

Recent Publications- February 15, 2010

Bone Marrow Transplantation (21 September 2009)

Outpatient Myeloablative Allo-SCT: A Comprehensive Approach Yields Decreased Hospital Utilization and Low TRM

Scott R. Solomon, MD; Rebecca H. Matthews, PharmD; Amy M. Barreras, PharmD; Asad Bashey, MD, PhD; Karen L. Manion, RN; Kathleen McNatt, RN; Dawn Spechart, PhD; D. Gerard Connaghan, MD; Lawrence E. Morris, MD; and H. Kent Holland, MD

American Society of Hematology Meeting (December 2009)

A Phase I/II Trial of 5-Azacytadine Prior to Gemtuzumab Ozogamicin (GO) for Patients with Relapsed Acute Myeloid Leukemia with Correlative Biomarker Studies

Edward D. Ball, MD; Bruno C. Medeiros, MD; Larissa Balaian, PhD; Tracy Roque; Sue Corringham, RN; Richa Rajwanshi; Steve Coutre, MD; Jason R Gotlib, MD, MS; Asad Bashey, MD, PhD; and Karen Messer, PhD

Low Dose Subcutaneous Alemtuzumab and Prophylactic Donor Lymphocyte Infusion Results in Favorable Outcomes for High Risk Recipients of Unrelated Donor Allogeneic Transplants

Scott R. Solomon, MD; Asad Bashey, MD, PhD; Lawrence E. Morris, MD; Karen L Manion; and H. Kent Holland, MD

Cryopreserved G-CSF Mobilized Donor Lymphocyte Infusion (DLI) without Withdrawal of Immunosuppression is Safe and Highly Effective for Treating Isolated Poor Donor T-cell Chimerism Following Reduced Intensity Allogeneic Transplantation (RICT)

Asad Bashey, MD, PhD; Karen L. Manion; Pauline Smith; Joan Mccollum, MT; H. Kent Holland, MD; Lawrence E. Morris, MD; and Scott R. Solomon, MD

Prospective Phase II Study of Pre-Administration of Rabbit Antithymocyte Globulin (rATG, Thymoglobulin®) to Maximize Early T-Cell Chimerism Following Allogeneic Reduced Intensity Conditioning Transplant (RICT) through Differential in-Vivo Depletion of Recipient Versus Donor T-Cells

Melissa Sanacore, PharmD; Stacey Brown, BA; Candice G Roth, RN, MSN; Ming Zhang, PhD; Pauline Smith, RN; H. Kent Holland, MD; Lawrence E. Morris, MD; Scott R. Solomon, MD; and Asad Bashey, MD, PhD

ASBMT/CIBMTR BMT Tandem Meeting (February 2010)

Poster:

A Comparison of Toxicity and Mobilization Efficacy Following Two Different Doses of Cyclophosphamide for Mobilization of Hematopoietic Stem Cells in Non-Hodgkins Lymphoma Patients

Connie A Sizemore, PharmD; Justin LaPorte, PharmD, BCOP; H. Kent Holland, MD; Joan Mccollum, MT; Jennifer Westerman, MT (ASCP); Lawrence E Morris, MD; Asad Bashey, PhD, MD; and Scott R Solomon, MD

Psychosocial Factors as Measured but the Transplant Evaluation Rating Scale (TERS) Predict Length of Hospitalization and Infectious Complications following Hematopoietic Stem Cell Transplantation.

Dawn Speckhart, PhD; Asad Bashey, M.D. PhD; Lawrence E. Morris, MD; Scott R. Solomon, MD; Tina Berry; and H. Kent Holland, MD

Presentation:

Comparison of Toxicity and Mobilization Efficacy Following Two Different Doses of Cyclophosphamide for Mobilization of Hematopoietic Stem Cells in Multiple Myeloma Patients

Connie A Sizemore, PharmD; Justin LaPorte, PharmD, BCOP; Melissa F. Sanacore, Pharm.D, BCOP; H. Kent Holland, MD;

Joan Mccollum, MT; Jennifer Westerman, MT (ASCP); Lawrence E Morris, MD; Asad Bashey, MD, PhD; and Scott R Solomon, MD

The Blood and Marrow Transplant Program at Northside Hospital
5670 Peachtree Dunwoody Rd NE, Suite 1000
Atlanta , GA 30342-1699

The Blood and Marrow Transplant Program at Northside Hospital

The Blood and Marrow Transplant Program at Northside Hospital (BMTNSH) is a collaborative effort between the Blood and Marrow Transplant Group of Georgia (BMTGA) and Northside Hospital (NSH). The program is one of the largest clinical transplant programs in the United States, serving patients undergoing bone marrow/stem cell transplant therapy and providing primary leukemia treatment. Our program has received National Center of Excellence Awards by major insurance companies and is nationally accredited by the following organizations:

- National Marrow Donor Program (NMDP) • Foundation for Accreditation of Cellular Therapy (FACT)
- American Association of Blood Banks (AABB) • Food and Drug Administration (FDA)

BMTNSH Facts

Northside Hospital is an award-winning comprehensive adult BMT Center that is designated by the National Marrow Donor Program (NMDP) as a qualified site to perform unrelated donor allogeneic bone marrow transplants. In addition, Northside Hospital is listed as a comprehensive transplant center with the Caitlin-Raymond International Bone Marrow Registry for national and international donor access. The Blood and Marrow Transplant Program offers:

- Autologous Stem Cell Transplants • Related and Unrelated Allogeneic Stem Cell Transplants
- Haploidentical Stem Cell Transplants • Cord Blood Transplants
- Nonmyeloablative / Reduced Intensity Stem Cell Transplants

The BMT Program operates seven days a week, 24 hours a day, and provides patients with team-based care that includes psychologists, pharmacists, nutritionists and physical therapist

Referrals can be made by calling 404-255-1930, and referrals can be made by a physician or any physician staff member. You will have the option of directly speaking to one of the physicians or a transplant / leukemia coordinator to make the referral. The coordinators will be in contact with your staff to obtain all appropriate records required for the consult and the patient will be contacted directly with the appointment date and time.

The Blood and Marrow Transplant Program at Northside Hospital • phone: 404 255 1930 • fax: 404 255 1939

Physicians at BMTGA:

H. Kent Holland, M.D.
FACT Program Director

Lawrence E. Morris, Jr., M.D.
Director of Leukemia Services

Scott R. Solomon, M.D.
Medical Director, Stem Cell Processing Lab

Asad Bashey, M.D., Ph. D.
Director of Clinical Research

IN THIS ISSUE:

The Blood and Marrow Transplant Program at Northside Hospital Recent Publications - February 15, 2010

Early Stem Cell Mobilization Recommended in Myeloma Patients Undergoing Lenalidomide (Revlimid) Based Initial Therapy

Stovall Foundation Provides No-Cost Lodging Options for Patients Undergoing Transplantation at the Blood and Marrow Transplant Program at Northside Hospital

New Thirty-Six Bed BMT & Leukemia Inpatient Unit Opens at Northside Hospital

The Blood and Marrow Transplant Program at Northside Hospital News

SPRING 2010

www.bmtga.com • www.northside.com



BMT Program at Northside Hospital Pioneers Outpatient Management of Myeloablative Allogeneic Transplants

Patients undergoing myeloablative allogeneic hematopoietic cell transplantation (HSCT) have traditionally been hospitalized starting with the high-dose preparative regimen until hematopoietic recovery and resolution of mucosal toxicity. Thus, the typical length of initial hospitalization ranges from four to five weeks. Such prolonged inpatient care was originally justified by concerns for mucosal toxicity and prolonged cytopenias with associated susceptibility to serious bacterial, invasive fungal and viral infections.

However, advancements in supportive care may enable outpatient management of most or all of the initial post-transplant care with resulting improved patient satisfaction and quality of life, reduced exposure to nosocomial pathogens, lower costs and reduced pressure on inpatient

beds. Several groups have demonstrated that autologous HSCT can be safely delivered in the outpatient setting with good outcomes and diminished cost. In addition, allogeneic transplantation following nonmyeloablative conditioning also appears feasible in the ambulatory care setting, given its significantly reduced regimen related toxicities compared with standard myeloablative allogeneic HSCT. Although a few pilot studies have explored the safety of outpatient myeloablative allogeneic HSCT^{1,2} in small numbers of selected patients, no prior study have shown whether this approach can be routinely applied to all patients undergoing myeloablative allogeneic HSCT.

The Blood and Marrow Transplant Program at Northside Hospital (BMTNSH) has invested extensively in the infrastructure necessary for such outpatient management and has developed

(Continued on next page)

(Continued from front page)

a comprehensive outpatient management program that is applied to all patients receiving allogeneic HSCT at the center. The results of 100 consecutive unselected patients who received a myeloablative allogeneic HSCT from a matched related donor at BMTNSH have recently been published.³ The published study evaluated the impact of outpatient management on safety, hospital utilization and clinical outcomes.

Patients who received their preparative regimen in the outpatient clinic, were hospitalized briefly for stem cell infusion and then discharged to the outpatient clinic for daily follow-up. Patients were readmitted expectantly for complications, more safely managed in the inpatient setting. The study demonstrated that outpatient management can safely be performed in almost all patients receiving myeloablative allogeneic HSCT. Only five of 100 patients were admitted prospectively to receive their high dose preparative regimen due to compliance⁴ or medical¹ concerns. Eighty-seven percent of patients received their entire preparative regimen in the outpatient infusion center. Almost 80% of patients were discharged from the hospital following their brief planned admission for stem cell infusion and were followed daily in the outpatient infusion center. Although the majority of patients are readmitted back to the hospital at a median of day +7 post-transplant, approximately one-fifth of patients are treated exclusively in the outpatient setting, excluding the brief planned admission for stem cell infusion. The median hospital length of stay was 12 days, which compares favorably to the 34-day median inpatient hospital stay seen at most US blood and marrow transplant centers.⁴ Transplant-related mortality at day 100 and six months was modest at 10% and 15% respectively, for all patients and 0% and 5% respectively, for standard risk patients.

This study of 100 consecutive patients, demonstrates the feasibility and safety of a comprehensive outpatient treatment approach for myeloablative allogeneic transplant recipients. This is most clearly demonstrated by the low transplant-related mortality seen in this patient population. Our results indicate that outpatient-based allogeneic HSCT is able to significantly reduce inpatient length of stay by more than half expected with traditional inpatient management without causing an increase in clinical complications.

This study adds to the growing literature regarding the safety of outpatient management of patients following high-dose chemotherapy. Prior concerns have included the increased risks of mucosal toxicity, infections, septic shock and organ failure associated with high-dose conditioning regimens and the possibility of worse outcomes if patients are not monitored closely in the hospital. Despite outpatient management, we noted a low incidence of serious infections. Although patients spent considerable time in their homes during the pancytopenic phase, outside of protective isolation, we documented no increase in the incidence of invasive aspergillus or other mold infections. 45 patients required readmission to the hospital secondary to neutropenic fever (ten with

documented bacteremia), but none of these patients died of sepsis or infectious death.

The low incidence of infectious complications and non-relapse mortality seen in this study, despite myeloablative conditioning, may in part be the result of a strict adherence to supportive care algorithms. Patients were evaluated daily by a mid-level practitioner, pharmacist and physician following hospital discharge. Compliance with antimicrobial prophylaxis, immunosuppressive therapy, and other medications, was reinforced using home medicine administration records. Patients were admitted promptly for complications requiring inpatient management such as neutropenic fever.

Although a formal quality-of-life survey was not included as part of the analysis, it was evident from satisfaction questionnaires that patients universally valued the treatment delivered in the outpatient setting. In fact, few patients requested to receive more traditional inpatient management and if they did it was usually due to transportation or caregiver concerns.

An outpatient management strategy significantly reduces hospitalization, which has an immediate benefit in reducing the pressure on available beds. Although a potential for cost savings exists, it is more difficult to demonstrate, as much of the inpatient cost reduction is simply shifted to the outpatient setting. However, several studies have documented a 25-45% decrease in total medical charges associated with an outpatient management strategy, which could translate into substantial savings if applied to a significant proportion of the more than 15,000 patients receiving HSCT in North America each year.

In summary, this study confirms that outpatient myeloablative allogeneic HSCT is feasible with regard to outpatient delivery of high-dose conditioning therapy and expectant management of post-transplant complications. Such a strategy can be safely applied to the vast majority of patients with low treatment related morbidity and mortality, and clinical outcomes comparable to that expected with traditional inpatient management. In addition to a dramatic reduction in hospital utilization, potential exists for cost reduction and improvements in quality-of-life.

References:

1. Rizzo JD, Vogelsang GB, Krumm S, Frink B, Mock V, Bass EB. Outpatient based bone marrow transplantation for hematologic malignancies: cost saving or cost shifting? *J Clin Oncol* 1999; 17:2811-2818.
2. Svahn DM, Ringdén O, Remberger M. Long-term follow-up of patients treated at home during the pancytopenic phase after allogeneic haematopoietic stem cell transplantation. *Bone Marrow Transplantation* 2005;36:511-516.
3. Bone Marrow Transplantation 2009; online publication, 21 September 2009 prior to print.
4. Millman Research Report: 2008 U.S. organ tissue transplant cost estimate and discussion. April 2008: 7.

Early Stem Cell Mobilization Recommended in Myeloma Patients Undergoing Lenalidomide (Revlimid) Based Initial Therapy

The use of novel agents (NA) such as lenalidomide and bortezomib in the initial therapy of myeloma patients has resulted in improved response rates and progression-free survival when compared to traditional induction regimens such as VAD (vincristine, adriamycin, dexamethasone). Furthermore, when novel agent based induction therapy is used prior to high-dose chemotherapy and autologous stem cell transplantation (ASCT), the post-transplant complete response and very good partial response rates are higher than using traditional induction regimens followed by ASCT. However, there is increasing data that prolonged use of some NA, particularly lenalidomide, may impair hematopoietic stem cell mobilization and collection.^{1,2} Given the rapid responses often generated by NA-based induction regimens, the International Myeloma Working Group has recently published a consensus document recommending early collection of autologous hematopoietic stem cells in patients who undergo NA-based induction and are candidates for either early or delayed therapy with ASCT.³ Specifically, attempted stem cell collection is recommended after three to four cycles of NA-based initial therapy. This is particularly important for patients receiving lenalidomide based initial therapy, in whom there is evidence that G-CSF based stem cell mobilization may be inadequate in patients who have received five to six cycles or greater of initial therapy.

1. Kumar S, Dispenzieri A, Lacy MQ, et al. Impact of lenalidomide therapy on stem cell mobilization and engraftment post-peripheral blood stem cell transplantation in patients with newly diagnosed myeloma. *Leukemia*. 2007;21:2035-2042.
2. Popat U, Saliba R, Thandi R, et al. Impairment of filgrastim-induced stem cell mobilization after prior lenalidomide in patients with multiple myeloma. *Biol Blood Marrow Transplant*. 2009;15:718-723.
3. Kumar S, Giral S, Stadmauer EA, et al. Mobilization in myeloma revisited: IMWG consensus perspectives on stem cell collection following initial therapy with thalidomide-, lenalidomide-, or bortezomib-containing regimens. *Blood*. 2009;114:1729-1735.

Stovall Foundation Provides No-Cost Lodging Options for Patients Undergoing Transplantation

Due to the personal impact of leukemia on their family, Ray and Martha Stovall went to their church community to help establish The Stovall Hope Foundation. The Foundation has grown to support three fully-furnished corporate apartments that are available to transplant and leukemia patients at The Blood and Marrow Transplant and Leukemia Programs at Northside Hospital. The apartments are available to patients and their caregivers at no cost, are fully furnished and are conveniently located close to Northside Hospital. The Stovall Hope Foundation has helped more than 120 families have a comfortable and convenient place to stay while they undergo transplant and/or leukemia treatments. Many patients who have lived in these apartments have then turned around and made contributions to help support their efforts. The Stovall's, through their Foundation, have provided an extraordinary gift that facilitates a patient's journey through leukemia and stem cell treatment.

New Thirty-Six Bed BMT & Leukemia Inpatient Unit Opens



The Blood and Marrow Transplant Program and Leukemia Programs at Northside Hospital have outgrown their original home and are replacing the previous 17-bed unit with a new 36 bed state-of-the-art facility.

Unique features of the new Unit:

- Closed & isolated facility for exclusive use by BMT and acute leukemia patients
- All private rooms with computerized electronic medical record documentation availability in each room
- State-of-the-art infection prevention including:
 - HEPA-filtered facility
 - Eight negative-pressure rooms with ante-rooms to prevent cross-contamination from patient with existing infections
 - Seamless surfaces through out the Unit to eliminate colonization with infectious organisms
- Dedicated exercise room for patients and caregivers
 - Exercise room has a dedicated bathroom and shower

- Specialized BMT pharmacy with the capacity to mix chemotherapy/immunotherapy agents. Pharmacy utilizes a computerized medication administration record (MAR) to decrease/eliminate medication errors.
- Dedicated Family Room with computer access, internet accessibility and disease related literature

Highly Specialized BMT Unit Staff

- Dedicated and trained nursing staff. All nursing staff is OCN chemotherapy and ACLS certified.
- Three dedicated nurse practitioners
- Dedicated Ph.D. health psychologist
- Five dedicated clinical PharmD's
- Inpatient attending BMT/acute leukemia physician's on call 24 hours a day/7 days a week. No interns or residents are utilized by the program.

The Blood and Marrow Transplant Program at Northside Hospital (BMTNSH) is one of the largest hematopoietic stem cell transplant and leukemia programs in the Southeastern United States. The Transplant Program is accredited by FACT/AABB/FDA. BMTNSH's clinical transplant program is the only hematopoietic stem cell transplant program in the United States that has been accredited without any deficiencies following three consecutive FACT inspections.

