil of professional ice pierced many times a day," observed the surgeon. So, thank you to our BMT nurses for their expertise, dedication and humanity.

The other reminder is that for those who survive such traumas, the scars are many, both seen and unseen. The late effects, never fully understood or imagined at the outside, once apparent, are often hidden or minimized. The recognition of what we have wrought and struggle to undue, perhaps shaming us to avoidance.

That is why I am so pleased with the attention being given to understanding the late effects of BMT and how to improve the long-term care of transplant survivors.

In this regard, I would like to highlight the recent Bone Marrow Transplantation Late Effects Consensus Conference sponsored by the National Institutes of Health. This conference, spearheaded by Drs. Minoo Battiwalla, Nonniekaye Shelbourne, Navneet Mahjail and others, was held June 21-22 in Washington, D.C. Representatives from transplant programs, payers, regulatory bodies and funding agencies, as well as patients, addressed this most challenging topic of hematopoietic cell transplantation survivorship. Six working groups discussed a broad range of topics focused on how to better understand the late effects of transplantation and how to improve survivor care over the many years that patients will have, usually distant from the specialized expertise of a transplant center.

Manuscripts summarizing the recommendations from the conference are being prepared and will appear in our journal, *Biology of Blood and Marrow Transplantation*, in the coming year. I encourage all to seek out these recommendations and work to implement them for patients.

Now I find that I cannot leave you without circling back to Canada, the First World War and poetry. One of the most famous war poems, "In Flanders Fields," was written May 3, 1915, by a young Canadian physician, Lieutenant-Colonel John McCrae, in response to the death of his friend at the Second Battle of Ypres. This poem was the origin of the remembrance poppy we wear on Memorial Day in the United States or Remembrance Day in Canada and the Commonwealth.

Take the time to read fiction this summer; we are all part of a shared story.

Chris

LEGISLATION AND REGULATION

Update on CMS Coverage Decision for Myelofibrosis, Multiple Myeloma and Sickle Cell Disease

In late January, the Centers for Medicare and Medicaid Services (CMS) issued a positive decision regarding coverage of allogeneic hematopoietic cell transplantation for myelofibrosis, multiple myeloma and sickle cell disease. CMS utilized the Coverage with Evidence Development (CED) mechanism, which means coverage is contingent on the Medicare beneficiary participating in a clinical study. Since that time, the Center for International Blood and Marrow Transplant Research (CIBMTR) has been working on preparing separate protocols for each indication. Development of the study protocols is happening concurrently, but the submission to CMS for review and approval is happening individually as the protocols become ready.

The sickle cell disease study, utilizing the BMT CTN 1503 protocol, was submitted a few weeks ago under the leadership of Mary Eapen, M.D., of the CIBMTR. The CMS has now **approved the protocol** for use with Medicare beneficiaries, pending a requested amendment to the analysis plan. ***However, because this study originated as a BMT CTN protocol independent of the CMS purpose, it will still be one to two months before accrual will begin.*** More specifically, the study is approved but is not yet open at any site. The BMT CTN 1503 protocol was released to the centers in early May, and sites will open as their individual institutional review boards approve the documents.

The myelofibrosis and multiple myeloma studies are still in development and have not yet been submitted for CMS consideration.

Links to key resources:

- Study information, including participating centers (when available)
- Study approval posting on the CMS website
- Billing guidance
- Decision Memo for Stem Cell Transplantation (Myelofibrosis, Multiple Myeloma and Sickle Cell Disease
- National Coverage Determination for Stem Cell Transplantation
- Coverage with Evidence Development background and policies

ASBMT Responds to CMS Proposed Rule on MACRA

The Centers for Medicare and Medicaid Services (CMS) has released a proposed rule regarding key parts of the Medicare Access and CHIP Reauthorization Act of 2015 (MACRA). It will affect numerous laws, regulations and government programs affecting physician reimbursement through Medicare.

The proposed MACRA rule contains two components: Merit-Based Incentive Payment System, which partially repeals the meaningful use program for electronic health records, and Alternative Payment Models.

You can review the ASBMT leadership response to the proposed rule on the ASBMT website by clicking here.

ASSOCIATION NEWS (CONTINUED FROM PAGE 1)

Sept. 14 Deadline for New Investigator Awards

Applications are now being accepted for the ASBMT New Investigator Awards! These awards –$60,000 each over two years – will be presented at the 2017 BMT Tandem Meetings. The deadline for applications is Sept. 14, 2016. Visit the ASBMT website for full details.

ASBMT Pharmacy Special Interest Group – Education Committee Standard of Care Guidelines and Resource Links

This resource is an online collection of citations for key publications in the field of hematopoietic cell transplantation (HCT). The purpose is to provide practitioners with significant literature sources that support the practice of HCT in adult patients. Each citation is listed in standard American Medical Association format and contains the link to the PubMed abstract as well as the PubMed identification number. The citations included in the collection have been selected and reviewed by members of the ASBMT Pharmacy Special Interest Group Education Committee and have been updated through October 2015.

New Resource for ASBMT Members

The much anticipated second edition of *Cellular Therapy: Principles, Methods, and Regulations* has just been released. This essential reference includes chapter contributions by more than 100 experts, as well as sample templates and methods for implementation. It is available as a hard copy, as a digital publication or as a bundle of both print and digital versions. The digital version includes access to printable excerpts for facility customization of the templates and procedures. ASBMT members receive a 10% discount on the list price when using the promo code ASBMT2 before July 15, 2016.

Advocacy Trainees Sought

The National Marrow Donor Program's (NMDP's) Legislative Affairs team is seeking physicians or other advanced practitioners willing to partner on outreach activities around key Medicare and Medicaid policy issues. Activities will include authorship of op-eds for placement in local and national newspapers, magazine and/or newsletter interviews regarding the impact of policies on patient care, and potential advocacy with congressional offices in Washington, D.C. Individual time commitments will be relatively minimal and policy novices are welcome. Physicians and advanced practitioners from anywhere in the country are encouraged to contact NMDP; those from D.C./Baltimore, Utah, Oregon, Texas, Michigan, Washington and New Jersey are currently of particular interest. Contact Kristen Bostrom at kbostrom@nmdp.org if you are interested.

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ASSOCIATION NEWS (CONTINUED FROM PAGE 4)

Become an ASBMT Leader…

The members of the ASBMT committees, special interest groups and task forces work diligently throughout each year to identify and implement objectives that strengthen our Society and the blood and marrow transplantation community.

We rely on the expertise and commitment of these highly valued leaders to guide the ASBMT into an ever-changing arena of medical care and regulatory guidelines.

Within the coming days, ASBMT will distribute a survey to members, asking for nominees to join the growing list of important committees, special interest groups and task forces that work to improve our organization and steer its future.

Please participate in the survey and consider sharing your knowledge and time.

Register for the 3rd Annual ASBMT Regional Conference for NPs, PAs and Fellows – Featuring "Best of Tandem 2016"

Click here to register today for the third annual ASBMT Regional Conference for NPs, PAs and Fellows Oct. 13-15 at the Loews Minneapolis Hotel.

The 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.

Attendees will leave more informed and ready to discuss current and further trends in the field, and the planned sessions will provide practice tools that can be used upon returning to work.

3rd Annual Regional Conference for NPs, PAs and Fellows
October 13-15, 2016
Loews Minneapolis Hotel
Minneapolis, Minnesota

BMT TANDEM MEETINGS

2016 BMT Tandem Meetings Audio and Slide Recordings Now Available

The 2016 BMT Tandem Meetings session recordings are now available through the online agenda. To access the recordings, click here.

Registration Opens Next Month for the 2017 BMT Tandem Meetings in Orlando

Online registration and housing will open in August for the 2017 BMT Tandem Meetings Feb. 22-26 at the Gaylord Palms Convention Center in Orlando. Links to meeting registration, housing reservations, the preliminary program, abstract submission and parallel conferences will all be found at asbmt.org. *Continue checking the website for further updates…*

Abstract Submission Deadline is Oct. 3 for BMT Tandem Meetings

The abstract submission process for the 2017 BMT Tandem Meetings in Orlando will open in August and close on Oct. 3. 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. *Continue checking the website for further updates…*

CLINICAL RESEARCH (CONTINUED FROM PAGE 1)

Early Post-HCT CMV Reactivation Increases Risk of Mortality and Relapse but Does Not Cause Relapse

A new study from the Center for International Blood and Marrow Transplant Research (CIBMTR) confirms that early cytomegalovirus (CMV) reactivation after allogeneic hematopoietic cell transplantation (HCT) is a risk factor for poor post-HCT outcomes and does not prevent relapse of hematologic disease. This is despite some single-center studies that have reported preventive relapse benefits of CMV recurrence for acute myeloid leukemia (AML) patients. For this study, researchers examined CIBMTR data on more than 9,400 hematologic malignancy patients, including 5,310 AML patients, 1,883 acute lymphoblastic leukemia patients, 1,079 chronic myeloid leukemia patients and 1,197 myelodysplastic syndrome patients. All of these patients received either a bone marrow or peripheral blood transplant between 2003 and 2010. The median time to CMV reactivation after HCT was 41 days, according to the study published in *Blood*. CMV reactivation did not prevent relapse in any of the disease categories and was found to be associated with higher nonrelapse mortality and lower overall survival. More...

Some Antibiotics Trigger GVHD and Related Mortality

Treating patients with certain antibiotics after allogeneic hematopoietic cell transplantation (HCT) increases their risk for colonic graft-versus-host disease (GVHD) and related mortality, reports new study findings published in *Science Translational Medicine*. Researchers reviewed the records of 857 transplant recipients and discovered that patients treated for neutropenic fever with imipenem-cilastatin or piperacillin-tazobactam were nearly twice as likely to die from GVHD-related complications within five years of HCT than untreated patients (21.5% for imipenem-cilastatin-treated patients vs. 13.1% for untreated patients and 19.8% piperacillin-tazobactam treatment vs. 11.9 % for untreated fever). However, treatment with the antibiotics aztreonam and cefepime did not appear to affect GVHD-related mortality. The researchers also analyzed stool samples and discovered that piperacillin-tazobactam recipients showed changes in gut microbials. The researchers confirmed their findings in mice and discovered that mice treated with imipenem-cilastatin lost the protective mucus lining the colon, which compromised intestinal barrier function. In addition, mouse stool samples had more *Akkermansia muciniphila*, a commensal bacterium with mucus-degrading capabilities, suggesting a link between mucus degradation and GVHD in mice. More...

TRANSLATIONAL SCIENCE STUDIES

Hematopoietic Cells With Low c-Kit Levels From Stem Cell Factor Exposure Still Transplantable

Low expression levels of c-Kit receptor membranes induced by stem cell factor do not prevent hematopoietic stem and progenitor cells (HSPCs) from replacing damaged hematopoietic tissue, according to a study in a recent issue of *Biology of Blood and Marrow Transplantation*. For the study, researchers transplanted HSPCs to bone marrow of mice to evaluate how these cells with different c-Kit expression levels affected engraftment. The researchers were surprised to discover that there were no defects in HSPCs with low numbers of c-Kit, regardless of short- or long-term engraftment, which they attributed to the ability of HSPCs downregulated by stem cell factor to replace missing c-Kit receptors within 12 hours. More...

Genome-Edited Hematopoietic Cells Capable of Long-Term, Multilineage Engraftment

A new study published in *Blood* shows that genome-edited hematopoietic stem and progenitor cells (HSPCs) can engraft and support long-term, multilineage repopulation after autologous transplantation. Researchers conducted the study with nonhuman primates to determine if zinc finger nucleases (ZFNs) were able to disrupt C-C chemokine receptor 5 (CCR5) locus in pigtailed macaque HSPCs. They discovered that shortly after transplantation macaque-specific CCR5 ZFNs disrupted CCR5 at levels as high as 64% ex vivo and 40% in vivo. In addition, CCR5 levels changed as much as 3%-5% in long-term repopulating cells over a six-month time period following transplantation. Among other study findings: genome-edited HSPCs generated cells that transferred to secondary tissues, including the gut, and ZFNs are highly specific for the CCR5 locus in primary cells. The researchers also developed a methodology that tracked individual CCR5 mutant cells over time in vivo, which enabled them to demonstrate that CCR5 gene-edited HSPCs are capable of long-term engraftment. More...

miR-146b-5p Gene Controls Hematopoietic Cell Transformation

Upregulation of cancer-inducing miRNA genes in microvesicles (MVs) enables the transformation of normal hematopoietic cells into leukemia-like cells, reports a study appearing in the journal *Cancer Research*. Using a model with MVs obtained from K562 chronic myelogenous leukemia cells, researchers discovered that during oncogenic transformation, antitumor miRNAs increased, new defense pathways formed and upregulation occurred. Several transcriptions factors and miRNAs were involved in the transformation, but miR-146b-5p, which was highly expressed in MVs, played a primary role in coordinating the cancerous gene-to-cell transformation process. In fact, recipient cells treated with MVs derived from K562 cells expressing mimics of miR-146b-5p accelerated transformation by stopping the tumor-suppressor *NUMB*. High levels of miR-146b-5p also heightened reactive oxygen species levels and genome instability of recipient cells. More...

Calendar of Events

•July

ASBMT
Clinical Research Training Course
July 13
Park City, Utah

University of Nebraska Medical Center
Pan Pacific Lymphoma Conference
July 18-22
Koloa, Hawaii

Society for Cryobiology
CRYO 2016
July 24-27
Ottawa, Canada

•August

International Society for Experimental Hematology
45th Annual Scientific Meeting
August 25-28
San Diego, California

•September

European Association for Haematopathology
18th Meeting
September 3-8
Basel, Switzerland

European School of Haematology
2nd International Conference on New Concepts in B-Cell Malignancies
September 9-11
Estoril, Portugal

European School of Haematology
18th Annual John Goldman Conference on Chronic Myeloid Leukemia: Biology & Therapy
September 15-18
Houston, Texas

American Association of Tissue Banks
Annual Meeting
September 20-24
New Orleans, Louisiana

Association of Physician Assistants in Oncology
19th Annual Conference
September 22-25
Orlando, Florida

•September

American Society for Histocompatibility & Immunogenetics
Annual Meeting
September 26-30
St. Louis, Missouri

Foundation for the Accreditation of Cellular Therapy
Cellular Therapy and Cord Blood Inspection and Accreditation Workshop
September 29
Memphis, Tennessee

National Comprehensive Cancer Network
11th Annual Congress: Hematologic Malignancies
September 30-October 1
New York, New York

International Society for Cellular Therapy
North America Regional Meeting
September 30-October 2
Memphis, Tennessee

•October

European School of Haematology
3rd International Conference on Multiple Myeloma
October 7-9
Milan, Italy

European Society for Medical Oncology
Annual Congress
October 7-11
Copenhagen, Denmark

ASBMT
3rd Annual Regional Meeting for NPs, PAs and Fellows
October 13-15
Minneapolis, Minnesota

Histiocyte Society
32nd Annual Meeting
October 17-19
Dublin, Ireland

European Society for Gene & Cell Therapy
Annual Congress
October 18-21
Florence, Italy

Association of Community Cancer Centers
33rd National Oncology Conference
October 19-21
St. Louis, Missouri

•October

AABB
Annual Meeting
October 22-25
Orlando, Florida

European School of Haematology
7th International Conference on Myeloproliferative Neoplasms
October 27-29
Estoril, Portugal

•November

Society for Immunotherapy of Cancer
Annual Meeting
November 9-13
National Harbor, Maryland

National Donor Marrow Program/Be The Match
Council Meeting
November 10-12
Minneapolis, Minnesota

European Association of Tissue Banks
25th Congress
November 23-25
Hannover, Germany

•December

American Society of Hematology
58th Annual Meeting
December 3-6
San Diego, California

European Society for Medical Oncology
Asia Congress
December 16-19
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

The editor for ASBMT eNews is Jean Sanders, M.D. ASBMT eNews services provided by Lori O'Keefe.
Do you have news, responses or opinions to share with us? Please e-mail the association office at enews@asbmt.org.