Full-Intensity Conditioning and Short Telomeres Risks for Cognitive Impairment Post-HCT
Patients who receive full-intensity conditioning are at risk for cognitive impairment after allogeneic hematopoietic stem cell transplantation (HCT), according to results of a prospective longitudinal study presented at the American Society of Hematology (ASH) annual meeting in December. Using 14 standardized neuropsychological tests, cognitive function was assessed in patients prior to HCT and again six months, one year and two years after transplantation. Results indicated that older age, male gender, Hispanic ethnicity, lower education, income and cognitive reserve, higher risk of relapse, and extreme fatigue contributed to cognitive impairment. After adjusting for these factors, patients who received full-intensity conditioning had deficiencies in executive function, processing speed, verbal fluency and motor dexterity after transplantation. Cognitive function in reduced-intensity conditioning recipients and healthy controls was not affected. The study also discovered that females with short telomeres prior to HCT were at risk for impairments in executive function, processing speed and verbal speed after transplantation. More...

Selective Graft Manipulation May Prevent GVHD and Improve Outcomes
In another abstract presentation at the ASH annual meeting, researchers presented results from a study that tested the safety and efficacy of a new method of graft manipulation in pediatric acute leukemia patients who lack an HLA-matched donor. Researchers removed alpha- and beta-positive T cells and CD19+ B cells from the grafts obtained from one parent of each patient, leaving mature natural killer cells and gamma- and delta-positive T cells. Of the 45 patients who received a hematopoietic stem cell transplantation with the manipulated grafts, 44 patients sustained primary engraftment, but the patient who had graft failure was successfully retransplanted from the other parent. The median times to reach an absolute neutrophil count greater than 0.5x10^9/L was 13 days and a platelet count greater than 50x10^9/L was 11 days. None of the patients developed gut or liver acute graft-versus-host disease (GVHD), 13 patients experienced skin-only grade I-II GVHD, and two patients developed skin limited chronic GVHD. The cumulative incidence of transplantation-related mortality (TRM) was 4%. Seven Continues on page 6
This Is Not a Homer Simpson Survey

“Aw, people can come up with statistics to prove anything, Kent. Forty percent of people know that.” Homer Simpson from “Homer the Vigilante”

This month we are asking medical directors and practice administrators of BMT programs in the United States to participate in a critical survey describing the clinical activity of BMT physicians. For many of our programs, these data will be used to set productivity metrics upon which compensation and staffing will be based.

As you are probably aware, the University Health Consortium (UHC) Faculty Practice Solutions Center (FPSC) provides a range of clinical activity metrics to subscribing faculty practice organizations and academic medical centers. Those metrics are developed by analysis of coding and billing data provided directly by our institutions, and adjustments are based on the clinical full-time equivalent activity (cFTE) of the physicians involved. The data are then used to inform management of the clinical productivity of physicians at the member institutions, relative to other physicians in the same organization and our peers at other institutions.

The FPSC captures line-item physician billing data from each member organization and calculates a variety of metrics, including Work RVUs, from this information. A significant benefit of the FPSC is that the data from all 96 participating organizations are cleaned, scrubbed and formatted in a consistent manner, including the application of a single algorithm to convert CPT code frequencies to Work RVUs. This standardization results in a high degree of apples-to-apples comparability. The FPSC develops its productivity metrics, reported on a per cFTE basis, from a sample of physicians in each clinical subspecialty for which it receives validated cFTE data. The cFTE data are obtained by survey, and the survey is fraught with potential problems, particularly if what is entered into the clinical time data is the budgeted clinical time rather than the actual clinical time.

Until recently, the FPSC did not report BMT-specific productivity metrics, and BMT was folded into the larger universe of academic medical oncology productivity, which generally had a favorable impact because we were seen to be highly productive. The FPSC now reports a BMT-specific metric, which is substantially higher than the medical oncology without infusion benchmark. The current metrics are potentially flawed because they are based on only a small number of providers from a handful of institutions. In addition, nurse practitioners and physician assistants, who are integral parts of most transplant teams, and the extended coverage our teams provide to patients are not considered.

Despite these critical flaws, many institutions have begun to use the data to set unrealistic productivity standards.

Under the leadership of Dr. Michael Lill, ASBMT and FPSC have been working together to further understand the data as they are currently reported and to identify what data needs to be collected so that the metrics reported are as robust and accurate as possible.

We must expand participation among the BMT community in this cFTE data collection process and, by extension, increase the cell size and statistical robustness of the BMT-specific productivity metrics. Our goal is to increase the cell size from the current 22 physicians to at least 120 BMT physicians from 30 academic medical centers.

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**President’s Message** (continued from page 2)

Program directors will receive an email discussing the survey by UHC by the end of the first week in January. We ask that all program directors return this information within two weeks of receipt, and that the details of the reported clinical activity be as accurate as possible and include all the non-billable time we spend on such activities as patient selection, quality management, etc. If you do not receive an email, please contact one of us directly and we will facilitate the delivery of the survey.

-Fred LeMaistre
-Michael Lill

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**BMT Tandem Meetings**

**Registration for BMT Tandem Meetings**
Please remember that registration for the 2014 BMT Tandem Meetings to be held Feb. 26 – March 2 in Grapevine, Texas, just north of Dallas, is open. Links to meeting registration, housing reservations, the preliminary program, abstract submission and parallel conferences can all be found in one convenient location. [More...](#)

**Housing for BMT Tandem Meetings**
Hotel reservations are first come, first served. Please remember that February is a popular vacation month in Dallas. On a single Web page, navigate to the meeting registration, housing reservations, the preliminary program, abstract submission and parallel conferences. [More...](#)

**Richard J. O’Reilly to Present E. Donnall Thomas Lecture**
Richard J. O’Reilly of the Memorial Sloan-Kettering Cancer Center will present the 17th annual E. Donnall Thomas Lecture at the 2014 BMT Tandem Meetings Feb. 26 - March 2 in Grapevine, Texas (just north of Dallas).

**2014 Lifetime Achievement Award and Public Service Award**
During 2014 BMT Tandem Meetings, ASBMT will present the 2014 Lifetime Achievement Award to Mary M. Horowitz, MD, MS, and will present the 2014 Public Service Award to Phyllis I. Warkentin, MD.

**BMT Trainees**
The 2014 BMT Tandem Meetings provide trainees with a variety of high-quality educational, career-development and networking opportunities. Fellows are encouraged to attend the [Fellows Orientation](#) session on Wednesday, Feb. 26. In addition, the BMT [Clinical Education Conference](#) held on Saturday, March 1, and Sunday, March 2, will provide a comprehensive up-to-date overview of BMT that is relevant to undergraduates, medical and graduate students, residents and fellows (MD and PhD). Trainees are also encouraged to attend and get involved in the [CIBMTR Working Committees](#).
Imatinib Treatment Response at Six Months May Predict Long-Term Survival

A phase 2 study from Italy confirms that imatinib is an effective treatment for steroid-refractory chronic graft-versus-host disease and suggests that how a patient responds to the treatment at six months may predict long-term survival. Of the 39 patients who received imatinib, 14 patients had partial responses and four had minor responses with relevant steroid sparing, according to Couriel criteria, and 20 patients had at least a partial response, based on National Institutes of Health (NIH) criteria and changes in NIH severity scores. Overall, the best responses were in the lungs (35%), gut (50%) and skin (32%), reports the study appearing in Blood. At follow-up three to four years later, 28 patients were alive; 72% of these patients had a three-year overall survival and 46% had event-free survival. However, researchers discovered that three-year overall survival was 94% for patients who responded to imatinib treatment at six months but only 58% for patients who did not respond to the treatment. In addition, anti-platelet-derived growth factor receptor stimulatory activity decreased in seven patients who responded to imatinib, yet it remained high in four patients who did not respond to imatinib. More...

Donor-Derived CAR T Cells Cause Malignancy Regression Without GVHD

Results of a study published in Blood indicate that donor-derived allogeneic anti-CD19 chimeric antigen receptor (CAR) T cells can cause B-cell malignancies that are resistant to standard donor lymphocyte infusions to regress without causing graft-versus-host disease (GVHD). Researchers conducted a clinical trial on 10 patients with B-cell malignancies that remained after allogeneic hematopoietic stem cell transplantation by genetically modifying allogeneic T cells taken from each patient’s donor to express a CAR targeting the B-cell antigen CD19. A single infusion of allogeneic anti-CD19-CAR T cells was given to each patient, who did not receive chemotherapy and were not lymphocyte depleted just prior to or at the time of the infusion. Following the infusion, three patients experienced malignancy regression, one patient with chronic lymphocytic leukemia (CLL) achieved ongoing complete remission, another patient with CLL had tumor lysis syndrome as the leukemia dramatically regressed, a patient with mantle cell lymphoma obtained an ongoing partial remission, and none of the patients developed GVHD. In addition, cells containing the anti-CD19-CAR gene were detected in eight of the patients. More...

Similar Outcomes for Pediatric Haploidentical and Matched Sibling Donor HCT Recipients

Pediatric acute leukemia patients showed similar results after haploidentical (HID) hematopoietic stem cell transplantation (HCT) as those for pediatric patients who underwent matched sibling donor (MSD) HCT, according to a study appearing in a recent issue of Bone Marrow Transplantation. The analysis of outcomes included patients who received a modified BuCy2 conditioning regimen and mobilized marrow and blood stem cell grafts. In addition, anti-thymoglobulin was used for HID HCT patients. All HID HCT recipients achieved neutrophil recovery and 97% platelet recovery, and the incidences of acute grade III-IV graft-versus-host disease (GVHD) and extensive chronic GVHD were 14% and 27%, respectively. The five-year leukemia-free survival (LFS) for patients in first complete remission who received an HID HCT was 69% for acute lymphoblastic leukemia (ALL) patients and 83% for acute myeloid leukemia (AML) patients, compared to 63% for ALL patients and 72% for AML patients who received an MSD HCT. The outcomes of the HID HCT for pediatric patients with acute leukemia were similar to those receiving MSD HCT. More...
ASSOCIATION NEWS

Membership Grows to All-Time Record of 2,086
ASBMT membership reached a new all-time record of 2,086 at the end of 2013, continuing 17 consecutive years of growth. The In-Training Member category saw the largest increase, growing at an annual rate of 31%. Health professionals outside the U.S. and Canada comprise 15% of ASBMT members.

Online Voting Continues for Officers, Directors
For the sixth time, the annual election of ASBMT officers and directors will be conducted online instead of by mailed paper ballot. Members qualified to vote in the election were sent instructions by broadcast email on Dec. 16, and the ballot deadline is Jan. 14.

March 1 Deadline for Clinical Research Training Course
The ASBMT Clinical Research Training Course for fellows-in-training and junior faculty is returning to Park City, Utah. Applications are being accepted through March 1 for the course that will be held July 9-14. More...

TRANSLATIONAL SCIENCE STUDIES

Study Explains Role of Ezh2 in GVHD Prevention
A study published in Blood reports that researchers have identified how the histone methyltransferase Ezh2 regulates allogeneic T-cell proliferation, differentiation and function. According to the study, loss of Ezh2 in donor T cells prevented graft-versus-host disease in mice after allogeneic bone marrow transplantation. Ezh2-deficient T cells had initially been activated to proliferate upon alloantigenic priming, but they were unable to continue proliferation and expansion during the late stages of graft-versus-host disease (GVHD) development. Ezh2 ablation was independent of the proapoptotic molecule Bim. Researchers discovered that Ezh2 was necessary for expressing transcription factors Tbx21 and Stat4. Loss of Ezh2 in T cells impaired their differentiation into interferon-γ-producing effector cells, but Ezh2 ablation retained antileukemia activity in alloreactive T cells, which improved overall survival of recipients. The researchers concluded that modulating Ezh2 to treat GVHD and other T cell-mediated inflammatory disorders warrants further investigation. More...

Continues on page 6
patients relapsed, and two-year leukemia-free survival (LFS) was 75%. However, patients who developed skin-only acute GVHD had an LFS of 83%, compared to 72% in patients who did not develop this complication. These results led researchers to conclude that selective modification of donor stem cells may prevent GVHD and contribute to quick neutrophil and platelet count recovery and low TRM. More...

Eliminating CD47 Signaling Induces HCT Tolerance of Humanized Mice and Prevents GVHD
To overcome the problem of xenotransplantation of the human immune system into certain mice, researchers performed genetic inactivation of CD47 on C57BL/6 Rag2\(^{-/-}\)γc\(^{-/-}\) background, eliminating the need for CD47-signal recognition protein α signaling and inducing tolerance to transplanted human hematopoietic stem cells. Triple-knockout, bone marrow, liver, thymus humanized mice used in the study developed lymphoid tissues with mesenteric lymph nodes, splenic follicles and gut-associated lymphoid tissue that demonstrated high levels of multilineage hematopoiesis. In addition, the mice had an intact complement system and did not show any signs of graft-versus-host disease more than seven months after transplantation. The mice exhibited characteristics of human HIV infection, such as CD4\(^{+}\) T-cell depletion, immune activation and development of HIV-specific B- and T-cell responses. This study appears in a recent issue of Blood. More...

Foxp3-Specific Spontaneous Immune Responses
Inducing transcription factor forkhead box P3 (Foxp3) specific cytotoxic T-cell responses may be an effective way to spontaneously provoke immune responses in cancer patients, according to a study published in Leukemia. Researchers identified and characterized spontaneous cytotoxic immune responses to Foxp3-expressing cells in the peripheral blood of both healthy and cancer patient study participants. The immune responses were directed against an HLA-A2-restricted peptide epitope resulting from Foxp3. The Foxp3-reactive T cells were characterized as cytotoxic CD8\(^{+}\) T cells, which recognized dendritic cells incubated with recombinant Foxp3 protein, indicating that it was internalized, processed and cross-presented in the context of HLA-A2. However, Foxp3-specific T cells were able to recognize regulatory T cells (Tregs), and Foxp3\(^{+}\) malignant T cells established from cutaneous T-cell lymphomas were destroyed by the Foxp3-specific cytotoxic T lymphocytes. The spontaneous presence of Foxp3-specific cytotoxic T-cell responses suggests that T cells play a role in immune regulation and possible elimination of Tregs. More...
CALENDAR OF EVENTS

• JANUARY
  Washington BioLeaders Forum
  January 27-29
  Washington, D.C.

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

• MARCH
  National Comprehensive Cancer Network
  19th Annual Conference
  March 13-15
  Hollywood, Florida

  Regenerative Medicine: Technologies Enabling Novel Therapies
  17th Annual Hilton Head Workshop
  March 20-23
  Hilton Head Island, South Carolina

  European Group for Blood and Marrow Transplantation
  Annual Meeting
  March 30-April 2
  Milan, Italy

  Association of Community Cancer Centers
  40th Annual Meeting
  March 31-April 4
  Arlington, Virginia

• APRIL
  International Society of Oncology Pharmacy Practitioners/Canadian Association of Pharmacy in Oncology
  XIV International Symposium on Oncology Pharmacy Practice
  April 2-5
  Montreal, Canada

  American Association for Cancer Research
  Annual Meeting
  April 5-9
  San Diego, California

  Leibniz Institute for Neurobiology Magdeburg
  8th International Symposium on Neuroprotection and Neurorepair
  April 9-12
  Sachsen-Anhalt, Germany

  International Society for Cellular Therapy
  20th Annual Meeting
  April 23-26
  Paris, France

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

• MAY
  Oncology Nursing Society
  Annual Congress
  May 1-4
  Anaheim, California

  American Association of Immunologists
  Annual Meeting
  May 2-6
  Pittsburgh, Pennsylvania

  American Society of Gene & Cell Therapy
  17th Annual Meeting
  May 21-24
  Washington, D.C.

  American Society of Clinical Oncology
  50th Annual Meeting
  May 30-June 3
  Chicago, Illinois

• JUNE
  European Hematology Association
  Annual Congress
  June 12-15
  Milan, Italy

  International Society for Stem Cell Research
  12th Annual Meeting
  June 18-21
  Vancouver, Canada

  Federation of Clinical Immunology Societies
  Annual Meeting
  June 25-28
  Chicago, Illinois

• 2015
  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