CIBMTR®
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

newsletter
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contents



# HLA-C MATCHING IMPORTANT IN CORD BLOOD TRANSPLANTATION: A NEW STUDY

*by Mary Eapen, MD, MS*

Selecting better matched recipients and donors for umbilical cord blood transplantation could substantially reduce transplant-related deaths, according to a new study led by Mary Eapen, MBBS, MS, Associate Professor of Medicine (Hematology/Oncology) at the Medical College of Wisconsin and Associate Scientific Director of the Center for International Blood and Marrow Transplant Research. The findings are published online at The Lancet Oncology (www.thelancet.com).

Currently, human leukocyte antigen (HLA) typing is used to ensure the antigens on the surface of umbilical cord cells are compatible with the recipient. Until now, it was believed that cord blood was more tolerant of differences between donor and recipient. The present criteria for selecting an unrelated umbilical cord blood unit do not usually include HLA-C, one of the genes that governs tissue type.

However, transplant-related deaths after umbilical cord blood transplantation (UCBT) are higher than after unrelated adult donor graft transplants. Dr. Eapen and co-authors investigated the effect of donor-recipient HLA matching on outcomes of 803 people (mostly children under 16 years old) with leukemia or myelodysplastic syndrome who had undergone UCBT in the United States and Europe between 1996 and 2008 to find out if matching for HLA-C changed outcomes.

The researchers found that additional matching for HLA-C significantly lowered transplant-related deaths after UCBT. Effects of matching for HLA-C were greatest with no HLA antigen differences between the donor and recipient and also with a single HLA antigen difference between the donor and recipient.

Dr. Eapen emphasized that these findings underscore a need for greater investment in public cord blood banks for better patient outcomes.

This article is available online at http://www.thelancet.com. Use the following citation: Eapen M, Klein JP, Sanz GF, Spellman S, Ruggeri A, Anasetti C, Brown M, Champlin RE, Garcia-Lopez J, Hattersely G, Koegler G, Laughlin MJ, Michel G, Nabhan SK, Smith FO, Horowitz MM, Gluckman E, Rocha V for the Eurocord-European Group for Blood and Marrow Transplantation, Netcord, and the Center for International Blood and Marrow Transplant Research. **Effect of donor-recipient HLA matching at HLA A, B, C, and DRB1 on outcomes after umbilical-cord blood transplantation for leukaemia and myelodysplastic syndrome: a retrospective analysis.** The Lancet Oncology, Early Online Publication, 7 October 2011.

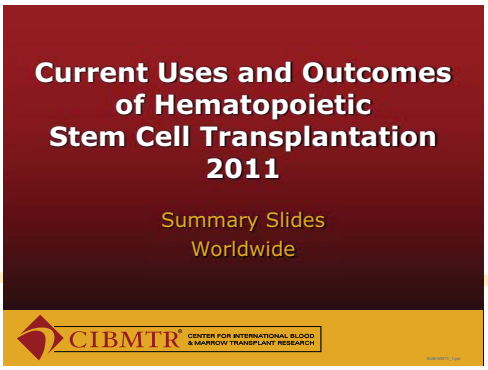
## ABBREVIATIONS USED IN THIS NEWSLETTER:

| | |
|---|---|
| **AML** | acute myeloid leukemia |
| **APBMT** | Asia-Pacific Blood and Marrow Transplantation Group |
| **APCC** | Asia Pacific Cancer Conference |
| **ASBMT** | American Society for Blood and Marrow Transplantation |
| **ASH** | American Society of Hematology |
| **ATG** | anti-thymocyte globulin |
| **BMT** | blood and marrow transplantation |
| **BMT CTN** | Blood and Marrow Transplant Clinical Trials Network |
| **CIBMTR** | Center for International Blood and Marrow Transplant Research |
| **CLL** | chronic lymphocytic leukemia |
| **CML** | chronic myeloid leukemia |
| **CTSI** | Clinical and Translational Science Institute |
| **DLBCL** | diffuse large B-cell lymphoma |
| **DUCBT** | double umbilical cord blood transplantation |
| **EMBMT** | Eastern Mediterranean Blood and Marrow Transplantation |
| **GVHD** | graft-versus-host disease |
| **HCT** | hematopoietic (stem) cell transplant |
| **HLA** | human leukocyte antigen |
| **HORCSCT** | Hematology-Oncology Research Center and Stem Cell Transplantation |
| **ISCT** | International Society for Cellular Therapy |
| **MCW** | Medical College of Wisconsin |
| **MM** | multiple myeloma |
| **MS** | multiple sclerosis |
| **NCI** | National Cancer Institute |
| **NHLBI** | National Heart, Lung, and Blood Institute |
| **NMDP** | National Marrow Donor Program |
| **NST** | non-myeloablative stem cell transplantation |
| **OS** | overall survival |
| **PBSC** | peripheral blood stem cell |
| **PFS** | Progression-free survival |
| **PI** | Principal Investigator |
| **RIC** | Reduced intensity conditioning |
| **SAA** | Severe aplastic anemia |
| **TED** | Transplant Essential Data (forms) |
| **TUMS** | Tehran University of Medical Sciences |
| **UCBT** | umbilical cord blood transplantation |
| **WBMT** | Worldwide Network for Blood & Marrow Transplantation |

# CIBMTR Summary Slides

*By Marcello Pasquini, MD, MS and Zhiwei Wang, MS*

The Summary Slides are an annual report on data submitted to the CIBMTR, focusing on trends, early outcomes, and transplant numbers. Here are 10 selected slides of particular interest. The complete set is available on our website at http://www.cibmtr.org/ReferenceCenter/SlidesReports/SummarySlides/pages/index.aspx.




Slides 1 to 20 exhibit data on frequency of transplants according to age, donor and transplant type, graft source and disease, and early outcomes such as 100-day mortality by disease and transplant type. All frequencies represent first transplants registered with the CIBMTR during the period, except when stating frequencies in the US. Slides 3,8 and 9 represent estimated frequencies of total number of transplants expected in the US. Slides 21 to 40 include overall survival outcomes according to disease, disease status, donor type, year of transplant and conditioning regimen intensity. Comparisons across survival curves are univariate and do not adjust for all potentially important factors; consequently, results should be interpreted cautiously.

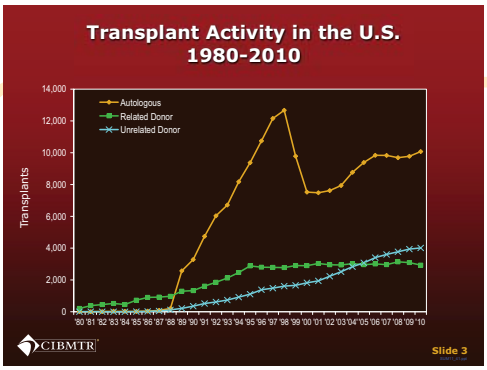
Acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), and chronic myelogenous leukemia (CML) are classified as early disease (first complete remission [CR1] or first chronic phase [CP1]), intermediate (second or subsequent CR or CP or accelerated phase [AP]), or advanced (primary induction failure, active disease, or blastic phase) disease. Myelodysplastic syndrome (MDS) is divided into early (refractory anemia [RA] or refractory anemia with ringed sideroblasts [RARS]), or advanced (refractory anemia with excess of blasts [RAEB] or chronic myelomonocytic leukemia [CMML]) disease. Lymphoma is classified according to sensitivity to prior chemotherapy (chemosensitive or chemoresistant).

The classification of conditioning regimen intensity is based on the agents, doses and schedules used. Several classification systems are available, and for this report we used a composite classification. Cases defined as reduced-intensity by the transplant center were classified as such. Cases without such information and with available data on chemotherapy agents, radiation and doses, were classified according to the CIBMTR operational definition of conditioning regimen intensity:

Myeloablative conditioning regimen: regimens with total body irradiation doses of ≥500 cGY, single fractionated doses of ≥800 cGY, busulfan doses of >9mg/kg, or melphalan doses of >150 mg/m2 given as single agents or in combination with other drugs.

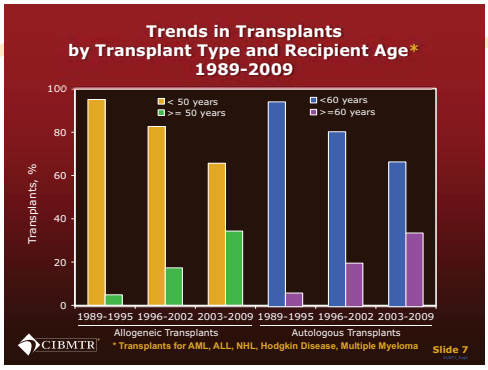
Reduced-intensity conditioning regimen: regimens with lower doses of total body irradiation, fractionated radiation therapy, busulfan, and melphalan than those used to define a myeloablative conditioning regimen (above).

Pasquini MC, Wang Z. Current use and outcome of hematopoietic stem cell transplantation: CIBMTR summary slides, 2011. Available at: http://www.cibmtr.org

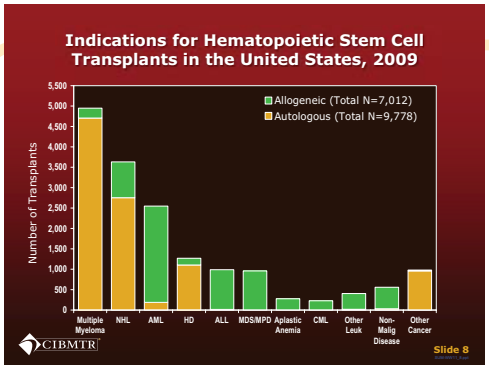



**Slide 3:** Estimated annual numbers of transplants in the U.S. were compiled according to the number registered with CIBMTR. Estimates of how closely the numbers reported are representative of actual transplant activity vary according to the type of transplant and number of centers reporting data per year. Prior to 2007, all except unrelated donor allogeneic transplant facilitated by the NMDP were reported voluntarily. It was estimated that the CIBMTR captured 90% of all unrelated donor transplants performed in the US, 60-90% of related donor allogeneic transplants and 65 to 75% of autologous transplants. These estimates were extrapolated from other databases that capture transplant center activity, accreditation or hospital discharges. After 2007, the Stem Cell Transplant Outcomes Database (SCTOD) was initiated which changed reporting requirements and data capture to an electronic format. The SCTOD requires that all allogeneic transplants performed in the US be registered with CIBMTR. Data reporting of autologous transplants remains voluntary and the numbers in the CIBMTR database are estimated to be 80%. US numbers of allogeneic transplants in the CIBMTR are representative of the actual transplant activity.

The number of autologous transplants in the U.S. has steadily increased since 2000. Allogeneic transplants from unrelated donors surpassed the number of allogeneic transplants from related donors after 2006. The major contributing factors to this trend are the growth of unrelated donor databases and improvements in unrelated donor transplant.



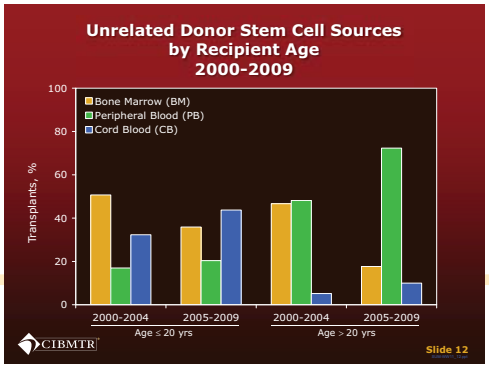

**Slide 7:** The proportion of patients treated for malignant diseases who are older than 50, and older than 60, after allogeneic and autologous transplants, respectively, has significantly increase in the last two decades. Improvements in supportive care, patient and donor selection, and use of reduced-intensity conditioning regimens for allogeneic transplants are the major contributors to this trend.



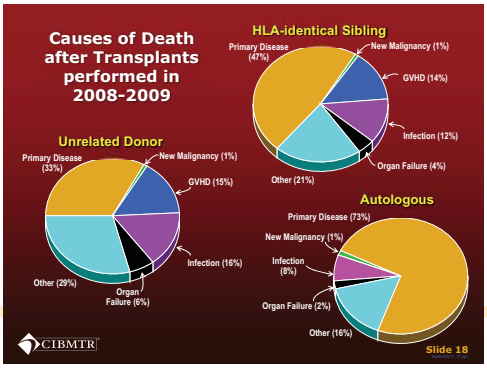

**Slide 8:** The most common indications for HCT in the United States in 2009 were multiple myeloma and lymphoma, accounting for 60% of all HCTs. Multiple myeloma continue to be the most common indication for autotransplantation and acute myeloid leukemia for allogeneic transplantation.



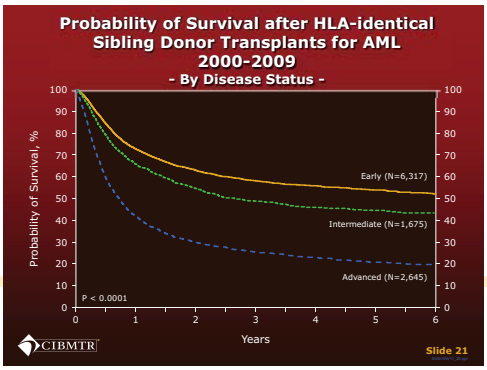
*>> continued on page 3*



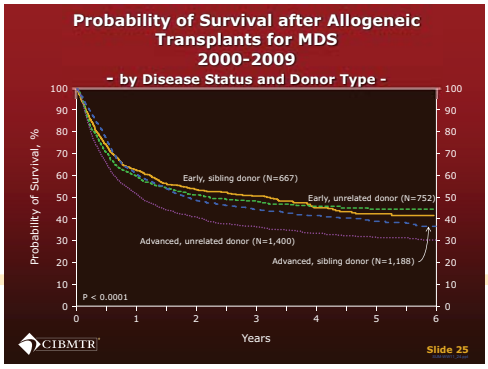

**Slide 12:** Comparison of unrelated donor graft sources between patients younger and older than 20 years demonstrates that the utilization of bone marrow as the preferred graft source has further decreased in the period from 2005 to 2009. Umbilical cord blood is the most common graft source for patients younger than 21 years (44%), and mobilized peripheral blood (72%) was the most common graft source for unrelated donor transplants in patients older than 20 during this period.



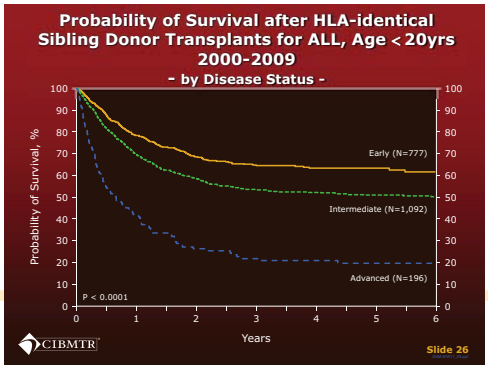

**Slide 18:** The causes of death in the first 100 days post-transplant mainly relate to the primary disease, graft-versus-host disease, infection and end-organ damage. After an autologous transplant, primary disease is the most commonly reported cause of death. Among allogeneic transplant recipients, unrelated donor transplants have fewer deaths related to the primary disease, however organ failure and infections are higher after unrelated donor transplants.



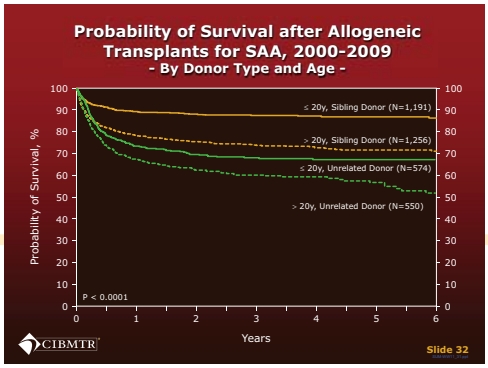

**Slides 21 and 22:** The CIBMTR has data for 20,934 patients receiving an HLA-matched sibling (n=10,637) or unrelated donor (n=10,297) transplant for AML between 2000 and 2009. Their disease status at the time of transplant and the donor type are the major predictors of post-transplant survival. The 3-year probabilities of survival after HLA-matched sibling transplant in this cohort was 58% ± 1%, 48% ± 1%, and 25% ± 1% for patients with early, intermediate, and advanced disease, respectively. The probabilities of survival after an unrelated donor transplant were 46% ± 1%, 44%± 1%, and 20% ± 1% for patients with early, intermediate, and advanced disease, respectively.




**Slides 25:** Allogeneic transplant is a potentially curative treatment for myelodysplastic syndrome (MDS). Outcomes differ according to disease status at the time of transplant and by donor type. The CIBMTR has data on 4,007 patients receiving an allotransplants for early (n=1,419) and advanced (n=2,588) MDS. The 3-year probabilities of survival were 51% ± 2% and 48% ± 2% for recipients of sibling and unrelated donor transplants for early MDS, respectively. Among patients with advanced MDS, corresponding probabilities were 44% ± 2% and 36% ± 2%.




**Slides 26-27:** Among young patients with ALL, for whom chemotherapy has a high success rate, allogeneic transplantation is generally reserved for patients with high-risk disease (i.e. high leukocyte count at diagnosis and the presence of poor-risk cytogenetic markers), who fail to achieve remission or who relapse after chemotherapy. Among the 2,065 patients younger than 20 receiving an HLA-matched sibling transplant for ALL between 2000 to 2009, the 3-year probabilities of survival were 64% ± 2%, 53% ± 2 %, and 22% ± 3% for patients with early, intermediate, and advanced disease, respectively. The corresponding probabilities of survival among the 2,958 recipients of an unrelated donor transplant were 61% ± 2%, 45% ± 1%, and 28% ± 3%.




**Slide 32:** Allogeneic HCT is the treatment of choice for young patients with severe aplastic anemia and available HLA-matched sibling donor. Among the 2,447 patients receiving HLA-matched HCT for severe aplastic anemia between 2000 and 2009, the 3-year probabilities of survival were 88% ±1% for those younger than 20 years and 74% ± 1% for those 20 years of age or older. Among the 1124 recipients of unrelated donor HCT, the corresponding probabilities of survival were 68% ± 2% and 60% ± 2%.

Interested in statistical study design? Check out this article by John Klein, Director of the Division of Biostatistics at the Medical College of Wisconsin (MCW) and Chief Statistical Director for CIBMTR. The article was originally published in Datum, a biostatistics newsletter published by the MCW Institute for Health and Society. It is available online at: http://www.mcw.edu/biostatistics/datum.htm.

# MATCHED PAIRS STUDY DESIGN

*By John Klein, PhD, Director of the Division of Biostatistics at the Medical College of Wisconsin (MCW) and Chief Statistical Director for CIBMTR*

The investigator designing a comparative study has a number of options for study design. In most studies, a simple cohort design is used. In the prospective study, design patients are randomized to one of two treatments and they are then followed. They may have a response measured, they may be evaluated for disease recovery at a particular point in time, or they may be followed until some event such as death or disease recurrence occurs. In this simple design, patients in the two arms are made to be, on the average, as alike as possible by the randomization scheme. This data, depending on what is to be tested, are analyzed, for example, by tests like the t-test or the Wilcoxon test for continuous response, the chi-square or Fisher's exact test for yes/no data, or the (weighted) log rank test for time to event data.

Cohort designs are also used in the analysis of cases and controls in large data bases. Here often there are relatively few cases and a very large number of controls. In a cohort study, all the data in the database is used and comparisons of the cases and controls are made in models adjusted for other covariates which may be affecting outcome. This regression adjustment is important when these covariates are imbalanced between the cases and controls and hopefully takes the place of randomization in the prospective study. Regression methods used are typically linear regression for continuous outcomes, logistic regression for dichotomous outcomes, and Cox regression for time to event data. These methods require that covariate information be available for all patients in the study.

An alternative design is the matched pairs design or the nested case-cohort study. When the study is a prospective study, treatment assignments are made on pairs of subjects. These pairs may be matched biologically or they may be matched on some set of key covariates. In this approach, the two subjects are assumed to be identical within a pair, except for their assigned treatment, but the response on a given treatment may be different from pair to pair. In some cases, the two treatments are studied on the same biological unit. Examples are animal studies where pairs are formed of litter mates, a seminal study of the use of LASER surgery in patients with diabetic retinopathy where one eye was given treatment and the other eye was the control, studies comparing treatments in twins, and studies of skin grafts for burn patients where good and poor matched grafts are compared on the same burn patients.

When analyzing treatment efficacy in large data bases, the analogue of a matched pairs experiment is a nested case-control study. Here the databases contain a relatively small number of case patients and a large number of control patients. Each case patient is matched to m control patients that have similar values of a number of covariates. Typically m is in the range 1 to 5 and more than 4 or 5 matches adds little to the power of the test comparing the treatment and control efficacy. A rough rule of thumb is that if one matches m controls to each case, the efficiency of the matched analysis is [1/ (m+1)] times that of the complete cohort analysis.

There are several reasons to consider a nested case-cohort design. First, if we match patients on a limited set of covariates, then it is likely they will be matched on other prognostic factors as well. This allows us to compare like to like when doing the test of differences in outcome between the cases and controls. A second, and often more important, reason for this design is logistical. In many instances, we need to collect additional information on the subjects selected. This may be additional covariates that need to be adjusted for in the analysis. It could be information that validates that the patient is correctly classified as a case or control, perhaps based on lab tests or path reports not in the database, or it could be more detailed measures of the outcome. This additional information is often quite time consuming, expensive, or impossible to obtain for all patients in a large retrospective database but can be obtained on a smaller set of nested case-cohort patients.

There are some concerns one needs to be aware of with nested case-cohort studies. First, when matching, it may be that some cases cannot find a match. In this design, these cases are deleted and there is a loss of efficiency. Second, when the outcome is the time to event, if the time for the case is censored and smaller than its controls, the 'pair' are essentially deleted when comparing the two treatments further reducing the sample size. Third, one cannot examine the effect of any factors used to match patients in any further analysis using these data. This design needs to be used with proper caution. A common fallacy is that these types of studies are more efficient than cohort studies which use all the data. This is in general not true and the relative efficiency depends on the correlation between pairs, the outcome measure, and the test being used.

An example of a nested case-control design is a study of the outcome of HCT using fludarabine, busulfan and Thymoglobulin based on the large database of the MCW Center for International Blood and Marrow Transplantation Research (CIBMTR). This conditioning regime is somewhat rare, while the control group of patients conditioned using busulfan and cyclophosphamide is fairly common in the database. Patients were matched on age, disease, and disease status to construct the nested case-cohort dataset. One motivation here for this design was that additional information on the dosages of the various drugs needed to be obtained from the reporting team who contributed to the database. For additional details, see Bredison et al, Biology of Blood and Marrow Transplantation 14, 993-1003, 2008.

For both the nested case-cohort design and the prospectively matched pairs experiments, the comparisons of treatments need to be adjusted for matching in the analysis. Two general approaches to analysis are used: A marginal or a conditional model. In the marginal approach, a test statistic based on an independence working model is used with a variance adjusted for possible association within pairs. A simple example is for continuous normal data where the test statistic is the difference of the two sample means, and the variance of this difference is variance of each sample mean minus twice the covariance between the sample means. In a conditional approach, tests tend to be based on differences or ratios of observations within a pair. An example is the paired t-test where one first takes the difference between the case and control responses and bases a one sample t-test on this difference. Note that for simple normal data matched pairs, the marginal and conditional methods described here give the same answer but this is not true in general.

The Biostatistics unit of the Clinical and Translational Science Institute (CTSI) recently received a one-year supplemental grant to study methods for matched data designs when the outcome is the time to some event. An annotated bibliography of references on techniques for analysis will soon appear on our website. In coming issues of Datum, we will be reporting results of this study. Stay tuned.

For this article, use the following citation: Klein, J. **Matched Pairs Study Design.** Datum Newsletter [serial online], September/October 2011; (17)3:1.

# DISTINGUISHED SERVICE AWARD FOR DR. ARDESHIR GHAVAMZADEH

The International Studies Working Committee of the CIBMTR is pleased to announce that Dr. Ardeshir Ghavamzadeh has been selected as the 2012 recipient of the CIBMTR Distinguished Service Award.

Dr. Ghavamzadeh received his MD from Vienna Medical School in Austria in 1971. He completed residencies in internal medicine and oncology in Kantonsspital Aarau, Switzerland, in 1977 and fellowships in Hematology and BMT at the University of Basel in Switzerland in 1991. In 1980, he was appointed Chief of Oncology-Hematology & BMT at Shariati Hospital in Tehran, where he began his work in stem cell transplantation.

Dr. Ghavamzadeh began contributing data to the IBMTR (now CIBMTR) in 1992 and served on its Advisory Committee in 1995. He is an executive board member of the Asia Pacific Blood and Marrow Transplantation Group (APBMT) and the Asia Pacific Cancer Congress (APCC).

Other notable positions include:

- Chief of Iranian Board of Hematology, Oncology (1991 – present)
- President of Iranian Society of Hematology-Oncology (1994 – 2002)
- Director and Professor of Medicine, Hematology-Oncology Research Center and Stem Cell Transplantation (HORCSCT), Tehran University of Medical Sciences (TUMS), Shariati Hospital (1999 – present)
- President of 2nd Congress of Hematology, Oncology and Bone Marrow Transplantation (2002)
- President of Hematology and Medical Oncology Iranian Society (2002 – present)
- President of Bone Marrow Transplantation Iranian Society (2003 – present)
- President of 9th Congress of Asia-Pacific Bone Marrow Transplantation Group (APBMTG) (2004)
- President of 19th Congress of Asian Pacific Cancer Conference (2007)
- President of Iranian Society for Internal Medicine Sub Specialty (2009 – present)
- Vice President of Eastern Mediterranean Blood and Marrow Transplantation (EMBMT) (2008 – present)

Additionally, Dr. Ghavamzadeh has served as president of numerous professional, regional Congresses. He served as PI/co-PI on numerous projects (including founding the Iranian Cancer Network), co-authored 2 books, published 51 papers (and also many in Persian), and authored nearly 300 abstracts.

Dr. Ghavamzadeh received Honorary Membership to the European Group for Blood & Marrow Transplantation in Vienna in 2009. He was also selected for Distinguished Professor of Tehran University of Medical Sciences in 2010. Dr. Ghavamzadeh oversees an active center that transplanted 377 patients in 2010. His team also educates transplantation teams at other centers in Tehran. In 2009, the HORCSCT began an unrelated stem cell banking project and is actively engaged in cord blood banking.

We wish to honor him for the successful development of a stem cell transplantation program in a setting with multiple challenges and also for his dedication to advancing the field of transplantation. Please join us in extending this honor to Dr. Ghavamzadeh during the CIBMTR Awards & Assembly Meeting at Tandem in San Diego on Thursday, February 2, 2012, at 6:30 PM PST.

# FORMSNET™3

FormsNet™3, the latest version of the CIBMTR forms submission tool, will include all of the highest priority requirements submitted by our stakeholders. This version will contain a more user-friendly design with improved navigation, customization capability, as well as a new Recipient Module, and a new Form Definition Manager.

FormsNet™3 will incorporate an "Agile Software Development" model, which is an iterative and incremental approach to software design and development. The goal of Agile Software Development is to successively refine and deliver a software system that meets the most stringent requirements of its audience. The process involves continuous planning, testing, and integration of both the project plan and the software. It also incorporates feedback at multiple points during each project phase, so that functionality and user experience are constantly refined and adjusted to meet the needs of its users. Look for this greatly improved version in November 2012.

***Some of the improvements you will see:***

- Auto-population of key fields
- Enabling/disabling of fields based on answers to prior questions
- Improved navigation and validation
- New user interface
- Field-level saving

# 2012 BMT TANDEM MEETINGS ON THE HORIZON

by D'Etta Waldoch

*The combined annual meetings of CIBMTR and ASBMT have been North America's largest international gathering of blood and marrow transplant clinicians and investigators, laboratory technicians, transplant nurses, pharmacists and clinical research associates since 1999.*

## 2011

It is November at the CIBMTR offices in Milwaukee and not exactly balmy, as I drift back to warm memories of the successful 2011 BMT Tandem Meetings on the beautiful island of Oahu, Hawaii, last February. The Hawaiian concept of "ohana" comes to mind, as I begin to consider what the 2012 meetings will bring and all the people who will attend. Ohana refers not only to one's biological family, but includes those we welcome into our presence as extended family. Over the years, it has been a pleasure to see many of the same people from around the world gather in February at our meetings. Colleagues and old friends—in many ways we become ohana with our common interests and various levels of expertise in hematopoietic cell transplantation. I can tell you for certain that the conference staff, a diverse mix of CIBMTR and ASBMT employees and outside contractors who work hard to bring the event together each year, very much consider themselves part of a "Tandem family." Our collective work in preparation for the BMT Tandem Meetings is often filled with the same sense of planning one might have for the upcoming holiday season, surrounded by and shared with extended family. It all somehow comes together on the heels of the holidays, and we find ourselves here in the flurry of Tandem activity once again looking forward to the welcoming smiles of familiar faces.

## 2012


Our 2012 BMT Tandem Meetings will return to the Manchester Grand Hyatt in sunny San Diego, California. Scientific Program Chairs for 2012 are Stella Davies, MBBS, PhD, representing CIBMTR, and John Levine, MD, MS, for ASBMT. This year's conference begins on Wednesday, February 1, a bit earlier than usual, and ends at noon on February 5, which is Super Bowl Sunday for the (US) National Football League. (Might be fun if some of the Tandem family hangs around to kick back and watch the football game together, before returning back home.)

Detailed information about the 2012 meeting, including conference registration and hotel reservations, is continuously updated on the CIBMTR (www.cibmtr.org) and ASBMT (www.asbmt.org) websites. Be sure to check in periodically for updates to the provisional agenda, where attendees may also use the Personal Scheduler tool to create custom itineraries for the 5-day BMT Tandem Meetings. Don't forget to get your ticket/s for the President's Reception on Saturday as the California sun sets, starting with food and friends poolside, followed by dancing and dessert into the wee hours.

Online abstract submission ended on October 13, with more than 550 presentations slotted for oral and poster sessions throughout the week. Educational topics slated for presentation at the San Diego meetings are listed in the box below.

Peripheral meetings will include the BMT CTN Steering Committee, BMT CTN Coordinator and Investigator Sessions, Foundation for Accreditation of Cellular Therapy (FACT) Training Workshops, Clinical Research Professionals Data Management Conference, BMT Center Administrative Directors Conference, BMT Pharmacists Conference, Advanced Practice Professionals Conference, Transplant Nursing Conference, Pediatric BMT Program, BMT Center Medical Directors Conference, and a Clinical Practice Forum designed to address clinically relevant topics for all allied health professionals working in transplantation. New this year, a group of nutritional experts working in transplantation will convene on Thursday.

For general information, please e-mail D'Etta Waldoch, CMP, at the conference office at bmttandem@cs.com. Questions about support opportunities at the 2012 BMT Tandem Meetings may be directed to Sherry Fisher at slfisher@mcw.edu.

### 2012 Meeting Topics

- Aging and transplants in the elderly
- Late effects/survivorship
- Biomarkers in HCT
- HCT for low-grade lymphoma
- Chronic GVHD
- Hematopoietic stem cell biology
- Dendritic cells
- GVHD prevention
- ATG vs. non-ATG therapy
- Transplantation for autoimmune disease
- Controversies in myeloma treatment
- HCT in the HIV+ population
- Natural killer cells in HCT and cellular therapy
- Donor selection: where is it going?
- Preventing relapse after HCT – myeloid malignancies
- Clinical trials: cooperative groups and networks of the future
- HCT/cellular therapy for CLL/CML
- Donor selection – HLA and other typing
- Supportive care/complementary therapies
- New treatment strategies
- Tolerance
- Next generation sequencing
- Training the next generation
- HCT for non-malignant disorders
- Sessions presented by NMDP, ISCT, and WBMT

# BLOOD AND MARROW TRANSPLANT CLINICAL TRIALS NETWORK

Effective August 2011, the Blood and Marrow Transplant Clinical Trials Network (BMT CTN) has expanded from 16 to 20 core centers and has enrolled over 4,000 patients since 2003. Additionally, the National Heart, Lung, and Blood Institute (NHLBI) awarded the BMT CTN a new 6-year grant for continued administration of the Data and Coordinating Center (DCC). The DCC is made up of three organizations—CIBMTR, NMDP, and The EMMES Corporation—that together support all BMT CTN activities.

This year, the American Society of Hematology (ASH) selected a BMT CTN protocol for the prestigious Plenary Session to be presented at the 2011 ASH Annual Meeting: **Increased Incidence of Chronic Graft-Versus-Host Disease (GVHD) and No Survival Advantage with Filgrastim-Mobilized Peripheral Blood Stem Cells (PBSC) Compared to Bone Marrow (BM) Transplants From Unrelated Donors: Results of Blood and Marrow Transplant Clinical Trials Network (BMT CTN) Protocol 0201, a Phase III, Prospective, Randomized Trial.** Anasetti C, Logan B, Lee SJ, Waller EK, Weisdorf D, Wingard JR, Cutler C, Westervelt P, Woolfrey A, Couban S, Jonston L, Maziarz R, Pulsipher M, Anderlini P, Bensinger W, Leitman S, Rowley SD, Carter SL, Horowitz MM, Confer DL.

Additionally, several studies were selected for oral and poster presentations:

**Randomized phase III trial of 131Iodine-Tositumomab (Bexxar)/Carmustine, Etoposide, Cytarabine, Melphalan (BEAM) vs. Rituximab/BEAM and autologous stem cell transplantation for relapsed diffuse large B-cell lymphoma (DLBCL): no difference in progression-free (PFS) or overall survival (OS).** Presenter: Julie Vose, MD.

**Larger numbers of donor naïve CD8+ T-cells and plasmacytoid dendritic cell precursors in allogeneic BM grafts from unrelated donors are associated with improved survival: results from BMT CTN 0201.** Presenter: Edmund K. Waller, MD, PhD.

**Immunoglobulin free light chain (FLC) and heavy chain/light chain (HLC) assays – comparison with electrophoretic responses in multiple myeloma (MM).** Presenter: Parameswaran Hari, MD, MRCP, MS (poster).

**Fludarabine-based conditioning for allogeneic marrow transplantation from unrelated donors in severe aplastic anemia (SAA): serious and unexpected adverse events in pre-defined cyclophosphamide (CY) dose levels.** Presenter: Jakub Tolar, MD, PhD (poster).

## Clinical trials - open enrollment

The BMT CTN encourages widespread transplant community participation in clinical trials. If your center is interested in participating, please visit the BMT CTN website at https://web.emmes.com/study/bmt2/index.html.

The following BMT CTN trials opened or will soon be opened for enrollment:

- **BMT CTN 0804/CALGB 100701 –** Reduced intensity allogeneic HSCT in high-risk CLL
- **BMT CTN 0805/SWOG 0805 –** Philadelphia (Ph) positive regimens in ALL
- **BMT CTN 0901 –** NST vs. myeloablative in MS or AML
- **BMT CTN 0902 –** Peri-transplant stress reduction
- **BMT CTN 0903 –** Allogeneic transplantation in HIV+
- **BMT CTN 1101 –** RIC in double UCBT vs. HLA-haploidentical (to be opened this year)

## Publications

The following manuscripts were published this year:

Krishnan A, Pasquini MC, Logan B, Stadtmauer EA, Vesole DH, Alyea E, Antin JH, Comenzo R, Goodman S, Hari P, Laport G, Qazilbash MH, Rowley S, Sahebi F, Somlo G, Vogl DT, Weisdorf D, Ewell M, Wu J, Geller NL, Horowitz MM, Giralt S, Maloney DG. **Autologous haemopoietic stem-cell transplantation followed by allogeneic or autologous haemopoietic stem-cell transplantation in patients with multiple myeloma (BMT CTN 0102): a phase 3 biological assignment trial.** The Lancet Oncology, 30 September 2011 online edition.

Devine SM, Carter S, Soiffer RJ, Pasquini MC, Hari PN, Stein A, Lazarus HM, Linker C, Stadtmauer EA, Alyea EP, Keever-Taylor CA, O'Reilly RJ. **Low Risk of Chronic Graft-versus-Host Disease and Relapse Associated with T Cell–Depleted Peripheral Blood Stem Cell Transplantation for Acute Myelogenous Leukemia in First Remission: Results of the Blood and Marrow Transplant Clinical Trials Network Protocol 0303.** Biol Blood and Marrow Transplantation. 17: 9, 1343-1351, September 2011.

Keever-Taylor CA, Devine SM, Soiffer RJ, Mendizabal A, Carter S, Pasquini MC, Hari PN, Stein A, Lazarus HM, Linker C, Goldstein SC, Stadtmauer EA, O'Reilly RJ. **Characteristics of CliniMACS® System CD34-Enriched T Cell-Depleted Grafts in a Multicenter Trial for Acute Myeloid Leukemia-Blood and Marrow Transplant Clinical Trials Network (BMT CTN) Protocol 0303.** Biol Blood and Marrow Transplantation. 2011 Aug 29. [Epub ahead of print].

Brunstein CG, Fuchs EJ, Carter SL, Karanes C, Costa LJ, Wu J, Devine SM, Wingard JR, Aljitawi OS, Cutler CS, Jagasia MH, Ballen KK, Eapen M, O'Donnell PV, and on behalf of the Blood and Marrow Transplant Clinical Trials Network. **Alternative donor transplantation after reduced intensity conditioning: results of parallel phase 2 trials using partially HLA-mismatched related bone marrow or unrelated double umbilical cord blood grafts.** Blood. 118: 2, 282-87, 2011 July 14.

Tomblyn MR, Ewell M, Bredeson C, Kahl BS, Goodman SA, Horowitz MM, Vose JM, Negrin RS, Laport GG. **Autologous vs. reduced intensity allogeneic hematopoietic cell transplantation for patients with chemosensitive follicular non-Hodgkin's lymphoma beyond first complete response or first partial response.** Biol Blood Marrow Transplant 17:1051-1057, 2011. (July)

Pulsipher MA, Young NS, Tolar J, Risitano AM, Deeg HJ, Anderlini P, Calado R, Kojima S, Eapen M, Harris R, Scheinberg P, Savage S, Maciejewski JP, Tiu RV, DiFronzo N, Horowitz MM, Antin JH. **Optimization of therapy for severe aplastic anemia based on clinical, biologic, and treatment response parameters: conclusions of an International Working Group on severe aplastic anemia convened by the Blood and Marrow Transplant Clinical Trials Network.** Biol Blood Marrow Transplant 17: 291-299, 2011. (Mar)

Horwitz EM, Horowitz MM, DiFronzo NL, Kohn DB, Heslop HE. **Guidance for developing PhaseII cell therapy trial proposals for consideration by the Blood and Marrow Transplant Clinical Trials Network.** Biol Blood Marrow Transplant 17:192-196, 2011. (Feb)

## Tandem

The BMT Tandem Meetings are the combined annual meetings of CIBMTR and the American Society of Blood and Marrow Transplantation (ASBMT). Attendees benefit from a full scientific program that addresses the most pertinent issues in hematopoietic cell transplantation.

The following BMT CTN protocols were presented at Tandem 2011:

**Phase II Trial of Non-Myeloablative Conditioning (NST) Double Umbilical Cord Blood Transplantation (DUCBT) from Unrelated Donors in Patients with Hematologic Malignancies: Results of Blood and Marrow Transplant Clinical Trials Network (BMT CTN) Protocol 0604.** Presented by Claudio Brunstein, MD, PhD.

**Phase II Trial of Non-Myeloablative Conditioning and Partially HLA-Mismatched (HLA-Haploidentical) Bone Marrow Transplantation (BMT) for Patients with Hematologic Malignancies: Results of Blood and Marrow Transplant Clinical Trials Network (BMT CTN) Protocol 0603.** Presented by Ephraim Fuchs, MD. This presentation received a Best Abstract Award.

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CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

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